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PI/PD Name: Susan L Graham

Gender: ☐ Male ☒ Female

Ethnicity: (Choose one response) ☐ Hispanic or Latino ☒ Not Hispanic or Latino

Race: (Select one or more)
- ☐ American Indian or Alaska Native
- ☐ Asian
- ☐ Black or African American
- ☐ Native Hawaiian or Other Pacific Islander
- ☒ White

Disability Status: (Select one or more)
- ☐ Hearing Impairment
- ☐ Visual Impairment
- ☐ Mobility/Orthopedic Impairment
- ☐ Other _____
- ☒ None

Citizenship: (Choose one) ☒ U.S. Citizen ☐ Permanent Resident ☐ Other non-U.S. Citizen

Check here if you do not wish to provide any or all of the above information (excluding PI/PD name): ☒

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PI/PD Name: Adam Arkin

Gender: ☒ Male ☐ Female

Ethnicity: (Choose one response) ☐ Hispanic or Latino ☒ Not Hispanic or Latino

Race: (Select one or more)
- ☐ American Indian or Alaska Native
- ☐ Asian
- ☐ Black or African American
- ☐ Native Hawaiian or Other Pacific Islander
- ☒ White

Disability Status: (Select one or more)
- ☐ Hearing Impairment
- ☐ Visual Impairment
- ☐ Mobility/Orthopedic Impairment
- ☐ Other _____
- ☒ None

Citizenship: (Choose one) ☒ U.S. Citizen ☐ Permanent Resident ☐ Other non-U.S. Citizen

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PI/PD Name: Paul N Hilfinger

Gender: ☒ Male ☐ Female

Ethnicity: (Choose one response) ☐ Hispanic or Latino ☒ Not Hispanic or Latino

Race: (Select one or more)
- ☐ American Indian or Alaska Native
- ☐ Asian
- ☐ Black or African American
- ☐ Native Hawaiian or Other Pacific Islander
- ☒ White

Disability Status: (Select one or more)
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- ☐ Mobility/Orthopedic Impairment
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PI/PD Name: Dorian Liepmann

Gender: ☒ Male ☐ Female

Ethnicity: (Choose one response) ☐ Hispanic or Latino ☐ Not Hispanic or Latino

Race: (Select one or more)
- ☐ American Indian or Alaska Native
- ☐ Asian
- ☐ Black or African American
- ☐ Native Hawaiian or Other Pacific Islander
- ☒ White

Disability Status: (Select one or more)
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- ☐ Mobility/Orthopedic Impairment
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PI/PD Name: Katherine A Yelick

Gender: ☐ Male ☒ Female

Ethnicity: (Choose one response) ☐ Hispanic or Latino ☒ Not Hispanic or Latino

Race: (Select one or more)
- ☐ American Indian or Alaska Native
- ☐ Asian
- ☐ Black or African American
- ☐ Native Hawaiian or Other Pacific Islander
- ☒ White

Disability Status: (Select one or more)
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- ☐ Other _____
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COVER SHEET FOR PROPOSAL TO THE NATIONAL SCIENCE FOUNDATION

PROGRAM ANNOUNCEMENT/SOLICITATION NO./CLOSING DATE/if not in response to a program announcement/solicitation enter NSF 00-2

NSF 99-167 **04/17/00**

FOR NSF USE ONLY

NSF PROPOSAL NUMBER

FOR CONSIDERATION BY NSF ORGANIZATION UNIT(S) (Indicate the most specific unit known, i.e. program, division, etc.)

INFORMATION TECHNOLOGY RESEARC

DATE RECEIVED	NUMBER OF COPIES	DIVISION ASSIGNED	FUND CODE	DUNS# (Data Universal Numbering System)	FILE LOCATION
				153881537	

EMPLOYER IDENTIFICATION NUMBER (EIN) OR TAXPAYER IDENTIFICATION NUMBER (TIN)

946002123

SHOW PREVIOUS AWARD NO. IF THIS IS
☐ A RENEWAL
☐ AN ACCOMPLISHMENT-BASED RENEWAL

IS THIS PROPOSAL BEING SUBMITTED TO ANOTHER FEDERAL AGENCY? YES ☐ NO ☒ IF YES, LIST ACRONYMS(S)

NAME OF ORGANIZATION TO WHICH AWARD SHOULD BE MADE

University of California-Berkeley

AWARDEE ORGANIZATION CODE (IF KNOWN)

0013128000

ADDRESS OF AWARDEE ORGANIZATION, INCLUDING 9 DIGIT ZIP CODE

University of California-Berkeley
336 Sproul Hall
Berkeley, CA. 947205940

NAME OF PERFORMING ORGANIZATION, IF DIFFERENT FROM ABOVE

PERFORMING ORGANIZATION CODE (IF KNOWN)

ADDRESS OF PERFORMING ORGANIZATION, IF DIFFERENT, INCLUDING 9 DIGIT ZIP CODE

IS AWARDEE ORGANIZATION (Check All That Apply)
(See GPG II.D.1 For Definitions) ☐ FOR-PROFIT ORGANIZATION ☐ SMALL BUSINESS ☐ MINORITY BUSINESS ☐ WOMAN-OWNED BUSINESS

TITLE OF PROPOSED PROJECT **ITR/ACS: Software for Numerical Simulation of Microscale Biological Systems**

REQUESTED AMOUNT	PROPOSED DURATION (1-60 MONTHS)	REQUESTED STARTING DATE	SHOW RELATED PREPROPOSAL NO., IF APPLICABLE
$ **4,999,971**	**60** months	**09/01/00**	**0077494**

CHECK APPROPRIATE BOX(ES) IF THIS PROPOSAL INCLUDES ANY OF THE ITEMS LISTED BELOW

☐ BEGINNING INVESTIGATOR (GPG 1.A.3)
☐ DISCLOSURE OF LOBBYING ACTIVITIES (GPG II.D.1)
☐ PROPRIETARY & PRIVILEGED INFORMATION (GPG II.D.10)
☐ NATIONAL ENVIRONMENTAL POLICY ACT (GPG II.D.10)
☐ HISTORIC PLACES (GPG II.D.10)
☐ SMALL GRANT FOR EXPLOR. RESEARCH (SGER) (GPG II.D.12)
☐ VERTEBRATE ANIMALS (GPG II.D.12) IACUC App. Date _____
☐ HUMAN SUBJECTS (GPG II.D.12)
Exemption Subsection _____ or IRB App. Date _____
☐ INTERNATIONAL COOPERATIVE ACTIVITIES: COUNTRY/COUNTRIES _____
☐ FACILITATION FOR SCIENTISTS/ENGINEERS WITH DISABILITIES (GPG V.G.)
☐ RESEARCH OPPORTUNITY AWARD (GPG V.H)

PI/PD DEPARTMENT
Electronics Research Lab.

PI/PD FAX NUMBER
510-642-3962

PI/PD POSTAL ADDRESS
771 Soda Hall
Computer Science Division
Berkeley, CA 947201776
United States

NAMES (TYPED)	High Degree	Yr of Degree	Telephone Number	Electronic Mail Address
PI/PD NAME **Susan L Graham**	**PH.D.**	**1971**	**510-642-2059**	**graham@cs.berkeley.edu**
CO-PI/PD **Adam Arkin**	**Ph.D**	**1992**	**510-495-2366**	**aparkin@uclink4.berkeley.edu**
CO-PI/PD **Paul N Hilfinger**	**PH.D.**	**1981**	**510-642-8401**	**hilfingr@cs.berkeley.edu**
CO-PI/PD **Dorian Liepmann**	**Ph.D**	**1990**	**510-642-9360**	**liepmann@me.berkeley.edu**
CO-PI/PD **Katherine A Yelick**	**Ph.D**	**1991**	**510-642-8900**	**yelick@cs.berkeley.edu**

CERTIFICATION PAGE

Certification for Principal Investigators and Co-Principal Investigators:

I certify to the best of my knowledge that:

(1) the statements herein (excluding scientific hypotheses and scientific opinions) are true and complete, and
(2) the text and graphics herein as well as any accompanying publications or other documents, unless otherwise indicated, are the original work of the signatories or individuals working under their supervision. I agree to accept responsibility for the scientific conduct of the project and to provide the required progress reports if an award is made as a result of this application.

I understand that the willful provision of false information or concealing a material fact in this proposal or any other communication submitted to NSF is a criminal offense (U.S.Code, Title 18, Section 1001).

Name (Typed)	Signature	Social Security No.*	Date
PI/PD **Susan L Graham**			
Co-PI/PD **Adam Arkin**			
Co-PI/PD **Paul N Hilfinger**			
Co-PI/PD **Dorian Liepmann**			
Co-PI/PD **Katherine A Yelick**			

SSN's are confidential and are not displayed *ON FASTLANE SUBMISSIONS*

Certification for Authorized Organizational Representative or Individual Applicant:

By signing and submitting this proposal, the individual applicant or the authorized official of the applicant institution is: (1) certifying that statements made herein are true and complete to the best of his/her knowledge; and (2) agreeing to accept the obligation to comply with NSF award terms and conditions if an award is made as a result of this application. Further, the applicant is hereby providing certifications regarding Federal debt status, debarment and suspension, drug-free workplace, and lobbying activities (see below), as set forth in Grant Proposal Guide (GPG), NSF 00-2. Willful provision of false information in this application and its supporting documents or in reports required under an ensuring award is a criminal offense (U. S. Code, Title 18, Section 1001).

In addition, if the applicant institution employs more than fifty persons, the authorized official of the applicant institution is certifying that the institution has implemented a written and enforced conflict of interest policy that is consistent with the provisions of Grant Policy Manual Section 510; that to the best of his/her knowledge, all financial disclosures required by that conflict of interest policy have been made; and that all identified conflicts of interest will have been satisfactorily managed, reduced or eliminated prior to the institution's expenditure of any funds under the award, in accordance with the institution's conflict of interest policy. Conflict which cannot be satisfactorily managed, reduced or eliminated must be disclosed to NSF.

Debt and Debarment Certifications

(If answer "yes" to either, please provide explanation.)

Is the organization delinquent on any Federal debt? Yes ☐ No ☒

Is the organization or its principals presently debarred, suspended, proposed for debarment, declared ineligible, or voluntarily excluded from covered transactions by any Federal department or agency? Yes ☐ No ☒

Certification Regarding Lobbying

This certification is required for an award of a Federal contract, grant, or cooperative agreement exceeding $100,000 and for an award of a Federal loan or a commitment providing for the United States to insure or guarantee a loan exceeding $150,000.

Certification for Contracts, Grants, Loans and Cooperative Agreements

The undersigned certifies, to the best of his or her knowledge and belief, that:

(1) No federal appropriated funds have been paid or will be paid, by or on behalf of the undersigned, to any person for influencing or attempting to influence an officer or employee of any agency, a Member of Congress, an officer or employee of Congress, or an employee of a Member of Congress in connection with the awarding of any federal contract, the making of any Federal grant, the making of any Federal loan, the entering into of any cooperative agreement, and the extension, continuation, renewal, amendment, or modification of any Federal contract, grant, loan, or cooperative agreement.

(2) If any funds other than Federal appropriated funds have been paid or will be paid to any person for influencing or attempting to influence an officer or employee of any agency, a Member of Congress, an officer or employee of Congress, or an employee of a Member of Congress in connection with this Federal contract, grant, loan, or cooperative agreement, the undersigned shall complete and submit Standard Form-LLL, ''Disclosure Form to Report Lobbying,'' in accordance with its instructions.

(3) The undersigned shall require that the language of this certification be included in the award documents for all subawards at all tiers including subcontracts, subgrants, and contracts under grants, loans, and cooperative agreements and that all subrecipients shall certify and disclose accordingly.

This certification is a material representation of fact upon which reliance was placed when this transaction was made or entered into. Submission of this certification is a prerequisite for making or entering into this transaction imposed by section 1352, title 31, U.S. Code. Any person who fails to file the required certification shall be subject to a civil penalty of not less than $10,000 and not more than $100,000 for each such failure.

AUTHORIZED ORGANIZATIONAL REPRESENTATIVE	SIGNATURE	DATE
NAME/TITLE (TYPED) **Jyl Baldwin**		

TELEPHONE NUMBER	ELECTRONIC MAIL ADDRESS	FAX NUMBER
510-642-8114	**jbaldwin@uclink.berkeley.edu**	**510-642-8236**

*SUBMISSION OF SOCIAL SECURITY NUMBERS IS VOLUNTARY AND WILL NOT AFFECT THE ORGANIZATION'S ELIGIBILITY FOR AN AWARD. HOWEVER, THEY ARE AN INTEGRAL PART OF THE INFORMATION SYSTEM AND ASSIST IN PROCESSING THE PROPOSAL. SSN SOLICITED UNDER NSF ACT OF 1950, AS AMENDED.

ITR/ACS: Software for Numerical Simulation of Microscale Biological Systems

Susan L. Graham, Adam Arkin, Paul Hilfinger, Dorian Liepmann, Oliver O'Reilly, and Katherine Yelick

Departments of Electrical Engineering and Computer Science, Bioengineering, Chemistry, and Mechanical Engineering
University of California, Berkeley

Numerical simulation, modeling, and analysis of physical systems are an increasingly important component of research in pure and applied science. Although the state of the art has advanced significantly in the last fifty years, progress has been slowed by the difficulty of developing the necessary software and algorithms. The algorithm and software problems are exacerbated by the emerging generation of high-end machines. These cluster-based machines offer enormous scaling potential, but are more difficult to use and to optimize for than the tightly integrated, homogeneous MPPs and vector supercomputers of the past. New algorithmic and software techniques are needed that will offer both ease of programming and high performance on modern architectures.

Improvements in computational modeling of microscale biological systems are essential to achieve improved understanding of cellular behavior, both to answer fundamental scientific problems and as a first step in developing new pharmacological and bio-MEMS based treatments for disease. For example, laboratory experiments have shown that cancer cells may exhibit either cancerous or non-cancerous characteristics, depending on the surrounding tissue; current models of cells cannot explain this phenomenon. Better understanding requires the development of new models and new algorithms, which in turn means a software environment that allows for fast turnaround and easy integration of separately developed modules. On the other hand, realistic simulations will use three-dimensional, time-dependent models with multiple spatial scales, which will require efficient use of large-scale machines.

In this project, two new biological modeling problems will be addressed:

Modeling the mechanics of biological fluids in microdevices. The insight gained from these simulations will be used for the development of new MEMS components for highly sensitive systems and sensors for biomedical applications, which must become more biomemetic as their size shrinks and increased sensitivity is needed.

Modeling how signals get from the membrane of a cell to the nucleus; simulating what happens when more than one growth factor or cytokine is present or when one or more molecular elements is damaged. Understanding those phenomena is an important step towards explaining the mechanisms of disease.

The feedback between these two tasks will subsequently be exploited to model larger systems and more complex interactions among factors affecting molecular and cellular behavior.

Novel numerical methods will be devised to support these models . Microscale biological systems involve chemical, fluidic, electromagnetic, and mechanical processes . Combinations of solvers for partial differential equations, ordinary differential equations, and stochastic differential equations will be used to capture these processes. Adaptive mesh refinement will be used for problems with multiple spatial scales, and embedded and immersed boundary methods will be used to couple of discrete and continuous components. These methods have applications in many areas besides microscale biological systems, including combustion, aerodynamics, astrophysics, engineering design, and blood flow in the human body.

To address the dual goals of programming ease and high performance, new techniques will be developed for expressing and optimizing the computational models, using the advanced numerical methods. BioFlow, a domain-specific dialect of Java, will be designed and implemented. Building on experience with the Titanium language and system, which targeted regular and adaptive meshes, an explicitly parallel model with a global address space and control over data structure layout will be used. Using the object-based framework provided by Java, data structures, solvers, and load balancing modules will be built that can easily be combined and extended as the models improve. The global address space will make it possible to explicitly represent large complex data structures that are spread over multiple computational nodes, and to compile the same programs for parallel computing systems with very different memory architectures. New compiler and runtime optimization techniques will be developed for all levels of the memory hierarchy, from registers and caches to networks and disks; these techniques will take into account memory and communication patterns that arise from irregular boundaries and the coupling of different types of solvers. Building on an existing language, rather than designing a new language from scratch, will lower the learning curve for scientific programmers and will provide a large base of supporting libraries and software on which to build. Using a linguistic approach, rather than a pure library-based one, will greatly improve expressiveness and enable better analysis and optimizations. The combination of new methods to achieve high performance of simulations run on modern architectures and a high-level linguistic framework in which to describe the simulations will have uses in all areas of computational modeling and simulation.

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ITR/ACS: Software for Numerical Simulation of Microscale Biological Systems

Project Description

Numerical simulation, modeling, and analysis of physical systems are an increasingly important component of research in pure and applied science. Although the state of the art has advanced significantly in the last fifty years, progress has been slowed by the difficulty and complexity of developing the needed software and the computationally appropriate algorithms. Consequently, many scientists are reluctant to relinquish their old codes as computing technology advances. Their computational conservatism is often passed on to their students. Other researchers express concern that they must invest large amounts of human effort in activities they see as peripheral to their main topic of investigation. The goal of this project is to address those limitations.

Our initial focus will be in the area of microscale biological systems, where we intend to facilitate fundamental research contributions. Simulation and modeling of biological systems at molecular and cellular scales is an essential tool for understanding the behavior of living organisms both in healthy and diseased states. Such understanding precedes the development of pharmacological and bio-MEMS-mediated therapy.

We propose to develop the algorithmic and software infrastructure to simulate both natural microscale biological systems, such as cells, and man-made bio-MEMS devices. Such systems have a high degree of complexity. They involve multiple physical processes: chemical kinetics, fluid dynamics and transport, electromagnetic effects, and mechanical components. This leads to complex combinations of diverse mathematical algorithms that must be implemented to simulate these problems: partial differential equation (PDE) solvers, ordinary differential equation (ODE) solvers, and stochastic differential equation (SDE) solvers. The currently available set of tools fall far short of providing high-fidelity representations of such complex systems. They are mostly based on lumped-parameter models. With few exceptions, the representation of spatial structure is at best extremely simplified, and often non-existent. When the problems involve low concentrations and small sizes, the spatial distributions become increasingly important in the prediction of systems behavior and performance. The more realistic the models, the stronger the performance demands on their computational realizations.

In order to develop new algorithms and new models in this area, there is a high premium on the ability to develop and test new ideas and approaches relatively quickly. On the other hand, the fundamental calculations are of time-dependent problems with three-dimensional spatial extent and multiple scales, i.e. ones that classically have placed the highest demands for computational performance. The simultaneous demand for a high degree of expressiveness and of performance places unique demands on the computing environment.

Our attack on this part of the problem centers on the development of a highly optimizing, yet portable compiler, runtime system, and tool suite for a high-level domain-specific dialect of Java for high-end parallel computing. An object-based framework an excellent basis for developing a collection of components that can be varied and modified easily as our understanding of the simulation and modeling calculations change. Building on a widely used linguistic base, namely Java, provides enormous advantages over creating a completely new language. It reduces the learning curve for scientific programmers, provides a large base of supporting libraries and software in which to embed our application code, and has a degree of platform independence that will enable us to focus our attention on the performance issues peculiar to scientific computing rather than starting from scratch. Compiler and runtime-system research will emphasize analysis of parallel program constructs and optimizations for memory hierarchies and inter-processor communication, particularly for this application domain.

The methods used to develop high-fidelity simulations of microscale biological systems will be based on recent advances in finite-difference methods for PDE's, the most computationally intensive component of the simulation problem for microscale biological systems. Among the techniques we will apply to this problem are adaptive mesh refinement for problems with multiple spatial scales; and embedded boundary methods and immersed boundary methods for representing the coupling of discrete and continuous components of a simulation.

Our initial work will concern two problems in biological simulations:

• Modeling the mechanics of biological fluids in microdevices. Insight gained from these simulations will be used to develop new MEMS components for highly sensitive systems and sensors for biomedical applications, which must become more biomemetic as their size shrinks and sensitivity must dramatically increase.

• Modeling how signals get from the membrane of a cell to the nucleus; simulating what happens when more than one growth factor or cytokine is present or when one or more molecular elements is damaged. These will involve detailed models of cell growth, cell locomotion and shape-change, and spatial inhomogeneity. Understanding these phenomena is an important step towards explaining the mechanisms of disease.

There is feedback between the two tasks; the biomemetic nature of the future sensors requires an understanding of how cells get so much done with so few molecules. Conversely, understanding the flow of complex fluids in controlled microenvironments will help develop tools to understand cellular mechanisms. Further, biological material, including whole cells, are increasingly an integral part of bioMEMS devices [37, 29, 28]. As our work proceeds, the results of each will influence the other. We will also expand both simulations to model larger systems and more complex interactions among factors affecting molecular and cellular behavior.

In order to have the development of these models for biological simulation and the development of the algorithmic and software tools needed to implement such models progress simultaneously, we will introduce two *prototype models* as intermediate targets for the development of the algorithmic and software tools. The prototype models collectively have many of the same numerical difficulties as are anticipated for the ultimate target models, but are sufficiently well-characterized to permit the immediate development and validation of the necessary mathematics and computer science research ideas. At the same time that this development is taking place, the bioengineering team will develop more comprehensive models. By the end of the second year of the project, both the software tools and the comprehensive models will reach the point that we can begin to implement simulation codes for the latter, and address the resulting mathematics and computer science research issues as they arise.

Research Issues

The three aspects of this project, the development of a high- performance language, compiler, and runtime system for scientific simulation and modeling applications, the development in that system of a suite of parallel programs realizing novel scalable algorithms for those simulations, and the use of that program suite for microscale biological system simulation are highly synergistic. The success of the project will depend on close collaboration and constant feedback from each of the three constituencies to the others. In the subsections that follow, we summarize the research challenges faced by each subgroup.

I. Computer Science

Several computer science challenges will need to be addressed before the biological simulations can proceed. Some of these challenges exist for any large-scale scientific simulation, while others are specific to the problems in computational fluid dynamics (CFD) that arise in microscale biological systems. The computer scientists in this project have developed an understanding of the application issues through many years of interdisciplinary projects, including collaborations with Colella's group on the FIDIL project in the late 1980's [47, 94] and the Titanium project starting in 1995 [103]. The proposed work will leverage algorithms and software from these prior efforts.

BioFlow: A Domain Specific Language and Optimizing Compiler

To address the needs of the application scientists for expressiveness, while meeting their goals for performance and portability, we will develop a domain-specific language and system for expressing mesh-based computations for mixed regular and irregular meshes. The BioFlow system will build on the results of the Titanium project, but because of the demands of the biological modeling applications, both a new language and a new implementation will be developed.

Titanium is a high-performance parallel dialect of Java that supports mesh-based computations on rectangular and adaptive rectangular meshes [103, 48]. Three major applications that have been developed in collaboration with Phillip Colella's group at LBNL are an adaptive 3D Poisson Solver [90], a 2D Poisson solver for infinite domains [12], and an adaptive solver for the compressible Euler equations for gas dynamics [76]. The Titanium compiler optimizes cache management, synchronization [2], communication scheduling [9, 64, 63, 101], and dynamic memory management [3]. The implementation of the Titanium language compiles programs to C (vendor compilers can then produce executables) and is portable across uniprocessors, shared-memory multiprocessors (SMPs) and distributed-memory multiprocessors (MPPs).

BioFlow will also be a parallel dialect of Java. Like Titanium, BioFlow will have domain-specific constructs to describe meshes (collections of elements indexed by points) and operations on meshes. In BioFlow, both regular and irregular hybrid data structures will be supported efficiently, and on challenging platforms.

We use a Java dialect in order to get the benefits of an object-oriented paradigm, to embed our domain-specific constructs in a familiar and modern framework, and to have the ability to adapt some Java tools and libraries for our use. That adaptation yields neither a subset nor a superset of Java, since we add new features and drop some others. In particular, we do not translate to JVM, nor do we support dynamic method linking, since they appear to have little value for our application domains, and inhibit optimizations that are essential for good performance. Using our approach, we have gotten performance on Titanium programs that is competitive with Fortran implementations of the same methods. The use of a Java framework enables us to create libraries of reusable methods, yet compile the library components that get used in an application in the context of that application.

Like Titanium, the BioFlow system will provide a global address space, enabling the programmer to refer explicitly to data structures that, on some platforms, may be distributed across multiple local processor memories. That capability facilitates reasoning about those structures, and enables the user to write programs that can be compiled for both shared-memory and distributed-memory platforms. Although the address space is global, or shared, the underlying memory model has a non-uniform (NUMA) cost model, reflecting the reality of large-scale machines. By using a language-based approach rather than one based purely on libraries (such as those we and others have developed for adaptive mesh refinement [62, 11, 72, 25]) some of the machine complexity can be hidden through good compiler analysis and optimizations, including the question of whether there is hardware support for a global address space. Some machines provide the illusion of a single shared memory, some use distinct hardware instructions to read or write memory on another processor [60], and some require message passing. A compiler can generate whatever primitives are necessary, using a lightweight communication layer [100, 39] on machines that require messaging.

By creating a system that is portable across architectures, and that enables the applications scientists to describe their models at a relatively high level, it becomes possible for them to use low-cost machines that are resident in their laboratories, and to have a fast development process for implementing and testing new models and performing parameter studies. Once the models have proven useful, larger simulations can be run either on local large parallel clusters (such as Berkeley's Millennium machine) or on very high-end platforms available through supercomputer centers.

Since many of the numerical models of microscale biological systems described later in this proposal are still under development, this way of working is much more attractive than the alternative of investing enormous effort in implementing newly developed models in a hard-to-use programming system, such as mixed C++ and Fortran with MPI. The computer science part of the project is to create a programming environment that is easy to use, yet provides portability and high performance across machines.

To meet the demands of rapid prototyping for the purpose of model development and evaluation, we will produce interactive tools for programming, debugging, and performance evaluation. The debugger and performance tools we developed for Titanium [79] will be extended to handle BioFlow and the programming environment research we are doing under other funding will be used to support BioFlow users [44].

Support for Large-Scale Computations

The memory and computational requirements for simulations that use adaptivity are particularly difficult to predict, since they depend on refinements based on numerical values that are not known in advance

[17, 21, 93]. Our rough estimates indicate that the microscale simulations described subsequently would require between 2 and 200 Gigabytes of memory and between 100 and 10,000 trillion floating point operations (TFlops). The smaller problems can be run on uniprocessors or SMPs, but the larger ones will require large-scale multiprocessors. Trends in supercomputing hardware are leading towards clusters of SMPs as a scalable and economically attractive choice for such high-end computing.

Clusters of SMPs leverage the hardware design efforts in high-performance processors and SMPs, but they have deep and complex memory hierarchies with different access primitives and costs at each level. This makes them more difficult to design algorithms for, generate code for, and tune performance for than their MPP and SMP predecessors. Ideally, a programmer should be able to produce high-performance parallel code on an SMP cluster using an abstract programming model that is not dependent on implementation details of the underlying machine. However, the programming model typically offered on these machines today is a low-level mixture of message passing (MPI) and either threads or compiler directives (OpenMP). Even users who are successfully using either message passing or threads are reluctant to move to a new model in which they must identify and manage two different kinds of parallelism in their applications. For application scientists still developing and testing models, such a level of effort is clearly unacceptable.

Our approach to handling clusters of SMPs will be to hide implementation differences between machines, while exposing in an abstract manner some of the key performance issues that must be handled by the algorithm designer. For example, although Titanium uses a global address space, there is a notion of local and remote memory; any processor can access any memory by simply dereferencing a pointer, but the cost difference is clear from the data type qualifications specified by the programmer [70]. For the purpose of algorithm and data-structure design, the programmer needs to be able to specify what data and computations need to be local (e.g. on the same SMP cluster node). Beyond that, our experience suggests that the multi-level hierarchy can be mostly hidden from the user, but will require new compilation and runtime techniques. At a minimum, either communication libraries must be made safe for multiple threads, or communication must be routed through a single communication processor [10]. In addition, the compiler must generate the appropriate type of communication or memory operations, and optimizations to globally coordinate communication on an SMP cluster.

In our experience, a key to performing these optimizations on explicitly parallel programs is analysis of the program synchronization [64]. This has the additional benefit that certain synchronization errors may be detected at compilation time [2]. Our prior work on synchronization is adequate for bulk-synchronous programs that use barriers, but cannot detect race conditions in programs with locks (expressed as synchronized blocks or methods in Java), nor can it handle programs that use a divide-and-conquer style in which subsets of processes may have to synchronize at a barrier. We will develop new techniques to handle both of these issues, which are important for handling more irregular and dynamic forms of parallelism in the applications.

Locality-Aware Algorithms

Our modeling approach is based largely on the use of high-resolution finite-difference methods for PDEs, for which the principal computations use relaxation operators – i.e., nearest-neighbor computations on the underlying mesh. The operators have a small constant number of floating point operations (often only one or two) per memory operation – in other words poor temporal locality. Without good temporal locality, register and cache values cannot be re-used and processing performance on a single node is low. For meshes with embedded boundaries, which create irregularities in the mesh, there is an additional problem of poor spatial locality, since the neighboring mesh elements may not be stored contiguously in memory.

Similar problems exist at the boundaries between processors or SMP nodes, particularly for solutions of elliptic equations, because the algorithms require a global exchange of information to implement the non-local effects that are inherent in physical systems such as incompressible fluids. We will use multigrid techniques that scale well with the problem size, requiring only linear computation in the number of mesh points. Even so, in conventional Poisson solvers the relaxation operators are evaluated on every iteration, which implies frequent communication that can significantly limit scalability.

Our approach to these locality problems is first to develop numerical methods that minimize communication and memory requirements and second to use the machine as efficiently as possible during communication by

performing aggregation, overlap, and global scheduling of the network resources.

For regular meshes both we and others have developed techniques to increase data reuse in registers and caches [77, 59]. The greatest benefits come from reorganizing the loops that sweep over mesh points along with an iteration loop, performing multiple iterations on a tile before moving to another. Such loop reorganization is a challenge for compilers due to the dependencies in the loops. By using a domain-specific language, we can largely avoid those difficulties by introducing iterators over meshes that simplify or eliminate some of the analysis necessary in C or Fortran compilers. In addition to the loop analysis problems, a fully automatic approach to data reuse requires some method for selecting tile sizes that work well on a particular memory hierarchy. In spite of significant research effort [31, 27, 50], automatic tile size selection has proven very difficult for arrays with three or more dimensions and for programs that access multiple arrays, because the conflict misses are difficult to model given the complex interactions between multiple levels of caches, and virtual memory. In another project, we are exploring the use of search techniques to select from among a large set of possible optimizations. This approach has been used successfully for dense linear algebra [20, 102] and Fast Fourier Transforms [36].

An example of a numerical algorithm designed for scalability is our new Poisson solver for infinite domains, which uses a kind of domain decomposition in which complete local solves are performed between communication steps [12]. Rather than performing communication on each iteration, there is a single communication step with a small additional cost in computation. This algorithm currently works only for regular meshes in 2D, but will be extended to 3D and to adaptive meshes as part of this proposed work.

Mixed Regular and Irregular Data Structures

All of the problems described so far become even more challenging when there is any kind of irregularity in the computation. It is more difficult to get good performance for adaptive meshes than for non-adaptive meshes because the data structures change dynamically. Nevertheless, adaptive meshes are handled effectively in the Titanium language. For the biological systems of interest, there are three new problems that arise from the models: immersed boundaries, embedded boundaries, and introduction of stochastic models. All of these are a kind of coupling or interfacing between data structures or between numerical methods. The most challenging are the embedded-boundary methods, because they change the mesh representation from a regular block-structured form to a hybrid of block-structured meshes and arbitrary unstructured meshes.

For all three of these problems, interfacing two different data structures in a large-scale NUMA environment creates a tension between data locality and computational load balance. In the immersed boundary method, for example, there is an underlying mesh used to compute fluid flow, which may be regular or adaptive, and a set of *fibers* represented as polygons (sets of points) that are specific to particular applications. The computation proceeds by computing fluid flow on the grid, mapping the values at underlying mesh points to the fibers, moving the fibers according to some application-specific physical laws, and propagating forces back to the fluid [97]. An ideal solution to the locality problem would co-locate the fibers with the underlying grid, but the fibers may not be evenly spread over the domain, so this would create load imbalance. Alternatively, the fibers may be distributed evenly in some way, but the communication between the grid and fibers would then be mostly non-local. While this locality and load balance trade-off is common to many settings, including particle-in-cell methods, the introduction of adaptive meshes, which we intend to use to reduce the overall computational demands and improve precision, complicates both locality and load imbalance.

The embedded-boundary methods will have locality and load-balance problems as well. In an embedded boundary, some of the grid cells (which are otherwise cubes) are divided into irregularly structured regions as shown in Figure 1. This complicates the data-structure representation and optimization, since a contiguous block of storage with simple indexing operations is no longer possible. A graph representation, as one might use for an unstructured mesh, is conceptually simple, but loses some of the locality advantages of a regular mesh. Our experience with sparse matrix performance, which is closely-related to relaxation operators on a graph, indicates that identifying and preserving any regular structure is key to high performance [52, 53]. In particular, storage and access overhead can be reduced by storing rectangular sub-blocks contiguously, and computations on these blocks can admit further optimization for register allocation and instruction scheduling. In addition, spatial locality can be improved by reorganizing the layout of data in memory, using graph-partitioning or reordering methods, although care must be taken to avoid destroying the regular

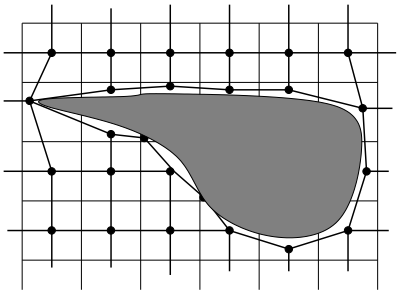

Figure 1: Graph of an embedded-boundary representation of geometry.

portion of the data structure. Finally, for relaxation operations on unstructured data, as in the structured case, there is a small potential for increasing temporal locality by ordering accesses, but this potential becomes much larger if one is performing multiple iterations of the relaxation operators.

Our approach to this problem will be to evaluate some data structure designs using a "by-hand" analysis of some of the key algorithms, taking both expressiveness and predicted performance into consideration. We will then choose a small set of representations and implement them for a uniprocessor, narrowing the choice to a single uniprocessor representation before moving on to a similar design phase for the parallel data structure. As a final step, we will identify transformations that the compiler might perform to further enhance performance, or to improve expressiveness (for example, allowing a kind of general indexing syntax when only nearest-neighbor computational patterns are ever needed).

II. Numerical Methods

The biological systems we propose to simulate exhibit a broad range of coupled mechanical and chemical behaviors. These include a variety of continuous and discrete mechanical behavior, as well as deterministic and stochastic chemical behavior. Our approach to representing these problems numerically will be based on a variety of state of the art discretization methods: adaptive finite-difference methods for solving PDEs in complex time-dependent domains, and novel methods for treating discrete mechanical systems and stochastic chemical systems. In describing these methods below, we will indicate the approach to be taken, the extent to which there are research questions that must be addressed, and the extent to which the computer science research discussed in the previous section addresses critical needs in the development of these algorithms.

Finite difference methods

We will be solving a variety of partial differential equations on time-varying domains: reaction-advection-diffusion equations, equations of motion for non-Newtonian and viscoelastic flows in the Stokes limit; and Poisson's equation for electrostatics. Our underlying spatial discretization for these problems will be high-resolution finite-difference methods (typically, second-order accurate in space). Our time discretization will be the semi-implicit predictor-corrector approach [13, 78]. When applied to systems such as incompressible viscoelastic flow or advection-diffusion equations, which arise in the biological applications, there are hyperbolic terms, parabolic viscous terms and an elliptic divergence-free constraint. In these circumstances, one obtains methods that are second-order accurate in space and time, have a time-step constraint based on the advective CFL number only, and involve the solution of well-behaved linear systems, i.e. ones coming from standard discretizations of second-order elliptic and parabolic operators. This allows us to use methods for solving these systems that are based on multigrid. Such algorithms scale linearly both in computation and memory required in the number of unknowns. However, they typically have a low ratio of computation to communication, making efficient implementation on platforms with deep memory hierarchies difficult.

Considerable effort has gone into developing efficient and robust versions of this approach for various incompressible and low-Mach number fluid-flow problems [14, 67, 68, 5]. More recently, this approach has been extended to problems with deforming boundaries [26], an essential requirement for the problems under

consideration. Some work has been done in applying these methods to viscoelastic flow problems [66], so we expect no serious difficulties in obtaining appropriate versions of the discretization methods for that case.

The development of efficient algorithms for coupled PDE's such as appear here depends on obtaining a decomposition of the system into components that can be solved efficiently, and for which each component is only weakly coupled to the others. If that is the case, the fully coupled system can be solved by combining the components using fractional step or predictor-corrector methods. For this problem domain, identifying such decompositions is nontrivial, due to the complexity of the continuous components of the system, to the requirements imposed by adaptivity and complex geometries, and to the coupling to the discrete mechanical components. Since the problems are complex and nonlinear, the development of robust algorithms will have a strongly experimental component. The need to carry out a rapid design-implementation-testing cycle places a premium on having a high degree of expressiveness in the programming system.

Adaptive Mesh Refinement

In order to represent multiple length and time scales and spatially intermittent phenomena, it is necessary to introduce adaptive numerical methods. In these methods, computational degrees of freedom are added and deleted at runtime as a function of space, time, and the data, thereby maintaining a uniform degree of accuracy throughout the computation at a minimum cost.

Our adaptive mesh methods are based on the block-structured adaptive mesh refinement (AMR) algorithms of Berger and Oliger [16, 18]. In this approach, the regions to be refined are organized into rectangular patches of several hundred to several thousand grid points per patch. Thus, one is able to use the high-resolution rectangular-grid methods described above to advance the solution in time. Furthermore, the overhead in managing the irregular data is amortized over relatively large amounts of floating point work on regular arrays. For time-dependent problems, refinement is performed in time as well as in space. Each level of spatial refinement uses its own stable time step, with the time steps at a level constrained to be integer multiples of the time steps at all finer levels. We have applied this method for a wide variety of problems in partial differential equations [87, 4, 98, 73, 88, 55, 51, 92, 91, 30, 19, 24]. In the present work, AMR constitutes an important capability to resolve spatially intermittent events. For example, in the bio-MEMS problem, only a small subset of the overall flow field will contain active molecules that are to be detected. Such regions will need increased spatial and temporal resolution relative to the background flow. We will also use the local refinement capability to resolve complex geometric behavior, for example, increasing the grid resolution in highly deformed regions of the cell membrane.

Numerical solution of PDE's on Complex Domains

We will represent the effect of the irregular geometry on the finite-difference grid using a Cartesian grid embedded boundary discretization [56, 81]. In this approach, the effect of the irregular boundary is represented by using a finite volume discretization of the differential operator, using control volumes that are obtained by intersecting the cubic control volumes centered around each grid point with the region on one or the other side of the irregular boundary. The primary unknowns are assumed to be centered at the centers of the Cartesian grid control volumes, i.e. as if the boundary weren't there. Such an approach has been shown to given consistent and stable discretizations, even in the case of moving boundaries. It is also routine to prescribe fluxes through the irregular boundaries using this approach [22, 15, 57].

There is a separate issue of representing the geometry of the irregular boundaries themselves. This is strongly dependent on the degree of deformation of the boundary, the dynamics of the boundary, and whether surface transport must be computed. In the prokaryotic cell model, the shape of the boundary is sufficiently regular to use a small number of overlapping rectangular mapped coordinate patches to represent the boundary geometry [23]. This will also facilitate the simulation of transport on the boundary. For bio-MEMS models, the device geometry is made up of rigid (though possibly moving) components. For this case, the geometry representation problem has been solved and the solution implemented in software [1]. At the other extreme, the endoplasmic reticulum is passively advected with the fluid. The surface can become highly distorted, but there is no diffusive transport along the surface. In that case, we will use a volume-of-fluid method that represents the evolution of the surface directly in terms of the transport of volume fractions occupied by each

side of the fluid [82, 49, 46]. Volume-of-fluid methods can represent large distortions, and are easily coupled to problems for which there is fluid on both sides of the boundary. A similar approach can be used in the representation of the vapor bubble that drives the positive displacement pump in the bio-MEMS problem.

There are a number of ways to represent the elastic forces on the membrane of a eukaryotic cell, based either on using the embedded boundary discretization supplemented by jump relations representing the effect of the elastic forces, or by using the immersed boundary approach to spread the elastic forces onto the grid [89]. The need to simulate diffusion on the surface presents a more difficult problem. The large aspect ratio and large deformations of the membrane would tax the limits of finite difference or finite element methods based on surface gridding, while the need to compute diffusive transport on the membrane makes the use of either a volume-of-fluid representation or the fiber representation used by Peskin [89] problematic. We view this problem as a key research question in the area of numerical algorithms for this project. One approach would be to use an Eulerian method (either volume-of-fluid method or a level-set method [84]) to represent the motion of the membrane surface, as well as for defining a grid system of a finite thickness region adjacent to the membrane for the purpose of computing the diffusive transport in the membrane.

The presence of multiple forms of irregularity in calculations that combine adaptivity and complex geometry present major challenges to almost all aspects of the programming environment. In practice, almost all of the data, and most of the computations, can be described using rectangular arrays and operations on such arrays, with only a small fraction of the data and the computation being truly irregular. However, it will require careful design of the data structures and associated compiler and runtime techniques to ensure that the irregularity can be expressed while performance advantage of regularity are exploited. Another open question is the development of appropriate load balancing techniques that preserve locality, because the semi-static approach used in purely adaptive methods rely on accurate estimates of communication and computation costs, which may not be possible.

Coupling to discrete models

In modeling the discrete mechanical subcomponents of the systems described here, there are two issues. The first is the representation of those subcomponents. The second is the coupling of the discrete components to the continuous problem.

There are several discrete components that require numerical simulation in this problem. The representation of the microtubules is discussed in the section of the proposal on models. In both the bio-MEMS and cell modeling settings, it is necessary to simulate the transport of a small number of large biological molecules such as DNA in a liquid medium. For this purpose, we will develop a new model for DNA and polymers. Rather than modeling the double helix using a single rod, the two sugar phosphate backbones of the DNA will each be modeled using a rod. The four nitrogenous bases that are bonded to the various locations of the backbone will be represented as discrete deformable attachments to the rods. Specifically, they will be modeled using a theory of a deformable continuum known as a Cosserat point or pseudo-rigid body [45]. The lateral surface of the Cosserat point will be equipped with attractive/repulsive fields that serve to model the hydrogen bonds and govern admissible base pairings. The resulting DNA model has many of the tractable advantages of the traditional single-rod models, while also being able to represent a greater range of the dynamical behavior of DNA, such as separation of the double helix during replication.

In coupling the discrete components to the continuum, we use fairly standard particle/mesh coupling ideas. For components such as ion channels, mitochondria and the nucleus that are chemical sources and sinks, we will represent them as smoothed sources on the grid. To represent the components with momentum coupling to the fluid, such as the microtubules and DNA strands, we will use the immersed boundary method [89]. In this approach, the forces induced by discrete mechanical components are represented on the grid as smoothed sources in the fluid momentum equation. The effect of these forces on the discrete components are mediated indirectly through the fluid motion. One of the important research issues to be addressed here is the extension of the immersed boundary approach to the Cosserat theory described above. A second issue is the parallelization of particle methods, which are well-understood on uniform meshes, but not on adaptive ones.

Coupling of stochastic and deterministic systems

When processes involve small numbers of molecules (like genetic reactions), stochastic algorithms must be used in order to capture accurately the fluctuating component of the chemical reaction process [74, 38, 40, 41, 42]. Currently, simulations of these cases require use of a physically rigorous algorithm for the Monte Carlo solution of the chemical master equation that is appropriate for this type of chemistry. Computationally, however, this algorithm is extremely intense. The number of cycles through the inner loop increases roughly exponentially with the number of modeled reactions and with the rate of the reactions. We will develop a more efficient method based on approximating the underlying jump Markov process by a continuous Markov process, and then simulating that process according to its Langevin equation.

One difficulty with such stochastic models is that the the accuracy of finite-difference methods depends on the cancellation of errors in differenced quantities, which in turn depends on the errors being sufficiently smooth, a property that is easily destroyed by stochastic noise or finite-state behavior. We will develop mechanisms for coupling stochastic and deterministic components that are sufficiently smooth to avoid a catastrophic loss of accuracy in the PDE solvers. We will also develop methods for performing the transition from stochastic to deterministic representations of the same physical processes in order to respond to changing conditions, e.g. the transition from a low-concentration regime to a high-concentration regime.

III. Microscale Modeling of Biological Systems

The processes of normal cellular life are not at all simple. An intricate and elaborate network of chemical interactions governs developmental processes, signal transduction, and metabolism. Though many biochemical subsystems are isolated from each other in first approximation, even these limited pathways involve at the least tens of proteins and at the most thousands. Individual differences in cellular activities of these and other components in the network and in genotype can cause quantitative and qualitative differences in individual development and responses to external perturbation such as introduction of a pharmaceutical. Attempting to understand, even qualitatively, how signals get from the membrane to the nucleus, what happens when more than one growth factor or cytokine is present or when one or more molecular element is damaged is difficult at best. Yet it is disruption of these very pathways that is implicated in a number of diseases and cancers [35, 61, 69].

The goal of the proposed work is to develop a set of algorithmic and software tools that allow one to represent in a computer model the complex spatial, mechanical and chemical interactions among cellular components. Typical components of an overall eukaryotic cellular modeling system would include systems of equations describing the membrane distribution of receptors, local concentrations of signaling proteins, and calcium concentration dynamics; stochastic differential equations describing molecular motors and chemical participants at locally low concentrations; electrochemical modeling of membrane potentials and ion gradient changes; mechanical models of the cytoskeletal structure and its rearrangements at the membrane; and viscoelastic modeling of lamellapodia formation, compartmentation and intercompartment transport and even nuclear structure.

We have already described the computer science and the numerical methods that are required to carry out this software development. In this section, we present a plan for developing the model requirements. While much is known about the models for simulating cells and bio-MEMS devices as mechanochemical systems, the overall complexity of comprehensive models is substantial. We discuss first the model requirements for the comprehensive models of eukaryotic cells and in-situ diagnostic devices. The purpose of this discussion is to establish model components that need to be characterised in the next two years in these areas. After that, we describe the prototype models that will serve as our initial targets.

Comprehensive Models for Eukaryotic Cells

Eukaryotic cells have a rich spatial and mechanical structure. The chemical environment is modified by a variety of continuous and discrete mechanical mechanisms. Mechanical behaviors of the cell include those of elastic, visco-elastic, fluid, and electrical continua, as well as those of discrete mechanical systems. Finally, the cell deforms in response to its chemical and mechanical environment.

Over the first two years of the project, we will develop model specifications in the several areas. These areas correspond to the principal mechanical and chemical components required for comprehensive models of eukaryotic cells. There is a substantial amount of prior art in these various areas, so a large part of our work will be to determine the extent of what is known, to fill in the gaps, and to develop the mechanisms for coupling the submodels in these various areas into integrated models. At the same time, we will identify and test appropriate analytical and numerical representations of these submodels that represent the state of the art in numerical methods.

The model specifications for eukaryotic cells fall into the following three broad categories of model: mechanical, transport, and network.

Mechanical Models.

• *Membrane Models.* The cell membrane is the flexible outer boundary of the cell with thickness a fraction of a percent of the cell diameter. Net motion of the cell is effected by means of adhesions on the outer surface of the membrane, which allow it to grab onto its surroundings (cells crawl).

• *Bulk motion of the cytoplasm.* Since the cell deforms as it moves, we will need a model for that fluid motion. This fluid motion takes place in a complex geometric environment: the cell walls deform, and there are complex geometric components inside the cell: the nucleus, mitochondria, and the endoplasmic and cytoplasmic reticula. These are all closed surfaces in the cell that are to various degrees deformable, that serve as reservoirs of active chemical species. These surfaces are passively advected with the cytoplasm.

• *Actin cortex.* The actin cortex is a network of polymers adjacent to the cell membrane. It occupies up to 20% of the cell thickness, with exponential falloff of the density of polymers as a function of the distance from the membrane. The actin cortex is a highly dynamic component of the cell, with the extent of the polymerization changing as a function of the local chemical environment and of the cell's shape.

• *Microtubules and molecular motors.* Microtubules are a set of more-or-less rigid rods connected at one end to various sites on the cell membrane, and at the other end to a common center in the cell. They can grow or shrink at either end, thus effecting motion of the cell wall. Molecular motors are adhesive patches attached to the microtubules that rachet themselves along the microtubules. They mediate transport in the cell by attaching themselves to molecules (or other cell components, such as an endoplasmic reticulum).

We will need models for both continuous and discrete mechanical components outlined above. These will include models for the constitutive properties of the continuous media (the cytoplasm, cell membrane, and actin cortex). These will typically be elastic models or non-Newtonian fluid models in the Stokes limit. These models must account properly for the response of the constitutive properties and of the adhesions to the local chemical composition of the membrane. The microtubules, for example, may be represented as inextensible strings with point mass sources at the ends. The axial motion of these strings can be represented using ideas developed for magnetic storage problems [83].

Transport models.

• *Continuous Transport.* We need to compute continuous (diffusive and advective) transport of active chemical species, both in the bulk cytoplasm and on the surface of the cell. We need to develop models for the diffusive species transport, possibly using simplified molecular dynamics calculations for that purpose. In addition, we will develop models of various sources and sinks of active species (mitochondria, nucleus, DNA, transport through the cell membrane). More generally, we need to model the interaction of the transport with the rest of the mechanical environment, e.g. species transport through the actin cortex.

• *Discrete Transport.* One of the principal discrete mechanisms for transport of chemical species through a surface is via discrete channels. These include transport through the cell membrane, and through the endoplasmic reticulum. We will develop models for transport through channels, including the computation of the response of the channels to the electric field environment. We will also develop models of active transport by the molecular motors.

Network models. These mechanical and diffusional processes control and respond to the cellular biochemical and genetic reaction networks. We will develop physical models for chromosome control, gene expression,

enzymatic activity, and small molecule/ion dynamics that we have derived in other contexts [8, 6, 74, 75, 7]. These will form the basis for models of cell cycle control, signal transduction, metabolism and development switches. The chemical network models of these systems will be extended to deal with spatial inhomogeneity, mechanochemical coupling, and transport.

Comprehensive Models for Bio-MEMS: In-Situ Continuous Diagnostic Devices

We wish to develop a comprehensive set of design tools for simulating next-generation bio-MEMS devices. An example of such a device is a continuous in-situ diagnostic system for monitoring disease processes or as part of a drug delivery system [71]. In this application, there is continuous sampling of blood from a patient, which is then analysed by the MEMS system, in a sequence of processing steps. For example, in an optical detection system, the sample would be mixed with a sequence of reagents in order to attach a fluorescent molecule to the molecules to be detected that would emit when exposed to a particular frequency of light. For continuous sampling systems to be practical, it is necessary for the sample sizes to be extremely small – on the order of microliters. In such small samples, there would be a few 10's of molecules that would need to be detected present in the system at any given moment, and it is essential that the systems be designed to maximize the number of molecules that are detected. In order to design such systems, simulation tools such as the ones to be developed here are essential.

Such a device will consist of a combination of several basic components:

• *Sampling system.* One or more microneedles inserted under the skin will take a continuous blood sample. Such a system will include some filtration system to reduce the flow and concentrate the reactive species, based either on a membrane or on a system of microchannels.

• *Pumping system.* Pumps will use a positive displacement system. In this approach, fluid is heated in a side chamber, creating a vapor bubble that displaces the fluid. When the heating is no longer applied, the bubble collapses. This is combined with a valve system that restricts the fluid flow to be unidirectional out of the pump in the first phase, and to refill the pump in the second phase [34].

• *Mixers.* Although MEMS devices are extremely small, the length scales for mixing via diffusion in a reasonable length of time are still smaller. Recent has shown that attempts to mix using dividers, T-channels or flow-convergent systems are not able to mix in a reasonable amount of time, even though complex geometries and flow paths are used to create thin striations of different fluids. Instead of using complex geometrical configurations to create thin striations of fluids, an alternative approach to mix fluids on the microscale is to create a chaotic flow field [85, 32, 33] (see Figure 2).

• *Optical systems.* The sensitivity of the optical system is often the limiting factor because of the presence of few molecules of interest in the small sample sizes associated with MEMS devices. Detection of single molecules is possible; its main limitation is the sampling volume because of reduced signal-to-noise. Therefore, reducing the sample size requires knowing where the molecules are and where the optical probes are focused, and predicting the interaction between labeled molecules and the optical probe.

Modeling issues

Bio-MEMS devices have modeling requirements typical of more general microfluidic systems. These are devices that have complex moving boundaries (typically rigid bodies), have large aspect ratios, and operate in the near-Stokesean regime [96]. Since microfluidic pumps are driven by vapor bubbles, we need to represent two-phase flow with a sharp phase boundary and surface tension. In addition, there are a number of requirements that are peculiar to the biological application. Biological fluids, such as blood, are typically non-Newtonian. Since we will be dealing with dilute solutions of biological molecules, we need to represent them as discrete particles, rather than as a continuous distribution; yet these particles interact with the continuous fluid system. Biological molecules are polar molecules, and silicon can carry an electric charge, so we need to be able to represent the interaction of the molecules with an electric field, as well as the fluid. At various points in the process, we need to represent the chemical interaction of these discrete molecules with reagents. As in the cellular case, this will require a stochastic representation of the chemistry, rather than a one based on solving a system of deterministic ODE's.

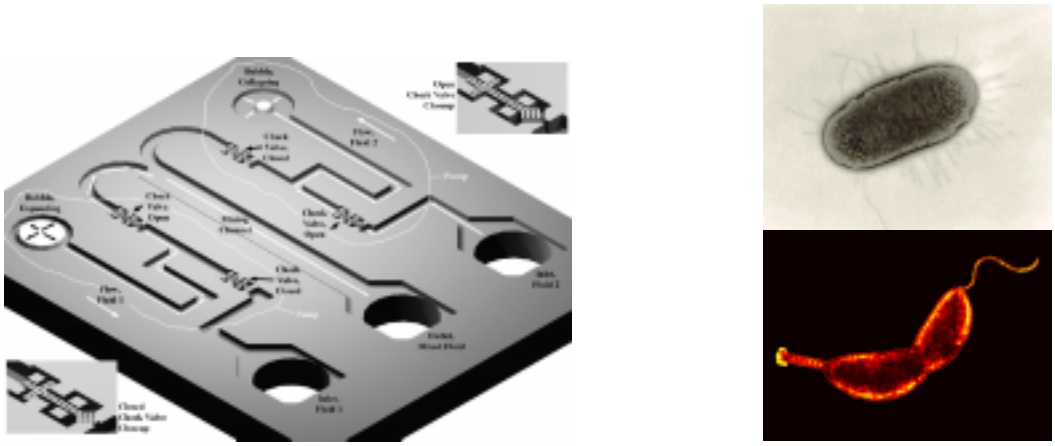

Figure 2: Left: A MEMS mixer. Top right: An E. Coli cell. Bottom right: Transmission electron micrograph of a Caulobacter crescentus cell in the process of cell division. The thin cylindrical tube on the left of the cell is the stalk and the wavy line on the right is the polar flagellum. The constriction in the middle is the site of cell division. This predivisional cell will divide and give rise to two different cell types: the motile swarmer cell with a polar flagellum, and the sessile stalked cell. (Photo courtesy of Yves V. Brun)

Prototype Models

Our initial target for modeling cellular dynamics will be to simulate the growth and division of the prokaryotic cells Escherichia Coli and Caulobacter Crecentus (figure 2) [54, 95, 58]. ¿From an algorithmic standpoint, the models for these cells contain many of the major components present in the more complex eukaryotic cells: deterministic and stochastic models for chemistry; moving boundaries across which there is mass transport; transport from the interior of the cell to the surface; and transport on the surface of the cell to discrete active sites where trapping can occur.

At any given instant in time, the state of the cell is given by specifying a surface in space that defines the boundary of the cell and by the concentration of chemical species at each point in space inside the cell. The number of active species can be as few as three for simple models of cell growth to 60 species for metabolic models[86]. The active species concentrations satisfy a system of reaction-diffusion equations with boundary conditions specified on the moving boundary of the cell. These boundary conditions represent the net effect of the flux of species carried from the intercellular medium as the cell grows and overtakes mass, and of the flux of chemical species that migrate into the cell walls and are transported along the boundary by surface diffusion[99].

The growth of the cell is represented by a single ODE for the rate at which the cell overtakes mass. The rate is a function of the cell-averaged concentrations of the active species. The time evolution of the surface is determined by the requirement that the cell grows at a uniform rate over its surface, except for a ring around the center of the cell that remains fixed. Initially, the surface is assumed to be a cylinder with hemispherical caps at each end. The active sites on the cell wall will move with the normal motion of the surface. There is also a stochastic component to the evolution that represents the effect of the cell DNA on the growth rate of the cell. In its simplest form, this is given by a master equation for the probability distribution that a reaction with the DNA will take place and affect the growth rate of the cell.

The prototype model for the bio-MEMS problem will be to simulate some of the individual fluid components of an in-situ diagnostic system, i.e. mixers, pumps, check valves, micro-needles, and an array of microchannels. The physical and numerical models for this problem are well understood, and will provide an appropriate prototype target for the development of the computer science ideas. For many of these components, we also have experimental data with which to validate the numerical methods.

An important role for the prototype systems will be as a test bed for the new numerical and modeling ideas required by the more comprehensive systems. An important example is the treatment of the various aspects of the discrete modeling of large molecules, such as DNA. The development of stable and accurate numerical

methods for coupling the stochastic models for chemistry of such dilute systems with a deterministic finite-difference model for the continuum mechanics will be investigated in a simplified form in the prokaryotic cell modeling, while the development of the models for discrete transport of DNA based on Cosserat theory will be tested in the bio-MEMS setting, for which there is experimental data [96]. Another example is the development of numerical models for the cell membrane. In the prokaryotic case, the geometry of the membrane is sufficiently regular that we can test various ideas for representing a moving surface on which there is simultaneously diffusive transport validated against a benchmark based on a surface coordinatization that is known to work in such simple geometries. The presence of both bio-MEMS and cell modeling in this proposal allows us to provide better coverage of the algorithm and modeling space in the prototype targets. For example, there is no fluid-flow modeling in the prokaryotic cell, only diffusive transport. However, that part of the modeling problem will appear in the prototype bio-MEMS problems.

Project Overview

In this section, we address some of the issues that arise from such a large, interdisciplinary project.

Project Scale and Duration

This project draws from three complementary areas of expertise, computer science, mathematics, and biomedical engineering, to attack fundamental problems in the modeling and simulation of microscale biological systems. We see all three as essential, and have included two application areas for several reasons.

- We want the programming system and the numerical methods we develop to have more general applicability and need the demands of two user groups to facilitate that genericity.
- As we gain the ability to support more complex coupled simulations, we expect aspects of these two application areas to merge, giving us a broader environment for modeling the biology and chemistry of intercellular phenomena.

We propose a five-year project both to leverage the human investment in creating a tightly knit interdisciplinary research team, and to be able to achieve our long-term goal of complex multi-faceted simulations.

Project Personnel

Professors Dorian Liepmann and Adam Arkin of the newly formed Berkeley Bioengineering Department and Professor Oliver O'Reilly of the Berkeley Department of Mechanical Engineering will lead the biological modeling group. Professor Liepmann directs the Berkeley Sensor and Actuator Center; Professor Arkin is an active participant in the Alliance for Cellular Signaling [43]. Their modeling work will enrich their separately funded research projects in biomedical engineering.

Professors Susan Graham, Paul Hilfinger, and Katherine Yelick will create the language and system in which the modeling will be realized. Professors Graham, Yelick, and Hilfinger have collaborated previously on the Titanium Project and other activities. Professor Hilfinger has done extensive research on language design, starting from his graduate work on the Ada language and continuing with languages for numerical mathematics (FIDIL), digital signal processing (Silage), and parallel programming (Titanium). Professor Graham has done research on virtually every aspect of compilation; Professor Yelick has outstanding credentials in runtime systems and libraries for parallel computing. All three of them have collaborated previously with scientists and engineers using high-performance computing for maodeling and simulation. They have significant experience developing programming tools as well.

Dr. Phillip Colella of the Applied Numerical Algorithms Group at Lawrence Berkeley National Laboratory will head the numerical mathematics effort (under the sponsorship of LBNL). Dr. Colella, a former member of the Berkeley Department of Mechanical Engineering, has been a participant in the Titanium Project. He is a world-class expert on numerical methods for fluid flow problems, and the advisor of many Ph.D. students on that topic. A former Ph.D. student of his is now a postdoc with Professor Liepmann.

The senior researchers will be joined by postdoctoral researchers, graduate students, and undergraduates from Berkeley and LBNL. We anticipate that the postdocs in the proposal budget will be computational biologists (i.e., experts in both the applications and in computational science), whereas most of the graduate and undergraduate students will be computer science and computational science students. That model has

worked well in the Titanium project. There are two postdocs on that project – a C.S. postdoc who is a former Ph.D. student of Dr. Colella's and an LBNL postdoc, together with computer science graduate and undergraduate students.

Project Plan

Although the proposed project draws on prior research by all of the senior participants, there are significant new challenges for all of them. We have structured the project so that the interdisciplinary collaboration takes place from the very beginning. The senior collaborators will meet frequently for project management and ccordination. There will be regularly scheduled research meetings of both disciplinary and cross-disciplinary subgroups to address technical issues, together with periodic meetings of the entire research team.

In the first year of the project, the biology team will design the prototype computational models that will be used initially, the numerical methods specialists will create the first version of the numerical mathematics to be used, and the computer scientists will design the language in which the modeling will be realized, and begin its implementation. We will start with simpler models and simpler algorithms. For example, the first algorithm implementations may not be adaptive, or may make simplifying assumptions about the physical problems. Starting in the second year, the implementation of the prototype models in the new system, using the new algorithms, will be carried out. The experience gained by the implementation effort will fuel the further model, algorithm, and system development, causing all three aspects to mature. As we become confident that we have the models, the language, and the algorithms right, we will place increasing emphasis on performance and on scaling the problems. We will also move from the prototypical models to the more complete models that will provide significant new insight and understanding to the biology community. Sometime during the third year we will be in a position to begin to exploit the feedback between the two application areas that will be achieved by carrying them out in the same computational environment.

Broader Impact of the Proposed Research

We expect to make fundamental research contributions in the areas of computer science, mathematical modeling, and biology. The algorithms and software techniques for programming clusters of SMPs can benefit users of these machines in science and engineering disciplines outside of biology. The demonstration of a single programming system that is effective on machines from desktops to supercomputers can also lower the cost of entry for users of large scale computational modeling. Two immediate sources of leverage in the dissemination our research are our colleagues at the Lawrence Berkeley National Laboratory and the National Partnership for Advanced Computational Infrastructure. Both of these institutions have indicated their support for this research in letters attached with this proposal. In addition, the Berkeley Millennium machines consist of several clusters that are available simulation and modeling efforts on the Berkeley campus.

The numerical techniques described in the proposal are relevant in many areas beyond microscale biological systems. In particular, adaptive mesh refinement is used in problems with a wide range of length and time scales, including combustion, aerodynamics, shock dynamics, and astrophysics. The general problem of coupling these methods to discrete, stochastic, and ODE methods could produce new simulation techniques for systems with fluids, chemistry, and structures. The embedded-boundary method also has wide applicability to engineering design problems that require the solution of PDE's in the presence of complex fixed or free boundaries. Examples include chemical and materials processing, automotive design, and subsurface flow problems arising in both environmental remediation and petroleum reservoir simulation. The immersed boundary is also used for problems in several areas that involve fluids interacting with flexible, elastic structures; these are typically biological systems, such as blood flow in the heart, clotting in blood vessels, and fluid in the inner ear.

The most dramatic potential impact of the proposed research on society as a whole comes from the possible improvements in the understanding and treatment of disease. Our cellular models will include representations of the pathways used to get signals from the membrane to the nucleus of a cell, and how these pathways are affected by damage to molecular elements or when multiple growth factors or cytokine exist. These fundamental questions are linked to our understanding a number of diseases and cancers. The bio-MEMS models could lead to improvement in the design of devices for monitoring and drug delivery that are more accurate and less invasive than conventional systems.

Integration of Research and Education

We have deliberately structured the project with a mixture of undergraduates, graduate students, and postdoctoral fellows rather than hiring professional software developers. Our previous experience with undergraduates has been excellent. The Titanium project has included several undergraduate researchers. Their recent projects include exploring new application domains by interfacing Titanium to PETSc and ParMetis for unstructured meshes, devising a new alias analysis for use in parallel optimization, developing Titanium implementations of common routines used in dense linear algebra and data-mining, and building a dynamic load-balancing framework for Titanium.

All of the senior researchers have been very successful graduate and postdoctoral research advisors as well. Many of the results of their work with these students are described earlier in the proposal. The cross-disciplinary nature of this project provides new education for the senior researchers as well.

Berkeley offers a graduate course in applications of parallel computers that is taken both by computer science students and by graduate students in other disciplines in which computational modeling and simulation are used. Student projects for the course team CS students with "applications" students. Research prototypes are often used in the course, and ongoing research projects are discussed. The course will provide both a technology transfer vehicle for the results of this project and a source of project participants.

Contributions to Diversity

The senior researchers have an excellent track record of working with members of under-represented groups. Professors Yelick and Graham constitute the entire female faculty in computer science at Berkeley. They have both been involved with the former Berkeley re-entry program in computer science, that helped prepare members of under-represented groups to enter graduate school, and both have had female and minority graduate students. One third of Dr. Colella's Ph.D. graduates at Berkeley were women.

Although it has been difficult, at Berkeley and elsewhere, to attract members of under-represented groups to graduate school in computer science, there are a significantly larger percentage of women entering bio-engineering. At the current time, 39% of the Berkeley graduate students in bio-engineering are women. By involving a diverse group of bio-engineering students in this project, we hope to attract at least some of them to careers in computational science.

Results from Prior NSF Support

In the last five years, Professors Graham and Yelick have received NSF support from the National Partnership for Advanced Computational Infrastructure (NPACI). Professor Graham is a co-PI of the cooperative agreement with the University of California, San Diego (ACI-9619020, up to $170,000,000, 10/1/97 - 9/30/02) and is the institutional PI for the subcontract to the University of California, Berkeley (ACI-9619020, $4,199,754, 10/1/97 - 9/30/02). The PACI program provides high-end computing resources to the science and engineering research community. In addition, it provides a symbiotic program to transfer leading-edge information technology to scientific and engineering researchers (the applications) and to use computational science and engineering research as a driver for high-end computing research (the enabling technologies) [1]. Professor Graham serves as the Chief Computer Scientist of NPACI, coordinating the enabling technology efforts and serving on the Leadership Team of the partnership.

As researchers, Professor Graham's and Professor Yelick's roles in the NPACI enabling technologies efforts centers around the UC Berkeley Titanium Project [103], a DARPA-sponsored collaborative effort that has developed the Titanium language and system, together with a collection of scientific applications implemented in Titanium (www.cs.berkeley.edu/Research/Projects/titanium). Under NPACI auspices, Titanium is being ported to the NPACI platforms and interfaces are being developed to the Active Data Repository (ADR) (www.cs.umd.edu/projects/hpsl/ResearchAreas/ADR.htm) and to the KeLP runtime system (www-cse.ucsd.edu/groups/hpcl/scg/kelp) . The compiler has been ported to the Cray T2E [65], Tera MTA [80], and IBM SP platforms and Linux platforms with Posix threads. The original implementation of Titanium ran on uniprocessors, shared memory machines, and the Berkeley NOW platform, all running Solaris.

[1] PACI is *not* a research program, but rather a service and technology transfer program.

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Education

1964 A.B. in Mathematics (with honors), Radcliffe College (Harvard University)
1966 M.S. in Computer Science, Stanford University
1971 Ph.D. in Computer Science, Stanford University

Appointments

University of California, Berkeley (1971-present)
Chancellor's Professor (1997-present), Professor, Computer Science (1981-present); Associate Professor, Computer Science (1976-1981); Assistant Professor, Computer Science (1971-1976).

Stanford University (1981)
Visiting Professor, Computer Systems Laboratory.

University of Chile, Santiago (1971)
Visiting Professor, Department of Mathematics.

Courant Institute of Mathematical Sciences, New York University (1969-1971)
Associate Research Scientists and Adjunct Assistant Professor, Department of Computer Science

Selected Publications

1. Susan L. Graham, Steven Lucco, and Oliver Sharp. Orchestrating interactions among parallel computations. *Proceedings of the ACM SIGPLAN '93 Conference on Programming Language Design and Implementation*, ACM Press, June 1993. Appeared as ACM SIGPLAN Notices 28 (6). http://www.acm.org/pubs/citations/proceedings/pldi/155090/p100-graham

2. David F. Bacon, Susan L. Graham, and Oliver J. Sharp. Compiler transformations for high-performance computing. *ACM Computing Surveys* 26(4): 345-420, 1994. http://www.acm.org/pubs/citations/journals/surveys/1994-26-4/p345-bacon/

3. Katherine Yelick, Luigi Semenzato, Geoffrey Pike, Carleton Miyamoto, Benjamin Liblit, Arvind Krishnamurthy, Paul Hilfnger, Susan Graham, David Gay, Philip Colella, and Alexander Aiken. Titanium: A high-performance Java dialect. *Concurrency: Practice and Experience* 10: 825-836, September 1998. http://www3.interscience.wiley.com/cgi-bin/issuetoc?ID=10050391

4. Joel Saltz, Alan Sussman, Susan Graham, James Demmel, Scott Baden, and Jack Dongarra. Programming Tools and Environments. *Communications of the ACM* 41 (11): 64-73, November 1998. http://www.acm.org/pubs/citations/journals/cacm/1998-41-11/p64-sussman/

5. Susan L. Graham. A computer science perspective on computing for the chemical sciences. *Impact of*

Advances in Computing and Communications Technologies on Chemical Science and Technology: Report of a Workshop, National Academy Press 1999. http://books.nap.edu/books/0309065771/html/109.html#pagetop1999

Selected Synergistic Activities

President's Information Technology Advisory Committee, 1997-2001
Advisory Committee, NSF, Div. of Mathematics and Physical Science, 1995-1998
National Research Council Computer Science and Telecommunications Board, 1996-2002
Chief Computer Scientist, National Partnership for Advanced Computational Infrastructure (NPACI), 1997-
Advisory Committee, National Institute for Science Education, 1996-2000

Recent Collaborators

Alexander Aiken, UCB
Russell Altman, Stanford
Peter Arzberger, UCSD/SDSC
Robert Ballance, Univ. New Mexico
Andrew Begel, UCB
John Boyland, Univ. Wisc., Milwaukee
Philip Colella, LBNL
Mark Ellisman, UCSD
David Gay, UCB
Andrew Grimshaw, U Virginia
Paul Hilfinger, UCB
Sid Karin, UCSD/SDSC
Arvind Krishnamurthy, Yale
Aron Kuppermann, Caltech
Ben Liblit, UCB
William Maddox, Sun Microsystems
William Martin, U Michigan
Steven McCanne, FastForward Networks
Paul Messina, Caltech & DOE
Jean-Bernard Minster, UCSD
Carlton Miyamoto , UCB
Reagan Moore, UCSD/SDSC
Gregory Moses, U Wisconsin
J.Tinsley Oden, U Texas
Arthur Olson, The Scripps Research Institute
Wayne Pfeiffer, UCSD/SDSC
Geoffrey Pike, UCB
James Pool, Caltech
Joel Saltz, U Maryland/Johns Hopkins
Luigi Semenzato, consultant
Peter Taylor, UCSD/SDSC
Caroline Tice, Compaq
Michael L. Van De Vanter, Sun Microsystems
Tim A. Wagner, Amazon.com
Katherine Yelick, UCB

Graduate and Postdoctoral Advisors

David Gries, Cornell

Thesis Advisor and Postgraduate-Scholar Sponsor (within past five years)

David F. Bacon, IBM
Andrew Begel, Grad. Student, UCB
Marat Boshernitsan, Grad. Student, UCB
John Boyland, Univ. Wisc., Milwaukee
Carol Hurwitz, Grad. Student, UCB
William Maddox, Sun Microsystems
Carlton Miyamoto, Grad. Student, UCB
Oliver Sharp, Microsoft
Caroline Tice, Compaq Research
Tim A. Wagner, Amazon.com

Approximately 40 graduate students advised
Approximately 7 postdoctoral scholars sponsored

Adam P. Arkin
Assistant Professor
Departments of Bioengineering and Chemistry
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aparkin@uclink.berkeley.edu

Education

1988	B.A., Chemistry	Carleton College, Minnesota
1992	Ph.D., Physical Chemistry	Massachusetts Institute of Technology
1992-1995	Post-doctoral researcher, Nonlinear Chemical Systems, Stanford University	
1995-1997	Post-doctoral researcher, Modeling Development, Stanford University	

Appointments

University of California, Berkeley (July 1999-present)
Assistant Professor, Departments of Bioengineering and Chemistry

Lawrence Berkeley National Laboratory, Berkeley, CA (January 1998 July 1999)
Faculty Scientist, Computational and Theoretical Biology Department, Physical Biosciences Division (July 1999-present)
Staff Scientist, Computational and Theoretical Biology Department, Physical Biosciences Division (January 1998-July 1999)

Selected Publications

1. McAdams, H., Arkin. A.P. (1997) Stochastic Mechanisms in Gene Expression. *Proc. Natl. Acad. Sci., USA* . 94(3):814.

2. Swanson, C., Arkin, A.P., Ross, J. (1997) An Endogenous Calcium Oscillator May Control Early Embryonic Division. *Proc. Natl. Acad. Sci., USA* . 94(4):1194.

3. McAdams, H. H., Arkin, A.P. (1998) Simulation of Prokaryotic Genetic Networks. *Annu.Rev. Biophys. Biomol. Struct.* 27: 199-244

4. Arkin, A.P., Ross, J., McAdams, H.H. (1998) Stochastic Kinetic Analysis of a Developmental Pathway Bifurcation in Phage-λ *Escherichia coli*. *Genetics.* 149(4):1633-1648.

5. Arkin, A.P. (1999) Signal Processing by Biochemical Reaction Networks. In: Biodynamics. J. Walleczek, ed. Cambridge University Press, Cambridge.In Press.

Selected Other Publications

1. Arkin, A.P., Youvan D.C. (1992) An Algorithm for Protein Engineering: Simulations of Recursive Ensemble Mutagenesis. *Proc. Natl. Acad. Sci. USA* 89(16):7811-7815.

2. Arkin, A.P., Youvan, D.C. (1992) Digital Imaging Spectroscopy. In: The Photosynthetic Reaction Center J. Deisenhofer & J.R. Norris eds. 133-154.

3. Arkin, A.P ,.Shen, P.-D., Ross, J. (1997) A Test Case of Correlation Metric Construction of a Reaction Pathways from Measurements. *Science*. 277(5330): 1275.

4. McAdams, H.H., Arkin, A.P (1999) Genetic Regulation at the Nanomolar Scale: It's a Noisy Business! *TIGS.* 15(2): 65-69.

Selected Synergistic Activities

1. Developed software suite for simulation of genetic networks that has been made available on the web and donated to a number of off-site groups for further development. Also forms the core of the Bio/Spice biological simulation and analysis tool.
2. Helped develop and write a proposal for a multisite Alliance for Cellular Signaling out of University of Texas, Southwestern Medical Center dedicated to forming a collaboration among more than forty experimentalist, computer scientists and computational biologists to understand G-protein signal transduction in B-Cells and cardiomyocytes.
3. Coordinating development, with Peter Karp (Stanford Research Institute), Milton Saier (UCSD), Fernando Valle (Genecor, Intl.), and Tyrrell Conway (U. Oaklahoma) of EcoReg and database of primary and secondary data on the kinetics, regulation, and expression in *E. coli* to create a synergy with EcoCyc, a knowledge base of *E. coli* pathways.

Graduate Advisor, Graduate and Post Graduate Advisees

Doctoral Advisors: Dr. Doug Youvan, President/CEO of Kairos, Inc (was assistant professor M.I.T.,main dissertation advisor); Prof. Keith Nelson, Department of Chemistry, M.I.T.

Post-doctoral Advisors: Prof. John Ross, Department of Chemistry, Stanford University, Prof. Lucy Shapiro & Dr. Harley McAdams, Developmental Biology, School of Medicine, Stanford University.

Post-Doctoral Advisees: Dr. Alex Gilman (chemistry) '98, Dr. Denise Wolf (engineering) '98, Dr. Chris Rao (chemical engineering) '00.

Collaborators in the Past 48 Months Other Than Above

H. McAdams, Stanford University
J. Doyle, California Institute of Technology
Antje Hofmeister, University of California, Berkeley
Guri Giaever, Ron Davis, Stanford University
Dan Rokhsar, University of California, Berkeley and Lawrence Berkeley National Laboratory
Stephen Holbrook, Lawrence Berkeley National Laboratory
Roger Brent, Molecular Sciences Institute

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Education

1973 A.B. in Mathematics, Princeton University
1981 Ph.D. in Computer Science, Carnegie-Mellon University

Appointments

University of California, Berkeley (1982-present)
Associate Professor, Computer Science Division,
Department of Electrical Engineering and Computer Science (1988-present)
Assistant Professor (1982-1988)

Carnegie-Mellon University (1981-1982)
Research Assistant in Computer Science

Selected Publications

1. Semenzato, L. and Hilfinger P. N., "Arrays in FIDIL", in *Arrays, Functional Languages, and Parallel Systems*, L. M. R. Mullin, M. Jenkins, G. Hains, R. Bernecky, and G. Gao, ed., Kluwer Academic Publishers, 1991, pp. 155-169.

2. Hilfinger, P. N., "FIDIL: A Language for Scientific Computation," Invited paper, *Advances in Computer Methods for Partial Differential Equations VII: Proceedings of the Seventh IMACS International Conference on Computer Methods for Partial Differential Equations*, R. Vichnevetsky, D. Knight, and G. Richter, ed., New Brunswick, June 22-24, 1992, pp. 349-355.

3. Alex Aiken, Phil Colella, David Gay, Susan Graham, Paul Hilfinger, Arvind Krishnamurthy, Ben Liblit, Carleton Miyamoto, Geoffery Pike, Luigi Semenzato, and Kathy Yelick, "Titanium: A High-Performance Java Dialect," Java '98 Workshop, 1998. In Concurrency and Experience.

Selected Other Publications

1. James Larus and Paul N. Hilfinger, "Detecting Conflicts Between Structure Accesses," *Proceedings of SIGPLAN '88 Conference on Programming Language Design and Implementation*, Atlanta, Georgia, June, 1988, pp. 21-34.

2. Wang, E. and Hilfinger, P. N., "Analysis of Structured Types in Lisp-like Languages," *Proceedings of the 1992 ACM Conference on LISP and Functional Programming*, June 22-24, 1992, pp. 216-225.

3. Paul Hilfinger and Jan Rabaey, "DSP Specification Using the Silage Language," in, Anatomy of a Silicon Compiler, Robert W. Brodersen, ed., Kluwer Academic Publishers, 1992, pp. 199-220.

4. Josh MacDonald and Paul N. Hilfinger, "PRCS: The Project Revision Control System," *Proceedings of the Eighth System Configuration Management Symposium* (SCM98), 1998.

5. James Shin Young, Josh MacDonald, Michael Shilman, Abdallah Tabbara, Paul Hilfinger, and A. Richard Newton, "Design and Specification of Embedded Systems in Java Using Successive, Formal Refinement," *Proceedings of the Design Automation Conference (DAC)*, 1998.

Synergistic Activities

1. Specified and supervised development of simplified source-code control system (PRCS), now widely distributed.
2. Developed compiler for Java for instructional use (Berkeley course CS 164), later used as initial basis for research compiler.
3. Served on National Research Council Study Committee: "Review of the Past and Present Contexts for Using Ada within the Department of Defense", 1995.

Recent Collaborators

Alex Aiken
Adam P. Arkin, LBNL
Phillip Colella, LBNL
David Gay
Susan Graham
Arvind Krishnamurthy, Yale
Ben Liblit
Dorian Liepmann
Joshua MacDonald
Carleton Miyamoto
A. Richard Newton
Geoffrey Pike
Luigi Semenzato (VMWareInc.)
Michael Shilman
Abdallah Tabbara
Katherine Yelick
James Shin Young

Unless otherwise noted, affiliation is the University of California, Berkeley.

Advisees

Total of 13 graduate advisees.

In the last 5 years: Joshua MacDonald (University of California, Berkeley), Geoffrey Pike (University of California, Berkeley), and Allen Downey (Colby College).

Thesis Advisor

Mary Shaw, Carnegie-Mellon University

Dorian Liepmann
Professor: Bioengineering and Mechanical Engineering
Director: Berkeley Sensor & Actuator Center
University of California
Dept. of Bioengineering
466 Evans Hall
Berkeley, CA 94720-1762

Education

1981 B.A., Combined Program-Chemistry, Occidental College
1981 B.S., Chemical Engineering, California Institute of Technology
1983 M.S., Chemical Engineering, California Institute of Technology
1990 Ph.D., Applied Mechanics, University of California, San Diego

Appointments

University of California, Berkeley (1998-present)
Associate Professor, Mechanical and Bio-Engineering

Berkeley Sensor & Actuator Center (1998-present)
Associate Director

Defense Sciences Research Council (1998-present)
Member

University of California, San Francisco/University of California, Berkeley Bioengineering Graduate Corp. (1993-present)
Former co-Chair and current Head Graduate Advisor

SAIC, La Jolla, CA (1984-1992)
Assistant in the Advanced Technology Group

Arroyo Center (1983-1984)
Provided technology and policy for the Army

Selected Publications

1. Papavasiliou, A.P., Liepmann, D., and Pisano, A.P., 1999 "Fabrication of a Free Floating Silicon Gate Valve," Proceedings of the ASME MEMS Division, 1999 IMECE, Vol.1 pp 435-440.

2. Srinivasan, U., Howe, R.T. and Liepmann, D., "Fluidic Assembly using Patterned Self-Assembled Monolayers and Shape Matching," *Transducers '99, The 10th International Conference on Solid-State Sensors and Actuators*, Sendai, Japan, June 7 – 10, 1999.

3. Shrewsbury, P.J., Muller, S.J., and Liepmann, D., "Characterization of DNA Flow Through Microchannels," *2nd International Conference on Modeling and Simulation of Microsystems, Semiconductors, Sensors and Actuators*, San Juan, Puerto Rico, April 19-21, 1999.

4. D. Fabris, S. J. Muller, and D. Liepmann, "Wake measurements for flow around a sphere in a visco-elastic fluid," *Physics of Fluids*, 11(12):3599-3612, 1999.

5. Lee, L.P., Berger, S.A., Pruitt, L., and Liepmann, D., "Key Elements of a Transparent Teflon Microfluidic System," □*-TAS '98 International Symposium*, Banff, Canada, Oct. 17-21, 1998.

Selected Other Publications

1. Evans, J. D. and Liepmann, D., "The Bubble Spring and Channel (BsaC) Valve: An Actuated, Bi-Stable Mechanical Valve for In-Plane Fluid Control," *Transducers '99, The 10th International Conference on Solid-State Sensors and Actuators,* Sendai, Japan, June 7-10, 1999 (to appear).

2. Evans, J.D., Liepmann, D. and Pisano, A.P. "Planar Laminar Mixer", MEMS97 (The Tenth Annual International Workshop on Micro Electro Mechanical Systems), January 26-30, 1997, Nagoya, Japan, pp. 96-101.

Synergistic Activities

As an Associate Professor of both Bioengineering and Mechanical Engineering, he has taught numerous courses in fluid mechanics at both the Graduate and Undergraduate levels as well as courses in Bioengineering and Mathematics. Dr. Liepmann was key player in the formation of the Bioengineering Department at Berkeley and was the first 100% member of the new department. His research has involved experimental work on biological flows, micro-fluidics, and macro-scale fluid mechanics. This work includes work on advanced diagnostic applications of hemodynamics, development of MEMS-based fluid control systems for applications such as drug delivery, and investigation of the micro-fluid mechanics of complex biological fluids. An example of his work is the development of a micro-mixer that employs chaotic advection to reduce mixing times by two orders of magnitude compared to diffusion. His group has developed new micro-valves and pumps. Dr. Liepmann has extensive experience in the synergistic application of numerical and experimental techniques for the understanding of complex fluid flows. He is the first researcher to use DPIV data to both provide initial conditions and extensive validation of the simulation. Recent work includes the first applications of DPIV in the investigation of viscoelastic (Boger) fluids including Taylor-Couette flow and wakes.

Recent Collaborators

Professors at UCB: Roger Howe, Luke Lee, Albert Pisano, Richard White, Ralph Grief, Costas Grigoropoulos, Carlos Fernandez-Pello, Omer Savas, Stanley Berger, Susan Muller, Jay Keasling, Adam Arkin, Lewei Lin, Mark Richardson, Oliver O'Reilley, Patrick Pagni, Terrance Leighton

Other: Philip Colella (LBL), Morteza Gharib (Caltech), David Sahn (Oregon Health Sciences Institute), Robin Shaundas (University of Denver), Ellen Longmire (Univ. of Minnesota), Greg Kovacs (Stanford)

Advisors and Advisees

Advisors:
Dr. Morteza Gharib, California Institute of Technology (current position)

Advisees:
PhD: John Evans (Becton Dickinson Technologies), Drazen Fabris (Santa Clara University), Luke Lee (UC Berkeley)

MS: Cathy Norton (Hewlett Packard), Rossana Quinones (IBM, Puerto Rico), Pablo Mitchell (UC Berkeley), Kendra Sharp (Illinois Institute of Technology), Lee Thomason (Berkeley Systems), William Edwards (Consultant), Evan Collier (Army Reserve Medical School).

Katherine A. Yelick
Associate Professor of Computer Science
Department of Electrical Engineering and Computer Science
University of California, Berkeley
Berkeley, CA 94720-1776
Office: (510) 642-8900
Fax: (510) 642-3962
yelick@cs.berkeley.edu

Education

1985 B.S. and M.S. in Computer Science, Massachusetts Institute of Technology
1991 Ph.D. in Computer Science, Massachusetts Institute of Technology

Appointments

University of California, Berkeley (1991-present)
Associate Professor, Computer Science (1996-present); Assistant Professor, Computer Science (1991-1996).

Lawrence Berkeley National Laboratory (1996-present)
Senior Research Scientist

ETH, Zurich, Switzerland (Summer, 1996)
Visiting Researcher

Massachusetts Institute of Technology (Fall, 1996)
Visiting Associate Professor

Clark University (Spring, 1985)
Visiting Instructor

Selected Publications

1. "Optimizing Sparse Matrix Vector Multiplication on SMPs," with E. Im. SIAM Conf. Parallel Processing for Scientific Computing, San Antonio, TX, March 1999
2. "Titanium: A High-Performance Java Dialect," with L. Semenzato, G. Pike, C. Miyamoto, B. Liblit, A. Krishnamurthy, P. Hilfinger, S. Graham, D. Gay, P. Colella, and A. Aiken. Concurrency: Practice and Experience, September-November 1998, pp. 825-36. Earlier version was presented at the ACM Workshop on Java for High-Performance Network Computing, February 1998.
3. "Models and Scheduling Algorithms for Mixed Data and Task Parallel Programs," with S. Chakrabarti and J. Demmel. Journal of Parallel and Distributed Computing, Vol. 47, pp. 168-184. December 1997.
4. "Analyses and Optimizations for Shared Address Space Programs," with A. Krishnamurthy. Journal of Parallel and Distributed Computation, vol.38, (no.2), Academic Press, 1 Nov. 1996. pp.130-44.
5. S. Chakrabarti, E. Deprit, J. Jones, A. Krishnamurthy, E.-J. Im, C.-P. Wen, and K. Yelick, "Multipol: A Distributed Data Structure Library." UCB//CSD-95-879, July 1995.

Selected Other Publications

1. "Scalable processors in the billion-transistor era: IRAM," with Kozyrakis, C.E., Perissakis, S., Patterson, D., Anderson, T., Asanovic, K., Cardwell, N., Fromm, R., Golbus, J., Gribstad, B.,Keeton, K., Thomas, R., and Treuhaft, N. *Computer*, vol.30, (no.9), IEEE Comput. Soc, Sept. 1997. p.75-8.
2. "The Energy Efficiency of IRAM Architectures," with R. Fromm, S. Perissakis, N. Cardwell, D. Patterson, and T. Anderson. Proceedings of the 24th Annual International Conference on Computer Architecture, June 1997.

3. C.-P. Wen, S. Chakrabarti, E. Deprit, A. Krishnamurthy and K. Yelick, “Runtime Support for Portable Distributed Data Structures," Proceedings of the Workshop on Languages, Compilers and Run-Time Systems for Scalable Computers, Troy, NY, USA, May 1995. Norwell, MA, USA: Kluwer Academic Publishers, 1996. pp. 111-120.
4. “Parallel Programming in Split-C,” with D. Culler, A. Dusseau, S. Goldstein, A. Krishnamurthy, S. Lumetta, and T. von Eiken. Supercomputing ‘93, November 1993.
5. “Unification in Combinations of Collapse-Free Regular Theories,” *Journal of Symbolic Computation*, March 1987, pp. 153-181.

Selected Synergistic Activities

Professor Yelick led the Multipol library project, a publicly available set of distributed data structures, scheduling algorithms, and irregular applications benchmarks. At the same time, she was developing a revised undergraduate data structures course, and used some of the scientific computing applications and data structures in the course. She collaborated with David Culler and their students on Split-C, and with several other faculty and students on the development of Titanium. Split-C and Titanium are both publicly available, explicitly parallel languages for high performance machines, and both have been used in graduate courses at Berkeley. The more recent project, Titanium, is a Java-based language with an optimizing compiler. Professor Yelick and one of her students devised new static compiler analyses for explicitly parallel programs and developed the first compiler that demonstrated such analyses could effectively be used to optimize parallel applications and to hide relaxed memory models. She has also completed several interdisciplinary applications projects in the areas of Computational Fluid Dynamics, CAD, cell biology, genetics, symbolic computation, and physics. She is currently leading the Sparsity project and the application and compiler efforts on the Intelligent RAM (IRAM) and Intelligent Storage (ISTORE) projects. Both projects involve close ties with industry. In addition to the 13 graduate students and 1 postdoc listed below, she has worked with over 20 undergraduates in her projects.

Recent Collaborators and Other Affiliations

U.C. Berkeley collaborators:

Alexander Aiken
Eric Anderson
Robert Brayton
Aaron Brown
David Culler
James Demmel
David Gay
Susan Graham
Paul Hilfinger
Joseph M. Hellerstein
Eun-Jin Im
Christoforos Kozyrakis
Ben Liblit
David Martin
Carleton Miyamoto
Thinh Nguyen
David A. Patterson
Stelios Perissakis
Geoff Pike
Noah Treuhaft
Avideh Zakhor

Others:

T. Anderson, U. Washington
R. Arpaci-Dusseau, U. Wisconsin
A. Arpaci-Dusseau, U. Wisconsin
K. Asanovic, MIT
Neal Cardwell
S. Chakrabarti, IIT Mumbai
Philip Colella, LBNL
Rich Fromm, Fastforward
Steve Garland, MIT
Jason Golbus, Myricomm
Ben Gribstad
Jeff Jones, Hyperparallel
Kimberly Keeton, Hewlett Packard
A. Krishnamurthy, Yale
A. Saldana
K. Schauser, UCSB
Chris Scheiman
L. Semenzato, VMware
R. Y. Wang, Princeton
Chih-Po Wen, Epiphany
G. York
Joseph Zachary, U. Utah

Graduate Advisor

John V. Guttag, Massachusetts Institute of Technology

Graduate Students and Postgraduate Scholars Advised

(13 total graduate students advised, one Postdoctoral Researcher sponsored)

G. Balls (Postdoc)
D. Bonachea, UCB
N. Bowman, UCB
S. Chakrabarti, IIT Mumbai
E. Deprit, UCB
Ruth Hinkins
Eun-Jin Im, UCB
A. Krishnamurthy, Yale
Chang Sun Lin, UCB
S. Steinberg
E. Thomas, UCB
N. Treuhaft, UCB
D. Weisser, CMU
C-P Wen, Epiphan

Phillip Colella
Senior Staff Scientist
NERSC Division
Lawrence Berkeley National Laboratory
Berkeley, CA 94720
Office: 510-486-5412
FAX: 510-495-2505
PColella@lbl.gov

Education

1974 A.B. in Applied Mathematics, UC Berkeley
1976 M.A. in Applied Mathematics, UC Berkeley
1979 Ph. D. in Applied Mathematics, UC Berkeley

Appointments

Lawrence Berkeley National Laboratory (1978-1986, 1996-present)
Senior Staff Scientist (1996-present); Staff Scientist (1978-1986)

University of California, Berkeley (1989-1998)
Professor in Residence, Mechanical Engineering (1995-1998)
Professor, Mechanical Engineering (1992-1995)
Associate Professor, Mechanical Engineering (1989-1992)

Lawrence Livermore National Laboratory (1986-1989, 1995-1996)
Staff Scientist / Mathematician

Courant Institute for the Mathematical Sciences, New York University (1985)
Visiting Scientist

University of Minnesota (1985)
Visiting Lecturer, School of Mathematics

Selected Publications

1. J. Helmsen, E.G. Puckett, P. Colella, and M. Dorr, "Two new methods for simulating photolithography development in 3D". SPIE Proceedings of Optical Microlithography IX, Santa Clara, CA, USA, 13-15 March 1996, p. 253-261.
2. A.S. Almgren, J.B. Bell, P. Colella, L.H. Howell, and M. Welcome, "A conservative adaptive projection method for the variable density incompressible Navier-Stokes equations", Journal of Computational Physics 142(1):1-46, May, 1998.
3. K. Yelick, L. Semenzato, G. Pike, C. Miyamoto, B. Liblit, A. Krishnamurthy, P. Hilfinger, S. Graham, D. Gay, P. Colella, A. Aiken, "Titanium: a high-Performance Java dialect", Concurrency: Practice and Experience 10:825-836, September, 1998.
4. H. Johansen and P. Colella, "A Cartesian grid embedded boundary method for Poisson's equation on irregular domains", Journal of Computational Physics 147(1):60-85, November, 1998.
5. P. Colella and D. Trebotich, "Numerical simulation of incompressible viscous flow in deforming domains", Proceedings of the National Academy of Sciences of the United States of America 96:5378-5381, March, 1999.

Additional Selected Publications

1. M. J. Berger and P. Colella, "Local adaptive mesh refinement for shock hydrodynamics", J. Comput. Phys. 82:64-84, May, 1989.
2. J. B. Bell, P. Colella and H. M. Glaz, "A second-order projection method for the incompressible Navier-Stokes equations", J. Comput. Phys. 85:257-283, December, 1989.
3. P. Colella, "Multidimensional upwind methods for hyperbolic conservation laws", J. Comput. Phys. 87:171-200, March, 1990.
4. J. B. Bell, P. Colella, and M. Welcome, "Conservative front tracking for inviscid compressible flow", Proceedings, 10th AIAA Computational Fluid Dynamics, Conference, Honolulu, HI June 24-27, 1991, p. 814 - 822.
5. J. A. Trangenstein and P. Colella, "A higher-order Godunov method for modeling finite deformation in elastic-plastic solids", Comm. Pure and Applied Math. 44:41-100, January, 1991.

Selected Synergistic Activities

Colella developed PPM and other robust second-order extensions of Godunov's method for a variety of time-dependent problems in hyperbolic conservation laws, including unsteady gas dynamics with complex equations of state, magnetohydrodynamics, and solid mechanics. He combined these methods with predictor-corrector ideas to obtain accurate and efficient algorithms for problems with a combination of hyperbolic and non-hyperbolic terms, and applied them to problems such as incompressible flow, porous media flows, and low Mach number combustion. He also used these ideas as the basis for new stable and well-conditioned algorithms for stiff problems in time-dependent PDE's, such as compressible flow at low Mach numbers and fluid models for plasmas.

Colella has developed a number of extensions to the volume of fluid approach to representing solutions to PDE's in complex geometries in which the geometry of the front is specified implicitly by giving the volume occupied in each grid cell by the domain on either side of the front. Recent accomplishments in that area include the development of formally consistent methods for solving elliptic and hyperbolic PDE's that are well-conditioned and second-order accurate.

In collaboration with Marsha Berger, Colella developed a version of block-structured adaptive mesh refinement (AMR) for unsteady shocks, and demonstrated that AMR could be implemented without significant memory or CPU overheads on high-performance computers. Since that time, he has worked on extending AMR to many of the applications described above.

Colella has been involved with several projects to improve the software environment for scientific computing, including the design of the FIDIL programming language with Paul Hilfinger, the development of C++ libraries to support adaptive finite difference calculations, and as a collaborator in the Titanium language project.

Colella has been a participant in a variety of multidisciplinary collaborations with experimentalists and theoretical fluid dynamicists, using various combinations of the algorithms described above. Areas of investigation include shock reflection and shock refraction, astrophysics, inertial confinement fusion, materials processing, combustion, and bio-MEMS simulations.

Recent Collaborators

Alexander Aiken, UCB
Ann Almgren, LBNL
Scott Baden, UCSD
Gregory Balls, UCB
John Bell, LBNL
Nicholas Cernansky, Drexel Univ.
Robert Crockett, UCB
Marcus Day, LBNL
Milo Dorr, LLNL
Scott Dudek, Babcock and Wilcox
Woodrow Fiveland, ABB
David Gay, UCB
Susan Graham, UCB
Daniel Graves, LBNL
Jeffrey Greenough, LLNL
John Helmsen, Applied Materials
James Hilditch, Ford Motor Co.
Paul Hilfinger, UCB
Louis Howell, LLNL
J. Patrick Jessee, Babcock and Wilcox
Hans Johansen, Esurance, Inc.
Anton Kast, LBNL
Christopher McKee, UCB
Richard Klein, LLNL / UCB
Arvind Krishnamurthy, Yale
Ben Liblit, UCB
Dorian Liepmann, UCB
Daniel Marcus, Speechwise, Inc.
Tyler Marthaler, Random Walk Computing
Daniel Martin, LBNL
Peter McCorquodale, LBNL
Gregory Miller, LBNL / UCD
Carleton Miyamoto, UCB
David Modiano, Crystal Design
Emily Nelson, NASA Glenn Research Center
Richard Pember, LLNL
Tadeuz Patzek, UCB
Geoffrey Pike, UCB
Richard Propp, LBNL
Elbridge Gerry Puckett, UCD
David Serafini, Arbitrade
Luigi Semenzato, VMware, Inc.
Mark Sussman, Florida State University
Rodney Tabaczynski, Ford Motor Co.
Kevin Tallio, Ford Motor Co.
David Trebotich, UCB
Marco Vegas-Landeau, UCB
Daniel Wake, Nonstop Solutions
Michael Welcome, LBNL
Katherine Yelick, UCB

Research Advisor

Alexandre Chorin, UCB

Thesis Advisor and Postdoctoral-Scholar Sponsor (Last Five Years)

Andrew Anderson, LLNL
Gregory Balls, UCB
Matthew Bettencourt, University of Southern Mississippi
Carolyn Chee, consultant
Scott Dudek, Babcock and Wilcox
John Helmsen, Applied Materials
James Hilditch, Ford Motor Co.
Hans Johansen, Esurance, Inc.
Daniel Martin, LBNL
Peter McCorquodale, LBNL
David Modiano, Crystal Design
Emily Nelson, NASA Glenn Research Center
Richard Propp, LBNL
David Serafini, Arbitrade
David Trebotich, UCB

16 Ph. D. Students supervised or co-supervised.
9 Postdoctoral Scholars Sponsored.

Oliver M. O'Reilly

Department of Mechanical Engineering
University of California at Berkeley
Berkeley California 94720
phone: 510-642-0877
email: oreilly@me.berkeley.edu

Education

1985 B.E. in Mechanical Engineering, National University of Ireland at Galway
1988 M.S. in Theoretical and Applied Mechanics, Cornell University
1989 Ph. D. in Theoretical and Applied Mechanics, Cornell University
1990 Postdoc., Rheology and Mechanics, Swiss Federal Institute of Technology (ETH-Zürich), to 1992

Appointments

University of California, Berkeley (1992-present)
Associate Professor, Department of Mechanical Engineering (1998-present)
Assistant Professor, Department of Mechanical Engineering (1992-1998)

Swiss Federal Institute of Technology, Zurich, Switzerland (1990-1992)
Postdoctoral Assistant, (1990-1992)

Cornell University (1986-1990)
Research and Teaching Assistant, Department of Theoretical and Applied Mechanics (1986-1990)

Related Publications

1. O. M. O'Reilly, On *Constitutive Relations for Elastic Rods*, International Journal of Solids and Structures, Vol. 35, pp. 1009-1024 (1998).

2. O. M. O'Reilly and J. S. Turcotte, Elastic *Rods with Moderate Rotation, Journal* of Elasticity, Vol. 48, pp. 195-216 (1997).

3. T. R. Nordenholz and O. M. O'Reilly, On *the Existence of Stretch for a Prescribed Stress in Isotropic, Incompressible Elastic Bodies*, Mathematics and Mechanics of Solids, Vol. 3, pp. 169-181 (1998).

4. O. M. O'Reilly and P. C. Varadi, Hoberman's *Sphere, Euler Parameters and Lagrange's Equations*, Journal of Elasticity, In Press (2000).

5. O. M. O'Reilly and P. C. Varadi, A *Treatment of Shocks in One-Dimensional Thermomechanical Media*, Continuum Mechanics and Thermodynamics, Vol. 11, pp. 339-352 (1999).

Other Significant Publications

1. T. R. Nordenholz and O. M. O'Reilly, On *Steady Motions of an Elastic Rod with Application to Contact Problems, International* Journal of Solids and Structures, Vol. 34, pp. 1123-1143 and 3211-3212 (1997).

2. O. M. O'Reilly, The *Dynamics of Rolling Disks and Sliding Disks*, Nonlinear Dynamics, Vol. 10, pp. 287-305 (1996).

3. O. M. O'Reilly, Steady *Motions of a Drawn Cable*, ASME: Journal of Applied Mechanics, Vol. 63, pp.180-189 (1996).

4. A. Mielke, P. Holmes and O. O'Reilly, *Cascades of Homoclinic Orbits to, and Chaos near, a Hamiltonian Saddle-Center*, Journal of Dynamics and Differential Equations, Vol. 4, pp. 95-126 (1992).

5. P. C. Varadi, G-J Lo, O. M. O'Reilly and P. Papadopoulos, A Novel Approach to Vehicle Dynamics using the theory of a Cosserat Point and its Application to Collision Analyses of Platooning Vehicles, Vehicle System Dynamics, Vol. 32, pp. 85-108 (1999).

Synergistic Activities

Presently, I serve as chair of the U.C. Berkeley Academic Senate Committee on Special Scholarships (a committee which is charged with increasing the numbers and assisting under-represented minority students). My teaching efforts have centered on modernizing the treatment of dynamics in several undergraduate and graduate courses. In addition, I teach a freshman seminar on "Movies and Mechanics" which aims to explain the pedagogy of undergraduate engineering education and also serves to attract undeclared students into mechanical engineering.

One of the goals of my research is to bring new methods to old problems. To this end, I feel that I have achieved significant advances in the introduction of new models to, and improved understanding of, various engineering problems ranging from wrist-exercisers (the dynabee) and vehicle collision dynamics to axially moving materials.

Collaborators

Philip Colella (Lawrence Berkeley National Laboratory)
Prof. Dorian Liepmann (University of California at Berkeley)
Prof. Panayiotis Papadopoulos (University of California at Berkeley)
Prof. Arun Srinivasa (University of California at Berkeley)

Graduate and Postgraduate Advisors

Prof. F. C. Moon (Cornell University)
Prof. P. J. Holmes (Princeton University, formerly at Cornell University)
Prof. J. Dual (ETH Zürich, Switzerland)

Graduate Students and Postdoctoral Scholars

David Gulick (High School Teacher, San Francisco)
Eva Kanso (University of California at Berkeley)
Ahrie Moon (Present address unknown)
Thomas R. Nordenholz (California Maritime Academy, Vallejo, California)
Jeffrey S. Turcotte (AFIT, Wright-Patterson Airforce Base, Ohio)
Peter C. Varadi (Siemens TTB and University of California at Berkeley)

I have supervised 6 graduate students and no postdoctoral scholars during the past five years.

SUMMARY PROPOSAL BUDGET

YEAR 1

FOR NSF USE ONLY		
PROPOSAL NO.	DURATION (months) Proposed	Granted
AWARD NO.		

ORGANIZATION: **University of California-Berkeley**

PRINCIPAL INVESTIGATOR / PROJECT DIRECTOR: **Susan L Graham**

A. SENIOR PERSONNEL: PI/PD, Co-PI's, Faculty and Other Senior Associates (List each separately with title, A.7. show number in brackets)	NSF Funded Person-mos. CAL	ACAD	SUMR	Funds Requested By proposer	Funds granted by NSF (if different)
1. **Susan L Graham - Prof 8**	**0.00**	**0.00**	**1.50**	$ **21,521**	$
2. **Adam Arkin - Asst Prof 6 OS**	**0.00**	**0.00**	**1.00**	**10,488**	
3. **Paul N Hilfinger - Assoc Prof 5 OS**	**0.00**	**0.00**	**1.50**	**14,820**	
4. **Dorian Liepmann - Assoc Prof 3**	**0.00**	**0.00**	**1.00**	**10,821**	
5. **Oliver M O'Reilly - Assoc Prof 4 OS**	**0.00**	**0.00**	**0.00**	**9,125**	
6. (**1**) OTHERS (LIST INDIVIDUALLY ON BUDGET JUSTIFICATION PAGE)	**0.00**	**0.00**	**1.50**	**13,959**	
7. (**6**) TOTAL SENIOR PERSONNEL (1 - 6)	**0.00**	**0.00**	**6.50**	**80,734**	
B. OTHER PERSONNEL (SHOW NUMBERS IN BRACKETS)					
1. (**2**) POST DOCTORAL ASSOCIATES	**12.00**	**0.00**	**0.00**	**123,220**	
2. (**0**) OTHER PROFESSIONALS (TECHNICIAN, PROGRAMMER, ETC.)	**0.00**	**0.00**	**0.00**	**0**	
3. (**7**) GRADUATE STUDENTS				**182,339**	
4. (**2**) UNDERGRADUATE STUDENTS				**22,750**	
5. (**0**) SECRETARIAL - CLERICAL (IF CHARGED DIRECTLY)				**0**	
6. (**1**) OTHER				**20,138**	
TOTAL SALARIES AND WAGES (A + B)				**429,181**	
C. FRINGE BENEFITS (IF CHARGED AS DIRECT COSTS)				**91,191**	
TOTAL SALARIES, WAGES AND FRINGE BENEFITS (A + B + C)				**520,372**	
D. EQUIPMENT (LIST ITEM AND DOLLAR AMOUNT FOR EACH ITEM EXCEEDING $5,000.) **4 Dell Precision Workstation (or equivalent)** $ **17,320**					
TOTAL EQUIPMENT				**17,320**	
E. TRAVEL 1. DOMESTIC (INCL. CANADA, MEXICO AND U.S. POSSESSIONS)				**43,650**	
2. FOREIGN				**0**	
F. PARTICIPANT SUPPORT COSTS					
1. STIPENDS $ **0**					
2. TRAVEL **0**					
3. SUBSISTENCE **0**					
4. OTHER **0**					
(**0**) TOTAL PARTICIPANT COSTS				**0**	
G. OTHER DIRECT COSTS					
1. MATERIALS AND SUPPLIES				**6,240**	
2. PUBLICATION COSTS/DOCUMENTATION/DISSEMINATION				**780**	
3. CONSULTANT SERVICES				**0**	
4. COMPUTER SERVICES				**35,568**	
5. SUBAWARDS				**0**	
6. OTHER				**3,744**	
TOTAL OTHER DIRECT COSTS				**46,332**	
H. TOTAL DIRECT COSTS (A THROUGH G)				**627,674**	
I. INDIRECT COSTS (F&A)(SPECIFY RATE AND BASE) **% of MTDC (Rate: 50.4000, Base: 569741)**					
TOTAL INDIRECT COSTS (F&A)				**287,149**	
J. TOTAL DIRECT AND INDIRECT COSTS (H + I)				**914,823**	
K. RESIDUAL FUNDS (IF FOR FURTHER SUPPORT OF CURRENT PROJECTS SEE GPG II.D.7.j.)				**0**	
L. AMOUNT OF THIS REQUEST (J) OR (J MINUS K)				$ **914,823**	$

M. COST SHARING PROPOSED LEVEL $ **0** AGREED LEVEL IF DIFFERENT $

PI / PD TYPED NAME & SIGNATURE*: **Susan L Graham** DATE

ORG. REP. TYPED NAME & SIGNATURE* DATE

FOR NSF USE ONLY		
INDIRECT COST RATE VERIFICATION		
Date Checked	Date Of Rate Sheet	Initials - ORG

SUMMARY PROPOSAL BUDGET COMMENTS - Year 1

Other Senior Personnel

Name - Title	Cal	Acad	Sumr	Funds Requested
Yelick, Katherine A - Assoc Prof 4	**0.00**	**0.00**	**1.50**	**13959**

**** I- Indirect Costs**
Modified Total Direct Costs excludepermanent equipment costs, Graduate Student Health Insurance payments, fee remission, and non-California resident tuition. As of July 1, 1999, the DHHS rate is 50.4%

SUMMARY PROPOSAL BUDGET

YEAR 2

FOR NSF USE ONLY		
PROPOSAL NO.	DURATION (months) Proposed	Granted
AWARD NO.		

ORGANIZATION: **University of California-Berkeley**

PRINCIPAL INVESTIGATOR / PROJECT DIRECTOR: **Susan L Graham**

A. SENIOR PERSONNEL: PI/PD, Co-PI's, Faculty and Other Senior Associates (List each separately with title, A.7. show number in brackets)	NSF Funded Person-mos. CAL	ACAD	SUMR	Funds Requested By proposer	Funds granted by NSF (if different)
1. **Susan L Graham - Prof 9**	**0.00**	**0.00**	**1.50**	$ **23,049**	$
2. **Adam Arkin - Asst Asst Prof 6 OS**	**0.00**	**0.00**	**1.00**	**10,803**	
3. **Paul N Hilfinger - Assoc Prof 5 OS**	**0.00**	**0.00**	**1.50**	**15,117**	
4. **Dorian Liepmann - Assoc Prof 3**	**0.00**	**0.00**	**1.00**	**11,037**	
5. **Oliver M O'Reilly - Assoc Prof 5 (OS)**	**0.00**	**0.00**	**1.00**	**9,773**	
6. (**1**) OTHERS (LIST INDIVIDUALLY ON BUDGET JUSTIFICATION PAGE)	**0.00**	**0.00**	**1.50**	**14,238**	
7. (**6**) TOTAL SENIOR PERSONNEL (1 - 6)	**0.00**	**0.00**	**7.50**	**84,017**	
B. OTHER PERSONNEL (SHOW NUMBERS IN BRACKETS)					
1. (**2**) POST DOCTORAL ASSOCIATES	**12.00**	**0.00**	**0.00**	**130,874**	
2. (**0**) OTHER PROFESSIONALS (TECHNICIAN, PROGRAMMER, ETC.)	**0.00**	**0.00**	**0.00**	**0**	
3. (**7**) GRADUATE STUDENTS				**193,450**	
4. (**2**) UNDERGRADUATE STUDENTS				**23,362**	
5. (**0**) SECRETARIAL - CLERICAL (IF CHARGED DIRECTLY)				**0**	
6. (**1**) OTHER				**20,728**	
TOTAL SALARIES AND WAGES (A + B)				**452,431**	
C. FRINGE BENEFITS (IF CHARGED AS DIRECT COSTS)				**98,907**	
TOTAL SALARIES, WAGES AND FRINGE BENEFITS (A + B + C)				**551,338**	
D. EQUIPMENT (LIST ITEM AND DOLLAR AMOUNT FOR EACH ITEM EXCEEDING $5,000.) **4 Dell Precision Workstation (or equivalent)** $ **17,320**					
TOTAL EQUIPMENT				**17,320**	
E. TRAVEL 1. DOMESTIC (INCL. CANADA, MEXICO AND U.S. POSSESSIONS)				**46,575**	
2. FOREIGN				**0**	
F. PARTICIPANT SUPPORT COSTS					
1. STIPENDS $ **0**					
2. TRAVEL **0**					
3. SUBSISTENCE **0**					
4. OTHER **0**					
(**0**) TOTAL PARTICIPANT COSTS				**0**	
G. OTHER DIRECT COSTS					
1. MATERIALS AND SUPPLIES				**6,365**	
2. PUBLICATION COSTS/DOCUMENTATION/DISSEMINATION				**796**	
3. CONSULTANT SERVICES				**0**	
4. COMPUTER SERVICES				**36,279**	
5. SUBAWARDS				**0**	
6. OTHER				**3,820**	
TOTAL OTHER DIRECT COSTS				**47,260**	
H. TOTAL DIRECT COSTS (A THROUGH G)				**662,493**	
I. INDIRECT COSTS (F&A)(SPECIFY RATE AND BASE) **% of MTDC (Rate: 50.4000, Base: 573078)**					
TOTAL INDIRECT COSTS (F&A)				**288,831**	
J. TOTAL DIRECT AND INDIRECT COSTS (H + I)				**951,324**	
K. RESIDUAL FUNDS (IF FOR FURTHER SUPPORT OF CURRENT PROJECTS SEE GPG II.D.7.j.)				**0**	
L. AMOUNT OF THIS REQUEST (J) OR (J MINUS K)				$ **951,324**	$

M. COST SHARING PROPOSED LEVEL $ **0** AGREED LEVEL IF DIFFERENT $

PI / PD TYPED NAME & SIGNATURE*: **Susan L Graham** DATE

ORG. REP. TYPED NAME & SIGNATURE* DATE

FOR NSF USE ONLY		
INDIRECT COST RATE VERIFICATION		
Date Checked	Date Of Rate Sheet	Initials - ORG

SUMMARY PROPOSAL BUDGET COMMENTS - Year 2

Other Senior Personnel

Name - Title	Cal	Acad	Sumr	Funds Requested
Yelick, Katherine A - Assoc Prof 4	**0.00**	**0.00**	**1.50**	**14238**

**** I- Indirect Costs**
Modified Total Direct Costs excludepermanent equipment costs, Graduate Student Health Insurance payments, fee remission, and non-California resident tuition. As of July 1, 1999, the DHHS rate is 50.4%

SUMMARY PROPOSAL BUDGET YEAR 3

FOR NSF USE ONLY		
PROPOSAL NO.	DURATION (months) Proposed	Granted
AWARD NO.		

ORGANIZATION: **University of California-Berkeley**

PRINCIPAL INVESTIGATOR / PROJECT DIRECTOR: **Susan L Graham**

A. SENIOR PERSONNEL: PI/PD, Co-PI's, Faculty and Other Senior Associates (List each separately with title, A.7. show number in brackets)	NSF Funded Person-mos. CAL	ACAD	SUMR	Funds Requested By proposer	Funds granted by NSF (if different)
1. **Susan L Graham - Prof 9**	**0.00**	**0.00**	**1.50**	$ **23,510**	$
2. **Adam Arkin - Asst Prof 6 OS**	**0.00**	**0.00**	**1.00**	**11,570**	
3. **Paul N Hilfinger - Assoc Prof 6 OS**	**0.00**	**0.00**	**1.50**	**16,191**	
4. **Dorian Liepmann - Assoc Prof 4**	**0.00**	**0.00**	**1.00**	**11,821**	
5. **Oliver M O'Reilly - Assoc Prof 5 OS**	**0.00**	**0.00**	**1.00**	**9,968**	
6. (**1**) OTHERS (LIST INDIVIDUALLY ON BUDGET JUSTIFICATION PAGE)	**0.00**	**0.00**	**1.50**	**16,191**	
7. (**6**) TOTAL SENIOR PERSONNEL (1 - 6)	**0.00**	**0.00**	**7.50**	**89,251**	
B. OTHER PERSONNEL (SHOW NUMBERS IN BRACKETS)					
1. (**2**) POST DOCTORAL ASSOCIATES	**12.00**	**0.00**	**0.00**	**134,602**	
2. (**0**) OTHER PROFESSIONALS (TECHNICIAN, PROGRAMMER, ETC.)	**0.00**	**0.00**	**0.00**	**0**	
3. (**7**) GRADUATE STUDENTS				**205,203**	
4. (**2**) UNDERGRADUATE STUDENTS				**23,834**	
5. (**0**) SECRETARIAL - CLERICAL (IF CHARGED DIRECTLY)				**0**	
6. (**1**) OTHER				**21,562**	
TOTAL SALARIES AND WAGES (A + B)				**474,452**	
C. FRINGE BENEFITS (IF CHARGED AS DIRECT COSTS)				**107,206**	
TOTAL SALARIES, WAGES AND FRINGE BENEFITS (A + B + C)				**581,658**	
D. EQUIPMENT (LIST ITEM AND DOLLAR AMOUNT FOR EACH ITEM EXCEEDING $5,000.)					
1 Laser printer $ **1,624**					
4 Dell Precision Workstation (or equivalent) **17,320**					
TOTAL EQUIPMENT				**18,944**	
E. TRAVEL 1. DOMESTIC (INCL. CANADA, MEXICO AND U.S. POSSESSIONS)				**47,325**	
2. FOREIGN				**0**	
F. PARTICIPANT SUPPORT COSTS					
1. STIPENDS $ **0**					
2. TRAVEL **0**					
3. SUBSISTENCE **0**					
4. OTHER **0**					
(**0**) TOTAL PARTICIPANT COSTS				**0**	
G. OTHER DIRECT COSTS					
1. MATERIALS AND SUPPLIES				**6,492**	
2. PUBLICATION COSTS/DOCUMENTATION/DISSEMINATION				**812**	
3. CONSULTANT SERVICES				**0**	
4. COMPUTER SERVICES				**37,005**	
5. SUBAWARDS				**0**	
6. OTHER				**3,896**	
TOTAL OTHER DIRECT COSTS				**48,205**	
H. TOTAL DIRECT COSTS (A THROUGH G)				**696,132**	
I. INDIRECT COSTS (F&A)(SPECIFY RATE AND BASE) **% of MTDC (Rate: 50.4000, Base: 597979)**					
TOTAL INDIRECT COSTS (F&A)				**301,381**	
J. TOTAL DIRECT AND INDIRECT COSTS (H + I)				**997,513**	
K. RESIDUAL FUNDS (IF FOR FURTHER SUPPORT OF CURRENT PROJECTS SEE GPG II.D.7.j.)				**0**	
L. AMOUNT OF THIS REQUEST (J) OR (J MINUS K)				$ **997,513**	$

M. COST SHARING PROPOSED LEVEL $ **0** AGREED LEVEL IF DIFFERENT $

PI / PD TYPED NAME & SIGNATURE*: **Susan L Graham** DATE

ORG. REP. TYPED NAME & SIGNATURE* DATE

FOR NSF USE ONLY

INDIRECT COST RATE VERIFICATION

Date Checked	Date Of Rate Sheet	Initials - ORG

SUMMARY PROPOSAL BUDGET COMMENTS - Year 3

Other Senior Personnel

Name - Title	Cal	Acad	Sumr	Funds Requested
Yelick, Katherine A - Assoc Prof 6 OS	0.00	0.00	1.50	16191

**** I- Indirect Costs**
Modified Total Direct Costs excludepermanent equipment costs, Graduate Student Health Insurance payments, fee remission, and non-California resident tuition. As of July 1, 1999, the DHHS rate is 50.4%

SUMMARY PROPOSAL BUDGET

YEAR 4

FOR NSF USE ONLY		
PROPOSAL NO.	DURATION (months) Proposed	Granted
AWARD NO.		

ORGANIZATION: **University of California-Berkeley**

PRINCIPAL INVESTIGATOR / PROJECT DIRECTOR: **Susan L Graham**

A. SENIOR PERSONNEL: PI/PD, Co-PI's, Faculty and Other Senior Associates (List each separately with title, A.7. show number in brackets)	NSF Funded Person-mos. CAL	ACAD	SUMR	Funds Requested By proposer	Funds granted by NSF (if different)
1. **Susan L Graham - Prof 10 OS**	**0.00**	**0.00**	**1.50**	$ **25,179**	$
2. **Adam Arkin - Asst Prof 6 OS**	**0.00**	**0.00**	**1.00**	**11,801**	
3. **Paul N Hilfinger - Assoc Prof 6 OS**	**0.00**	**0.00**	**1.50**	**16,515**	
4. **Dorian Liepmann - Assoc Prof 4**	**0.00**	**0.00**	**1.00**	**12,057**	
5. **Oliver M O'Reilly - Assoc Prof 5 OS**	**0.00**	**0.00**	**1.00**	**10,167**	
6. (**1**) OTHERS (LIST INDIVIDUALLY ON BUDGET JUSTIFICATION PAGE)	**0.00**	**0.00**	**1.50**	**16,515**	
7. (**6**) TOTAL SENIOR PERSONNEL (1 - 6)	**0.00**	**0.00**	**7.50**	**92,234**	
B. OTHER PERSONNEL (SHOW NUMBERS IN BRACKETS)					
1. (**2**) POST DOCTORAL ASSOCIATES	**12.00**	**0.00**	**0.00**	**142,974**	
2. (**0**) OTHER PROFESSIONALS (TECHNICIAN, PROGRAMMER, ETC.)	**0.00**	**0.00**	**0.00**	**0**	
3. (**7**) GRADUATE STUDENTS				**217,700**	
4. (**2**) UNDERGRADUATE STUDENTS				**24,306**	
5. (**0**) SECRETARIAL - CLERICAL (IF CHARGED DIRECTLY)				**0**	
6. (**1**) OTHER				**22,223**	
TOTAL SALARIES AND WAGES (A + B)				**499,437**	
C. FRINGE BENEFITS (IF CHARGED AS DIRECT COSTS)				**116,307**	
TOTAL SALARIES, WAGES AND FRINGE BENEFITS (A + B + C)				**615,744**	
D. EQUIPMENT (LIST ITEM AND DOLLAR AMOUNT FOR EACH ITEM EXCEEDING $5,000.)					
4 Dell Precision Workstation (or equivalent) **$ 17,320**					
TOTAL EQUIPMENT				**17,320**	
E. TRAVEL 1. DOMESTIC (INCL. CANADA, MEXICO AND U.S. POSSESSIONS)				**48,090**	
2. FOREIGN				**0**	
F. PARTICIPANT SUPPORT COSTS					
1. STIPENDS $ **0**					
2. TRAVEL **0**					
3. SUBSISTENCE **0**					
4. OTHER **0**					
(**0**) TOTAL PARTICIPANT COSTS				**0**	
G. OTHER DIRECT COSTS					
1. MATERIALS AND SUPPLIES				**6,622**	
2. PUBLICATION COSTS/DOCUMENTATION/DISSEMINATION				**828**	
3. CONSULTANT SERVICES				**0**	
4. COMPUTER SERVICES				**37,745**	
5. SUBAWARDS				**0**	
6. OTHER				**3,973**	
TOTAL OTHER DIRECT COSTS				**49,168**	
H. TOTAL DIRECT COSTS (A THROUGH G)				**730,322**	
I. INDIRECT COSTS (F&A)(SPECIFY RATE AND BASE)					
% of MTDC (Rate: 50.4000, Base: 625983)					
TOTAL INDIRECT COSTS (F&A)				**315,495**	
J. TOTAL DIRECT AND INDIRECT COSTS (H + I)				**1,045,817**	
K. RESIDUAL FUNDS (IF FOR FURTHER SUPPORT OF CURRENT PROJECTS SEE GPG II.D.7.j.)				**0**	
L. AMOUNT OF THIS REQUEST (J) OR (J MINUS K)				$ **1,045,817**	$

M. COST SHARING PROPOSED LEVEL $ **0** AGREED LEVEL IF DIFFERENT $

PI / PD TYPED NAME & SIGNATURE*: **Susan L Graham** DATE

ORG. REP. TYPED NAME & SIGNATURE* DATE

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INDIRECT COST RATE VERIFICATION

Date Checked	Date Of Rate Sheet	Initials - ORG

SUMMARY PROPOSAL BUDGET COMMENTS - Year 4

Other Senior Personnel

Name - Title	Cal	Acad	Sumr	Funds Requested
Yelick, Katherine A - Assoc Prof 6 OS	0.00	0.00	1.50	16515

**** I- Indirect Costs**
Modified Total Direct Costs excludepermanent equipment costs, Graduate Student Health Insurance payments, fee remission, and non-California resident tuition. As of July 1, 1999, the DHHS rate is 50.4%

SUMMARY PROPOSAL BUDGET

YEAR 5

FOR NSF USE ONLY		
PROPOSAL NO.	DURATION (months) Proposed	Granted
AWARD NO.		

ORGANIZATION: **University of California-Berkeley**

PRINCIPAL INVESTIGATOR / PROJECT DIRECTOR: **Susan L Graham**

A. SENIOR PERSONNEL: PI/PD, Co-PI's, Faculty and Other Senior Associates (List each separately with title, A.7. show number in brackets)	NSF Funded Person-mos. CAL	ACAD	SUMR	Funds Requested By proposer	Funds granted by NSF (if different)
1. **Susan L Graham - Prof 10 OS**	**0.00**	**0.00**	**1.50**	$ **25,935**	$
2. **Adam Arkin - Asst Prof 6 OS**	**0.00**	**0.00**	**1.00**	**12,155**	
3. **Paul N Hilfinger - Assoc Prof 6 OS**	**0.00**	**0.00**	**1.50**	**17,010**	
4. **Dorian Liepmann - Assoc Prof 4**	**0.00**	**0.00**	**1.00**	**12,419**	
5. **Oliver M O'Reilly - Assoc Prof 5 OS**	**0.00**	**0.00**	**1.00**	**10,472**	
6. (**1**) OTHERS (LIST INDIVIDUALLY ON BUDGET JUSTIFICATION PAGE)	**0.00**	**0.00**	**1.50**	**17,010**	
7. (**6**) TOTAL SENIOR PERSONNEL (1 - 6)	**0.00**	**0.00**	**7.50**	**95,001**	
B. OTHER PERSONNEL (SHOW NUMBERS IN BRACKETS)					
1. (**2**) POST DOCTORAL ASSOCIATES	**12.00**	**0.00**	**0.00**	**147,042**	
2. (**0**) OTHER PROFESSIONALS (TECHNICIAN, PROGRAMMER, ETC.)	**0.00**	**0.00**	**0.00**	**0**	
3. (**7**) GRADUATE STUDENTS				**230,984**	
4. (**2**) UNDERGRADUATE STUDENTS				**24,789**	
5. (**0**) SECRETARIAL - CLERICAL (IF CHARGED DIRECTLY)				**0**	
6. (**1**) OTHER				**22,876**	
TOTAL SALARIES AND WAGES (A + B)				**520,692**	
C. FRINGE BENEFITS (IF CHARGED AS DIRECT COSTS)				**125,873**	
TOTAL SALARIES, WAGES AND FRINGE BENEFITS (A + B + C)				**646,565**	
D. EQUIPMENT (LIST ITEM AND DOLLAR AMOUNT FOR EACH ITEM EXCEEDING $5,000.) **4 Dell Precision Workstation (or equivalent)** $ **17,320**					
TOTAL EQUIPMENT				**17,320**	
E. TRAVEL 1. DOMESTIC (INCL. CANADA, MEXICO AND U.S. POSSESSIONS)				**48,870**	
2. FOREIGN				**0**	
F. PARTICIPANT SUPPORT COSTS					
1. STIPENDS $ **0**					
2. TRAVEL **0**					
3. SUBSISTENCE **0**					
4. OTHER **0**					
(**0**) TOTAL PARTICIPANT COSTS				**0**	
G. OTHER DIRECT COSTS					
1. MATERIALS AND SUPPLIES				**6,754**	
2. PUBLICATION COSTS/DOCUMENTATION/DISSEMINATION				**845**	
3. CONSULTANT SERVICES				**0**	
4. COMPUTER SERVICES				**38,500**	
5. SUBAWARDS				**0**	
6. OTHER				**4,053**	
TOTAL OTHER DIRECT COSTS				**50,152**	
H. TOTAL DIRECT COSTS (A THROUGH G)				**762,907**	
I. INDIRECT COSTS (F&A)(SPECIFY RATE AND BASE) **% of MTDC (Rate: 50.4000, Base: 649971)**					
TOTAL INDIRECT COSTS (F&A)				**327,585**	
J. TOTAL DIRECT AND INDIRECT COSTS (H + I)				**1,090,492**	
K. RESIDUAL FUNDS (IF FOR FURTHER SUPPORT OF CURRENT PROJECTS SEE GPG II.D.7.j.)				**0**	
L. AMOUNT OF THIS REQUEST (J) OR (J MINUS K)				$ **1,090,492**	$

M. COST SHARING PROPOSED LEVEL $ **0** AGREED LEVEL IF DIFFERENT $

PI / PD TYPED NAME & SIGNATURE*: **Susan L Graham** DATE

ORG. REP. TYPED NAME & SIGNATURE* DATE

FOR NSF USE ONLY

INDIRECT COST RATE VERIFICATION

Date Checked	Date Of Rate Sheet	Initials - ORG

SUMMARY PROPOSAL BUDGET COMMENTS - Year 5

Other Senior Personnel

Name - Title	Cal	Acad	Sumr	Funds Requested
Yelick, Katherine A - Assoc Prof 6 OS	0.00	0.00	1.50	17010

**** B-3 Graduate Students**
7 GSRs for 12 months.
**** I- Indirect Costs**
Modified Total Direct Costs excludepermanent equipment costs, Graduate Student Health Insurance payments, fee remission, and non-California resident tuition. As of July 1, 1999, the DHHS rate is 50.4%

SUMMARY PROPOSAL BUDGET

Cumulative

FOR NSF USE ONLY		
PROPOSAL NO.	DURATION (months) Proposed	Granted
AWARD NO.		

ORGANIZATION: **University of California-Berkeley**

PRINCIPAL INVESTIGATOR / PROJECT DIRECTOR: **Susan L Graham**

A. SENIOR PERSONNEL: PI/PD, Co-PI's, Faculty and Other Senior Associates (List each separately with title, A.7. show number in brackets)	NSF Funded Person-mos. CAL	ACAD	SUMR	Funds Requested By proposer	Funds granted by NSF (if different)
1. **Susan L Graham - Prof 8**	**0.00**	**0.00**	**7.50**	$ **119,194**	$
2. **Adam Arkin - Asst Prof 6 OS**	**0.00**	**0.00**	**5.00**	**56,817**	
3. **Paul N Hilfinger - Assoc Prof 5 OS**	**0.00**	**0.00**	**7.50**	**79,653**	
4. **Dorian Liepmann - Assoc Prof 3**	**0.00**	**0.00**	**5.00**	**58,155**	
5. **Oliver M O'Reilly - Assoc Prof 4 OS**	**0.00**	**0.00**	**4.00**	**49,505**	
6. (**1**) OTHERS (LIST INDIVIDUALLY ON BUDGET JUSTIFICATION PAGE)	**0.00**	**0.00**	**7.50**	**77,913**	
7. (**6**) TOTAL SENIOR PERSONNEL (1 - 6)	**0.00**	**0.00**	**36.50**	**441,237**	
B. OTHER PERSONNEL (SHOW NUMBERS IN BRACKETS)					
1. (**10**) POST DOCTORAL ASSOCIATES	**60.00**	**0.00**	**0.00**	**678,712**	
2. (**0**) OTHER PROFESSIONALS (TECHNICIAN, PROGRAMMER, ETC.)	**0.00**	**0.00**	**0.00**	**0**	
3. (**35**) GRADUATE STUDENTS				**1,029,676**	
4. (**10**) UNDERGRADUATE STUDENTS				**119,041**	
5. (**0**) SECRETARIAL - CLERICAL (IF CHARGED DIRECTLY)				**0**	
6. (**5**) OTHER				**107,527**	
TOTAL SALARIES AND WAGES (A + B)				**2,376,193**	
C. FRINGE BENEFITS (IF CHARGED AS DIRECT COSTS)				**539,484**	
TOTAL SALARIES, WAGES AND FRINGE BENEFITS (A + B + C)				**2,915,677**	
D. EQUIPMENT (LIST ITEM AND DOLLAR AMOUNT FOR EACH ITEM EXCEEDING $5,000.) $ **88,224**					
TOTAL EQUIPMENT				**88,224**	
E. TRAVEL 1. DOMESTIC (INCL. CANADA, MEXICO AND U.S. POSSESSIONS)				**234,510**	
2. FOREIGN				**0**	
F. PARTICIPANT SUPPORT COSTS					
1. STIPENDS $ **0**					
2. TRAVEL **0**					
3. SUBSISTENCE **0**					
4. OTHER **0**					
(**0**) TOTAL PARTICIPANT COSTS				**0**	
G. OTHER DIRECT COSTS					
1. MATERIALS AND SUPPLIES				**32,473**	
2. PUBLICATION COSTS/DOCUMENTATION/DISSEMINATION				**4,061**	
3. CONSULTANT SERVICES				**0**	
4. COMPUTER SERVICES				**185,097**	
5. SUBAWARDS				**0**	
6. OTHER				**19,486**	
TOTAL OTHER DIRECT COSTS				**241,117**	
H. TOTAL DIRECT COSTS (A THROUGH G)				**3,479,528**	
I. INDIRECT COSTS (F&A)(SPECIFY RATE AND BASE)					
TOTAL INDIRECT COSTS (F&A)				**1,520,442**	
J. TOTAL DIRECT AND INDIRECT COSTS (H + I)				**4,999,970**	
K. RESIDUAL FUNDS (IF FOR FURTHER SUPPORT OF CURRENT PROJECTS SEE GPG II.D.7.j.)				**0**	
L. AMOUNT OF THIS REQUEST (J) OR (J MINUS K)				$ **4,999,970**	$

M. COST SHARING PROPOSED LEVEL $ **0** AGREED LEVEL IF DIFFERENT $

PI / PD TYPED NAME & SIGNATURE*	DATE	FOR NSF USE ONLY
Susan L Graham		INDIRECT COST RATE VERIFICATION
ORG. REP. TYPED NAME & SIGNATURE*	DATE	Date Checked / Date Of Rate Sheet / Initials - ORG

NSF Form 1030 (10/98) Supersedes all previous editions

C***SIGNATURES REQUIRED ONLY FOR REVISED BUDGET (GPG III.B)**

Susan L. Graham, PI
University of California, Berkeley
NSF – Information Technology Research (ITR)
9/1/00 – 8/31/05

"ITR/ACS: Software for Numerical Simulation of Microscale Biological Systems"

Budget Justification

Salary and associated costs of education are provided for 7 Graduate Student Researchers for 9 academic year months and 3 summer months (3 of the 7 are budgeted as non-resident students), and for 2 undergraduate student researchers at 25% time during the academic year and 100% time during the summer. Professors Graham, Yelick, and Hilfinger each receive 1.5 summer months of support in each project year, and Professors Liepmann, Arkin, and O'Reilly each receive 1 summer month of support each year. Other personnel are 2 Visiting Postdoctoral Researchers full time each year, and 50% of a Research Administration position who will provide specific support functions for contract/grant compliance, including: Post-award grant management, financial analysis, projections, record keeping, billing coordination, procurement, travel, reimbursement and travel voucher preparation, receiving and processing deliveries, monitoring equipment inventory, and payroll (initial hiring, processing, etc.). These services are not included in the campus indirect cost rate, nor do central campus units provide them.

All salaries are current with cost-of-living increases projected as follows: 2.0% for all faculty and students, effective every October 1. Merit raises are also included, where applicable, effective July 1.

Benefits rates are 9.2% for Faculty Summer salary, 1.3% for Graduate Student Researcher academic year salary, 3% for Graduate Student Researcher summer salary, and 4.3% for undergraduate researchers. GSR Health Insurance is $247/student/semester, and Partial Fee remission for residents is $2,076/resident student/semester, and $2,199/non-resident student per semester, beginning Fall 2000.

Requested equipment for this project includes 4 personal computers per year, for a total of 20 over five years (replacing outdated equipment on a regular basis), for the 17 researchers on this project. The requested model is identified for its technical specifications, but actual equipment purchased may vary according to advances in technological development. The current quotation was obtained from Dell, and pricing reflects the maximum educational discount possible. One printer is also purchased in year 3, again to replace outdated equipment for this project.

Travel costs are obtained via estimated costs for round-trip, coach, non-restricted trips to Washington, D.C., and average per diem and registration costs. Fifteen trips per year are allocated for the 17 researchers, for a total of 75 trips over 5 years. The purpose is to attend technical conferences and to present research results.

Computer support expenses include a Computer Infrastructure Fee, system software and hardware administration, back-up charges, printer charges, and hardware maintenance. Other charges include mailing, phones, and photocopying expenses.

For verification of rates, please see the University of California, Sponsored Projects Office web site: `http://www.spo.berkeley.edu/Policy/benefits/beneft99.html`.

Current and Pending Support

See GPG Section II.D.8 for guidance on information to include on this form.)

The following information should be provided for each investigator and other senior personnel. Failure to provide this information may delay consideration of this proposal.

Investigator: Susan L. Graham	Other agencies (including NSF) to which this proposal has been/will be

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: National Partnership for Advanced Computational Infrastructure (NPACI)

(Susan L. Graham, PI, James Demmel, co-PI, David Culler, co-PI; supports research of 11 faculty)

Source of Support: UCSD/NSF

Total Award Amount: $3,830,525 Total Award Period Covered: 10/1/97 - 9/30/02

Location of Project: U.C. Berkeley

Person-Months Per Year Committed to the Project. Cal: Acad: Sumr: 1.25

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: Titanium Language and Compiler Program

Source of Support: Subcontract, Lawrence-Berkeley National Laboratory (DOE)

Total Award Amount: $117,742 Total Award Period Covered: 5/23/99 – 5/20/00

Location of Project: U.C. Berkeley

Person-Months Per Year Committed to the Project. Cal: Acad: Sumr:

Support: ☐ Current ☒ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: Frameworks for Interactive Software Development

Source of Support: NSF

Total Award Amount: $255,020 Total Award Period Covered: 5/1/00 – 4/30/02

Location of Project: U.C. Berkeley

Person-Months Per Year Committed to the Project. Cal: Acad: 0 Sumr: .5

Support: ☐ Current ☒ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: ITR/ACS: Software for Numerical Simulation of Microscale Biological Systems (Susan Graham, PI; Co-PIs: Adam Arkin, Paul Hilfinger, Dorian Liepmann, Katherine Yelick)

Source of Support: NSF

Total Award Amount: $4,999,971 Total Award Period Covered: 9/1/00 – 8/31/05

Location of Project: U.C. Berkeley

Person-Months Per Year Committed to the Project. Cal: Acad: 0 Sumr: 1.5

Support: ☐ Current ☒ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: ITR/SW: Multi-modal Interfaces for Programming and Software Development

(Susan Graham, PI; Michael Clancy, Co-PI)

Source of Support: NSF

Total Award Amount: $2,982,776 Total Award Period Covered: 9/1/00 – 8/31/05

Location of Project: U.C. Berkeley

Person-Months Per Year Committed to the Project. Cal: Acad: Sumr: 2

*If this project has previously been funded by another agency, please list and furnish information for immediately preceding funding period.

Current and Pending Support

(See GPG Section II.D.8 for guidance on information to include on this form.)

The following information should be provided for each investigator and other senior personnel. Failure to provide this information may delay consideration of this proposal.

Other agencies (including NSF) to which this proposal has been/will be submitted. None

Investigator: Arkin, Adam

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support
Project/Proposal Title: Integrated Computational Biology of Stress Response in *D. radiodurans* and *B. subtilis*.
Source of Support: DOE
Total Award Amount: $250,000
Total Award Period Covered: 10/1/99-9/30/00
Location of Project: Lawrence Berkeley National Laboratory
Person-Months Per Year Committed to the Project. Cal: Acad: Sumr:

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support
Project/Proposal Title: Molecular Design Institute II: Construction of Genetic Circuitry in *Saccharomyces cerivisiae*
Source of Support: ONR
Total Award Amount: $ 100,000
Total Award Period Covered: 10/1/99-9/30/00
Location of Project: Lawrence Berkeley National Laboratory
Person-Months Per Year Committed to the Project. Cal: Acad: Sumr: 0.20

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support
Project/Proposal Title: Instant Cell Analysis, Bio/Spice, Cellular Devices and Exquisite Detection
Source of Support: ONR/DARPA
Total Award Amount: $251,069
Total Award Period Covered: 9/1/99-12/31/01
Location of Project: Lawrence Berkeley National Laboratory
Person-Months Per Year Committed to the Project. Cal: Acad: Sumr: 0.25

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support
Project/Proposal Title: Bio/Spice: A Tool for Integrated Cellular Bioinformatics and Dynamical Genomics
Computational Tool for Simulating Cellular Development and Genetic Pathways
Source of Support: DOE
Total Award Amount: $ 180,000
Total Award Period Covered: 10/1/99-9/30/00
Location of Project: Lawrence Berkeley National Laboratory
Person-Months Per Year Committed to the Project. Cal: Acad: Sumr: 0.25

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support
Project/Proposal Title: Interaction of Genome and Cellular Microenvironment: How One-Dimensional (Linear Sequence) Information is Selectively Utilized to make a Three-Dimensional (Complex) Tissue
Source of Support: DOE
Total Award Amount: $35,000 (of $771.5K total)
Total Award Period Covered: 10/1/99-9/30/00
Location of Project: Lawrence Berkeley National Laboratory
Person-Months Per Year Committed to the Project. Cal: Acad: Sumr: 0.05

Support:☐ Current ☒ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support
Project/Proposal Title: Biocomplexity: Complex and Orthogonal Control of Gene Expression – Engineering Model Systems for Industrial Application
Source of Support: NSF
Total Award Amount: 1,127,909
Total Award Period Covered: 9/1/00-8/31/03
Location of Project: Berkeley
Person-Months Per Year Committed to the Project. Cal: Acad: Sumr: 1.0

Support: ☐ Current ☒ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support
Project/Proposal Title: Engineering Analysis of a Genetic Switch
Source of Support: ONR
Total Award Amount: $ 225,466
Total Award Period Covered: 6/1/00-5/31/03
Location of Project: Berkeley
Person-Months Per Year Committed to the Project. Cal: Acad: Sumr: 0.20

Support: ☐ Current ☒ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support
Project/Proposal Title: Alliance for Cellular Signaling
Source of Support: NIH/Univ. of Southwestern Medical Center
Total Award Amount: $ 793,144
Total Award Period Covered: 9/1/00- 8/31/05
Location of Project: Berkeley
Person-Months Per Year Committed to the Project. Cal: Acad: Sumr: 0.15

Support: ☐ Current ☒ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support
Project/Proposal Title: Miniature bioprocess array: a platform for quantitative physiology
Source of Support: DARPA
Total Award Amount: $3,802,606
Total Award Period Covered: 7/1/00- 6/31/03
Location of Project: Berkeley
Person-Months Per Year Committed to the Project. Cal: Acad: Sumr: 0.15

Support: ☐ Current ☒ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support
Project/Proposal Title: High-Throughput Instrumentation for the Selection of Genomic Affinity Reagents and Predictive Informatics
Source of Support: DARPA
Total Award Amount: $787,000 (of ~$4,000,000)
Total Award Period Covered: 7/1/00- 6/20/05
Location of Project: Berkeley
Person-Months Per Year Committed to the Project. Cal: Acad: Sumr: 0.15

Support: ☐ Current ☒ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support
Project/Proposal Title: ITR/ACS: Software for Numerical Simulation of Microscale Biological Systems (Susan Graham, PI; Co-PIs: Adam Arkin, Paul Hilfinger, Dorian Liepmann, Katherine Yelick)
Source of Support: NSF
Total Award Amount: $4,999,971
Total Award Period Covered: 9/1/00 – 8/31/05
Location of Project: U.C. Berkeley
Person-Months Per Year Committed to the Project. Cal: Acad: Sumr: 1

Current and Pending Support

See GPG Section II.D.8 for guidance on information to include on this form.)

The following information should be provided for each investigator and other senior personnel. Failure to provide this information may delay consideration of this proposal.

Investigator: Paul Hilfinger	Other agencies (including NSF) to which this proposal has been/will be

Support: ☐ Current ☒ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: ITR/ACS: Software for Numerical Simulation of Microscale Biological Systems

(Susan Graham, PI; Co-PIs: Adam Arkin, Paul Hilfinger, Dorian Liepmann, Katherine Yelick)

Source of Support: NSF

Total Award Amount: $4,999,971 Total Award Period Covered: 9/1/00 – 8/31/05

Location of Project: U.C. Berkeley

Person-Months Per Year Committed to the Project. Cal: Acad: Sumr: 1.5

Support: ☐ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:

Source of Support:

Total Award Amount: Total Award Period Covered:

Location of Project:

Person-Months Per Year Committed to the Project. Cal: Acad: Sumr:

Support: ☐ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:

Source of Support:

Total Award Amount: Total Award Period Covered:

Location of Project:

Person-Months Per Year Committed to the Project. Cal: Acad: 0 Sumr:

Support: ☐ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:

Source of Support:

Total Award Amount: Total Award Period Covered:

Location of Project:

Person-Months Per Year Committed to the Project. Cal: Acad: 0 Sumr:

Support: ☐ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title

Source of Support:

Total Award Amount: Total Award Period Covered:

Location of Project:

Person-Months Per Year Committed to the Project. Cal: Acad: Sumr:

*If this project has previously been funded by another agency, please list and furnish information for immediately preceding funding period.

Current and Pending Support

See GPG Section II.D.8 for guidance on information to include on this form.)

The following information should be provided for each investigator and other senior personnel. Failure to provide this information may delay consideration of this proposal.

Investigator: Dorian Liepmann

Other agencies (including NSF) to which this proposal has been/will be submitted.

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: Integrated Microfluid Transport Fabrication Technologies

Source of Support: Becton Dickinson

Total Award Amount: $143,445 Total Award Period Covered: 1-Oct-1995 to 31-Dec-2000

Location of Project: U.C. Berkeley

Person-Months Per Year Committed to the Project. Cal: Acad: Sumr: 0

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: Concerning Mixed-Dimensional VLSI-Type Configurable Simulation Tools For Virtual Prototyping Of Bio-Mic

Source of Support: CFD Research Corporation

Total Award Amount: $285,000 Total Award Period Covered: 18-Jun-1998 to 17-Jun-2001

Location of Project: UC Berkeley

Person-Months Per Year Committed to the Project. Cal: Acad: Sumr: 0

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: MEMS Rotary Internal Combustion Engine

Source of Support: DARPA

Total Award Amount: $1,549,331 Total Award Period Covered: 29-Jun-1998 28-Jun-2001

Location of Project: UC Berkeley

Person-Months Per Year Committed to the Project. Cal: Acad: Sumr: 1

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: Micro-Cooler For Chip Level Temperature Control

Source of Support: DAF Wright-Patterson AFB

Total Award Amount: $ 350,000 Total Award Period Covered: 16-Sep-1997 to 15-Jan-2001

Location of Project: UC Berkeley

Person-Months Per Year Committed to the Project. Cal: Acad: Sumr:

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title Mixing and Processing of Complex Biological Fluids in Micro Flumes

Source of Support: DARPA

Total Award Amount: 1,273,060 Total Award Period Covered: 16-Sep-1998 to 15-Jan-2002

Location of Project: UC Berkeley

Person-Months Per Year Committed to the Project. Cal: Acad: Sumr: 1

*If this project has previously been funded by another agency, please list and furnish information for immediately preceding funding period.

Current and Pending Support

See GPG Section II.D.8 for guidance on information to include on this form.)

The following information should be provided for each investigator and other senior personnel. Failure to provide this information may delay consideration of this proposal.

Investigator: Dorian Liepmann

Other agencies (including NSF) to which this proposal has been/will be

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: Integrated MEMS Delivery System for both Liquid and Reconstituted Drugs

Source of Support: : DARPA

Total Award Amount: $1,222,000 Total Award Period Covered: 3-Apr-1997 to 2-Apr-2000 (expecting no-cost extension)

Location of Project: U.C. Berkeley

Person-Months Per Year Committed to the Project. Cal: Acad: Sumr: 0

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: Integrated Micro-Cooler Module for High Thermal Flux Removal

Source of Support: DARPA

Total Award Amount: $ 3,022,532 Total Award Period Covered: 7-May-1999 to 6-May-2002

Location of Project: UC Berkeley

Person-Months Per Year Committed to the Project. Cal: Acad: Sumr: 1

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: Integrated mFLUME Reconstitution System for Biological and Medical Supplies

Source of Support: DARPA/ETO

Total Award Amount: $1,222,000 Total Award Period Covered: 4/97 – 3/00

Location of Project: UC Berkeley

Person-Months Per Year Committed to the Project. Cal: Acad: Sumr:

Support: ☐ Current ☒ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: Bio-Fluidic Chips

Source of Support: DARPA

Total Award Amount: $2,271,930 Total Award Period Covered: 4/1/00 – 3/31/03

Location of Project: UC Berkeley

Person-Months Per Year Committed to the Project. Cal: Acad: Sumr: 1

Support: ☐ Current ☒ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: ITR/ACS: Software for Numerical Simulation of Microscale Biological Systems

(Susan Graham, PI; Adam Arkin, Paul Hilfinger, Dorian Liepmann, Katherine Yelick, Co-PIs)

Source of Support: NSF

Total Award Amount: $4,999,971 Total Award Period Covered: 9/1/00 – 8/31/05

Location of Project: UC Berkeley

Person-Months Per Year Committed to the Project. Cal: Acad: Sumr: 1

*If this project has previously been funded by another agency, please list and furnish information for immediately preceding funding period.

Current and Pending Support

The following information should be provided for each investigator and other senior personnel. Failure to provide this information may delay consideration of this proposal.

Investigator: Katherine Yelick

Other agencies to which this proposal has been/will be submitted.

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support
Project/Proposal Title: Young Investigator Program

Source of Support: ARO
Total Award Amount: $ 150,000 Total Award Period Covered: 6/1/96 - 5/31/00 (no-cost extension)
Location of Project: U.C. Berkeley
Person-Months Per Year Committed to the Project. Cal: Acad: Sumr: 0

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support
Project/Proposal Title: Automated Perturbation Theory for Hamiltonian Systems

Source of Support: NSF
Total Award Amount: $ 97,230 Total Award Period Covered: 9/1/97 - 8/31/00 (no cost extension)
Location of Project: U.C. Berkeley
Person-Months Per Year Committed to the Project. Cal: Acad: Sumr: 0

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support
Project/Proposal Title: Bridging the Processor-Memory Gap (David Patterson, PI)

Source of Support: California State MICRO 99-094
Total Award Amount: $126,096 Total Award Period Covered: 7/1/99-12/31/00
Location of Project: U.C. Berkeley
Person-Months Per Year Committed to the Project. Cal: Acad: 0 Sumr: 0

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support
Project/Proposal Title: Intelligent DRAM (IRAM)
(David Patterson, PI; Katherine Yelick, co-PI; Tom Anderson, co-PI)

Source of Support: DARPA
Total Award Amount: $5,707,616 Total Award Period Covered: 7/1/96 – 3/31/01
Location of Project: U.C. Berkeley
Person-Months Per Year Committed to the Project. Cal: Acad: Sumr: 1.89

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support
Project/Proposal Title: National Partnership for Advanced Computational Infrastructure (NPACI) (Susan L. Graham, PI, James Demmel, co-PI, David Culler, co-PI; supports research of 11 faculty)

Source of Support: UCSD/NSF
Total Award Amount: $3,830,525 Total Award Period Covered: 10/1/97- 9/30/2002
Location of Project: U.C. Berkeley
Person-Months Per Year Committed to the Project. Cal: Acad: Sumr: .5

*If this project has previously been funded by another agency, please list and furnish information for immediately preceding funding period.

USE ADDITIONAL SHEETS AS NECESSARY

Current and Pending Support

The following information should be provided for each investigator and other senior personnel. Failure to provide this information may delay consideration of this proposal.

Investigator: Katherine Yelick	Other agencies to which this proposal has been/will be submitted.

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: AASERT: System Support for Unstructured Meshes on Clusters of SMPs

Source of Support: ARO

Total Award Amount: $104,000 Total Award Period Covered: 4/1/98 – 3/31/01 (no-cost extension)

Location of Project: U.C. Berkeley

Person-Months Per Year Committed to the Project. Cal: Acad: Sumr:

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: Tools for Scalable High Performance Computing
(James Demmel, PI; David Culler and Katherine Yelick, co-PIs)

Source of Support: LLNL/DOE

Total Award Amount: $969,124 Total Award Period Covered: 4/1/99 – 3/31/02

Location of Project: U.C. Berkeley

Person-Months Per Year Committed to the Project. Cal: Acad: Sumr: 0

Support: ☐ Current ☒ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: Bridging the Processor Memory Gap
(David Patterson, Katherine Yelick,

Source of Support California State MICRO

Total Award Amount: $ 71,739 Total Award Period Covered: 7/1/00 – 6/30/01

Location of Project: U.C. Berkeley

Person-Months Per Year Committed to the Project. Cal: Acad: Sumr: 1

Support: ☐ Current ☒ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: ITR/ACS: Automatic Performance Tuning of Numerical Kernels
(Katherine Yelick, PI, James Demmel, co-PI)

Source of Support: NSF

Total Award Amount: $497,739 Total Award Period Covered: 9/1/00 – 8/31/03

Location of Project: U.C. Berkeley

Person-Months Per Year Committed to the Project. Cal: Acad: Sumr: .5

Support: ☐ Current ☒ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: ITR/SII: Taming the Data Flood: Systems that Evolve, are Available, and Maintainable
(David Patterson, PI; Katherine Yelick, John Kubiatowicz, Co-PIs; includes subcontract to Mills College)

Source of Support: NSF

Total Award Amount: $2,993,827 Total Award Period Covered: 9/01/00-8/31/03

Location of Project: U.C. Berkeley

Person-Months Per Year Committed to the Project. Cal: Acad: 0 Sumr: 1.5

*If this project has previously been funded by another agency, please list and furnish information for immediately preceding funding period.

USE ADDITIONAL SHEETS AS NECESSARY

Current and Pending Support

The following information should be provided for each investigator and other senior personnel. Failure to provide this information may delay consideration of this proposal.

Investigator: Katherine Yelick

Other agencies to which this proposal has been/will be submitted.

Support: ☐ Current ☒ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: ITR/ACS: Software for Numerical Simulation of Microscale Biological Systems (Susan Graham, PI; Co-PIs: Adam Arkin, Paul Hilfinger, Dorian Liepmann, Katherine Yelick)

Source of Support: NSF

Total Award Amount: $4,999,971 Total Award Period Covered: 9/1/00 – 8/31/05

Location of Project: U.C. Berkeley

Person-Months Per Year Committed to the Project. Cal: Acad: Sumr: 1.5

Support: ☐ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:

Source of Support:

Total Award Amount: Total Award Period Covered:

Location of Project:

Person-Months Per Year Committed to the Project. Cal: Acad: Sumr:

Support: ☐ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:

Source of Support:

Total Award Amount: Total Award Period Covered:

Location of Project:

Person-Months Per Year Committed to the Project. Cal: Acad: Sumr:

Support: ☐ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:

Source of Support:

Total Award Amount: Total Award Period Covered:

Location of Project:

Person-Months Per Year Committed to the Project. Cal: Acad: Sumr:

Support: ☐ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:

Source of Support:

Total Award Amount Total Award Period Covered:

Location of Project:

Person-Months Per Year Committed to the Project. Cal: Acad: Sumr:

*If this project has previously been funded by another agency, please list and furnish information for immediately preceding funding period.

USE ADDITIONAL SHEETS AS NECESSARY

Current and Pending Support

See GPG Section II.D.8 for guidance on information to include on this form.)

The following information should be provided for each investigator and other senior personnel. Failure to provide this information may delay consideration of this proposal.

Investigator: Phillip Colella

Other agencies (including NSF) to which this proposal has been/will be

Support: ☐ Current ☒ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: ITR/ACS: Software for Numerical Simulation of Microscale Biological Systems

(Susan Graham, PI; Co-PIs: Adam Arkin, Paul Hilfinger, Dorian Liepmann, Katherine Yelick)

Source of Support: NSF

Total Award Amount: $4,999,971 Total Award Period Covered: 9/1/00 – 8/31/05

Location of Project: U.C. Berkeley

Person-Months Per Year Committed to the Project. Cal: Acad: Sumr: 0

Support: ☐ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:

Source of Support:

Total Award Amount: Total Award Period Covered:

Location of Project:

Person-Months Per Year Committed to the Project. Cal: Acad: Sumr:

Support: ☐ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:

Source of Support:

Total Award Amount: Total Award Period Covered:

Location of Project:

Person-Months Per Year Committed to the Project. Cal: Acad: 0 Sumr:

Support: ☐ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:

Source of Support:

Total Award Amount: Total Award Period Covered:

Location of Project:

Person-Months Per Year Committed to the Project. Cal: Acad: 0 Sumr:

Support: ☐ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title

Source of Support:

Total Award Amount: Total Award Period Covered:

Location of Project:

Person-Months Per Year Committed to the Project. Cal: Acad: Sumr:

*If this project has previously been funded by another agency, please list and furnish information for immediately preceding funding period.

Current and Pending Support

(See GPG Section II.D.8 for guidance on information to include on this form.)

The following information should be provided for each investigator and other senior personnel. Failure to provide this information may delay consideration of this proposal.

Investigator: Oliver O'Reilly

Other agencies (including NSF) to which this proposal has been/will be submit-
None

Support: ☐ Current ☒ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: Mechanics of Contact with Application to Brake Squeal and Axially Moving Media

(This proposal, shared with one other co-investigator)

Source of Support: NSF

Total Award Amount: $168,896 Total Award Period Covered: 9/01/00 – 8/31/03

Location of Project: University of California, Berkeley

Person-Months Per Year Committed to the Project. Cal: Acad: Sumr: .50

Support: ☐ Current ☒ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: ITR/ACS: Software for Numerical Simulation of Microscale Biological Systems (Susan Graham, PI; Co-PIs: Adam Arkin, Paul Hilfinger, Dorian Liepmann, Katherine Yelick)

Source of Support: NSF

Total Award Amount: $4,999,971 Total Award Period Covered: 9/1/00 – 8/31/05

Location of Project: University of California, Berkeley

Person-Months Per Year Committed to the Project. Cal: Acad: Sumr: 1

Support: ☐ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:

Source of Support:

Total Award Amount: $ Total Award Period Covered:

Location of Project: University of California, Berkeley

Person-Months Per Year Committed to the Project. Cal: Acad: Sumr:

Support: ☐ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:

Source of Support:

Total Award Amount: $ Total Award Period Covered:

Location of Project:

Person-Months Per Year Committed to the Project. Cal: Acad: Sumr:

Support: ☐ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:

Source of Support:

Total Award Amount: $ Total Award Period Covered:

Location of Project:

Person-Months Per Year Committed to the Project. Cal: Acad: Sumr: none

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*If this project has previously been funded by another agency, please list and furnish information for immediately preceding funding period.

Susan Graham, PI
University of California, Berkeley
NSF – Information Technology Research (ITR)
1/1/99 – 12/31/05

"ITR/ACS: Software for Numerical Simulation of Microscale Biological Systems"

(H) Facilities, Equipment, and Other Resources

The researchers on this project will use state of the art workstations (primarily PCs and Sparcs) for day-to-day development activities. Larger-scale computation will be done on a variety of high-performance computing systems. The workstations used by the computer scientists are connected to the major 100 Mbit networking infrastructure housed in various machine rooms in the Computer Science building, Soda Hall. The facilities used by the biological modelers are similar, but are more geographically dispersed; much of the numerical methods computing will be carried out at the Lawrence Berkeley Laboratory facilities. In all cases, researchers rely on department-wide services including system administration services, backup services, and software support services.

U.C. Berkeley houses the Millennium machine, a campus-wide computing facility for the support of simulation activities in several departments. The core consists of 8 departmental SMP clusters of 16-20 processors each, connected over a high-speed network to one another and to a central cluster of several hundred processors, which is currently under construction. The Millennium infrastructure was paid for by an Intel donation of $6M of equipment, with additional support of approximately equal dollar value from NSF, IBM, Microsoft, SMCC, Nortel, and the campus. The Millennium system will be available for use on this project. Through their appointments at NERSC/LBNL, Professors Graham, Yelick, and Arkin, and Dr. Colella will have access to high performance computing at NERSC. Through their involvement in the NPACI partnership, they will have access to high-performance machines at the San Diego Supercomputer Center. The latter sources computer time are in addition to those obtained through national allocation programs, and letters of collaboration are attached in the Supplemental Documents section.

Faculty on this project will use their current office space, and office space for graduate and undergraduate students and post-doctoral researchers will be provided. The research administration staff will use existing current office space. Office space will be available at LBNL for project participants from the Laboratory.

CERTIFICATION PAGE

Certification for Principal Investigators and Co-Principal Investigators:

I certify to the best of my knowledge that:

(1) the statements herein (excluding scientific hypotheses and scientific opinions) are true and complete, and
(2) the text and graphics herein as well as any accompanying publications or other documents, unless otherwise indicated, are the original work of the signatories or individuals working under their supervision. I agree to accept responsibility for the scientific conduct of the project and to provide the required progress reports if an award is made as a result of this application.

I understand that the willful provision of false information or concealing a material fact in this proposal or any other communication submitted to NSF is a criminal offense (U.S.Code, Title 18, Section 1001).

Name (Typed)	Signature	Social Security No.*	Date
PI/PD **Susan L Graham**	Susan L Graham	SSNs are confidential and are not displayed *ON FASTLANE SUBMISSIONS*	4-10-00
Co-PI/PD **Adam Arkin**			4/4/00
Co-PI/PD **Paul N Hilfinger**			4/10/00
Co-PI/PD **Dorian Liepmann**			4/9/00
Co-PI/PD **Katherine A Yelick**			4-12-00

Certification for Authorized Organizational Representative or Individual Applicant:

By signing and submitting this proposal, the individual applicant or the authorized official of the applicant institution is: (1) certifying that statements made herein are true and complete to the best of his/her knowledge; and (2) agreeing to accept the obligation to comply with NSF award terms and conditions if an award is made as a result of this application. Further, the applicant is hereby providing certifications regarding Federal debt status, debarment and suspension, drug-free workplace, and lobbying activities (see below), as set forth in Grant Proposal Guide (GPG), NSF 00-2. Willful provision of false information in this application and its supporting documents or in reports required under an ensuring award is a criminal offense (U. S. Code, Title 18, Section 1001).

In addition, if the applicant institution employs more than fifty persons, the authorized official of the applicant institution is certifying that the institution has implemented a written and enforced conflict of interest policy that is consistent with the provisions of Grant Policy Manual Section 510; that to the best of his/her knowledge, all financial disclosures required by that conflict of interest policy have been made; and that all identified conflicts of interest will have been satisfactorily managed, reduced or eliminated prior to the institution's expenditure of any funds under the award, in accordance with the institution's conflict of interest policy. Conflict which cannot be satisfactorily managed, reduced or eliminated must be disclosed to NSF.

Debt and Debarment Certifications

(If answer "yes" to either, please provide explanation.)

Is the organization delinquent on any Federal debt? Yes ☐ No ☒

Is the organization or its principals presently debarred, suspended, proposed for debarment, declared ineligible, or voluntarily excluded from covered transactions by any Federal department or agency? Yes ☐ No ☒

Certification Regarding Lobbying

This certification is required for an award of a Federal contract, grant, or cooperative agreement exceeding $100,000 and for an award of a Federal loan or a commitment providing for the United States to insure or guarantee a loan exceeding $150,000.

Certification for Contracts, Grants, Loans and Cooperative Agreements

The undersigned certifies, to the best of his or her knowledge and belief, that:

(1) No federal appropriated funds have been paid or will be paid, by or on behalf of the undersigned, to any person for influencing or attempting to influence an officer or employee of any agency, a Member of Congress, an officer or employee of Congress, or an employee of a Member of Congress in connection with the awarding of any federal contract, the making of any Federal grant, the making of any Federal loan, the entering into of any cooperative agreement, and the extension, continuation, renewal, amendment, or modification of any Federal contract, grant, loan, or cooperative agreement.

(2) If any funds other than Federal appropriated funds have been paid or will be paid to any person for influencing or attempting to influence an officer or employee of any agency, a Member of Congress, an officer or employee of Congress, or an employee of a Member of Congress in connection with this Federal contract, grant, loan, or cooperative agreement, the undersigned shall complete and submit Standard Form-LLL, "Disclosure Form to Report Lobbying," in accordance with its instructions.

(3) The undersigned shall require that the language of this certification be included in the award documents for all subawards at all tiers including subcontracts, subgrants, and contracts under grants, loans, and cooperative agreements and that all subrecipients shall certify and disclose accordingly.

This certification is a material representation of fact upon which reliance was placed when this transaction was made or entered into. Submission of this certification is a prerequisite for making or entering into this transaction imposed by section 1352, title 31, U.S. Code. Any person who fails to file the required certification shall be subject to a civil penalty of not less than $10,000 and not more than $100,000 for each such failure.

AUTHORIZED ORGANIZATIONAL REPRESENTATIVE	SIGNATURE	DATE
NAME/TITLE (TYPED) **Jyl Baldwin** For	C-T.	**04/10/00**

TELEPHONE NUMBER	ELECTRONIC MAIL ADDRESS	FAX NUMBER
510-642-8114	**jbaldwin@uclink.berkeley.edu**	**510-642-8236**

*SUBMISSION OF SOCIAL SECURITY NUMBERS IS VOLUNTARY AND WILL NOT AFFECT THE ORGANIZATION'S ELIGIBILITY FOR AN AWARD. HOWEVER, THEY ARE AN INTEGRAL PART OF THE INFORMATION SYSTEM AND ASSIST IN PROCESSING THE PROPOSAL. SSN SOLICITED UNDER NSF ACT OF 1950, AS AMENDED.

April 10, 2000

Professor Susan Graham
EECS/Computer Science
University of California Berkeley
771 Soda
Berkeley, CA 94720-1776

RE: Support for the NSF Proposal, "Software for Numerical Simulation of Microscale Biological Systems"

Dear Professor Graham,

On behalf of the National Energy Research Supercomputing Center at the Lawrence Berkeley National Laboratory, I am writing to support your effort at developing a set of software tools to simulate fundamental biological processes at the cellular level. The proposed activities resonate well with computational science research that has been supported for some time at NERSC.

NERSC / LBNL will continue to provide salary and facilities support to Dr. Phillip Colella and other scientific and technical staff who currently carry out research in numerical PDE's being leveraged by this proposal. Researchers directly affiliated with this proposal will also have access to NERSC's general computational and data storage facilities as well as its dedicated visualization capabilities based on the LBNL special allocation process at NERSC. I would also encourage you beyond that to take advantage of the general allocation process at NERSC, which is open to all researchers with projects of relevance to the DOE mission.

This project is particularly appropriate for the support of NERSC and LBNL. The principal investigators include three faculty staff (yourself, Professor Adam Arkin, and Professor Katherine Yelick) who hold joint appointments with LBNL. In addition, it touches on a number of research areas that are central to LBNL core research efforts, both in the biological sciences and in high-end computing. I wholeheartedly endorse the research goals of your proposal, and I am looking forward to the prospect of expanding our collaboration through this project.

Sincerely,

Dr. Horst D. Simon
Director, National Energy Research Scientific Computing (NERSC) Center
Lawrence Berkeley National Laboratory
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April 11, 2000

Professor Adam P. Arkin
Division of Physical Biosciences
Lawrence Berkeley National Laboratory
Berkeley, CA 94720

Dear Adam:

The project you described to me, "Software for Numerical Simulation of Microscale Biological Systems," seems ambitious but it promises to be of great value to biological research. The regulation of central cellular systems such as signal transduction, chemotatic behavior, and development involve processes that span many tens and hundreds of molecules and possibly thousands of reactions. These processes are spatially localized or disperse, and are coupled to the mechanical properties of the cell and its environment, which, in turn, feeds back on the chemistry.

The ability of our laboratory, in collaboration with others, to generate data on these processes has begun to outstrip our ability to systematize it all, bring this data into self-consistency and form a picture of why these biological networks work so well, when they fail, and how we can control them. This will only get worse as large collaborative data collection efforts such as the Alliance for Cellular Signalling (http://afcs.swmed.edu/) start to take off and gigabytes of information about a particular system (B-cell and cardiomyocyte chemotaxis) are generated per year. I believe it will be very helpful to have the ability to build dynamical models based on this data and be able to generate and test complex hypotheses about the microscopic biochemical and genetic chemistry leads to macroscopic physiological and cell biological behavior. It is clear that the technology to do this does not yet exist.

The problems you are addressing in the project you described are exactly those that need to be solved for such a simulation program to be useful. I know that much data analysis and experiment must be performed before such models become maximally useful, but I want to put my strong support forward for this project. It is only by starting now that experiment and theory can grow together, each motivating the other to address mutual problems. I see your project as an excellent start to this interaction and I look forward one day even working with the tools your team is developing.

Yours sincerely,

Henry R. Bourne

UNIVERSITY OF CALIFORNIA, SAN DIEGO UCSD

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April 7, 2000

Dr. Susan Graham
Computer Science Division - EECS
776 Soda Hall #1776
University of California
Berkeley, CA 94720-1776

Dear Susan:

As the director of both the San Diego Supercomputer Center and the National Partnership for Advanced Computational Infrastructure (NPACI), I am extremely pleased to write this letter of support for your proposal "Software for Numerical Simulation of Microscale Biological Systems" submitted to NSF's Information Technology Research Program.

You, as NPACI Chief Computer Scientist, and I have worked together over the past several years to plan and implement the partnership. I respect your expertise and commitment greatly, and I believe both have been critical to NPACI's success.

Your proposed work is extremely relevant to enhancing the usefulness of large-scale compute resources, such as those at SDSC. More specifically, your goals to develop new algorithmic and software techniques emphasizing ease of programming and high performance on modern cluster-based architectures dovetail exactly with SDSC's need to enable the most effective use of our cluster-based IBM system, the most powerful supercomputer available for academic research in the U.S.

Furthermore, your work, with its focus on linking the molecular and cellular scales, will be an important step in developing new software approaches that link models across a range of time and space scales to enable more comprehensive, realistic modeling. This is a goal shared by the four NPACI applications thrust areas—Molecular Science, Neuroscience, Earth Systems Science, and Engineering.

The proposed work, of course, will build on your prior Titanium development done in collaboration with professors Katherine Yelick and Phil Colella and ongoing work in the NPACI Programming Tools and Environments thrust area. In particular, it will build on a recently approved "alpha" project led by Yelick. Such projects, because they integrate multiple smaller projects and offer the potential to benefit a variety of disciplines, receive greater NPACI support and management attention to ensure their success.

In short, your work will benefit users of high-end compute systems, leverage NPACI goals and software development, and, in the application you've chosen, help increase our understanding of the mechanisms of disease.

Enthusiastically,

Sid Karin