Research Projects on Hydra

Multiscale Molecular Dynamics and its Applications in Nano–Fluid Dynamics and Computer–Assisted Drug Design

Qun Ma

Molecular dynamics (MD) solves a system of ordinary differential equations governing the motion of the particles (atoms) in a system [2]. MD is very useful in many applications. In a biomolecular system such as solvated proteins, for example, one can use MD to study the coordinated motion of the side chains, the closing and opening of certain binding domains, the diffusion of small molecules inside the channels within the proteins, or the interaction of ligand (drug) molecules and proteins [12, 29]. These studies are crucial in providing deep insights on a molecular level as to why certain molecules are useful for regulating protein function, thereby acting as an effective drug. In a fluid system, one can use MD to study the dynamics of the fluid on a nanoscale, helping to elucidate, say, heat and mass transfer [11]. Time stepping algorithms are at the heart of molecular dynamics simulations. Even a modest improvement in time stepping algorithms will result in significant reduction in turnaround time since most MD simulations of real biological systems take days or even months to finish. A closely related technique is called coarsening. Coarsening aims at speeding up simulations by using a coarsened representation of the system, allowing a reasonable compromise between fidelity and speed.

Nano-devices refer to systems that have characteristic length of less than 1 micron. Understanding the unconventional physics involved in the operation of such minute devices is critical for the advancement of nano-technology. Unfortunately, fluid flows in such devices cannot be reliably predicted by conventional continuum models such as Navier-Stokes (NS) equations with no-slip boundary condition. Further complicating matters, molecular scale numerical computations of an entire fluid system using an all-atom MD approach are prohibitively expensive. However, an exciting new approach has been proposed recently which uses a hybrid scheme to study the fluids in nano-devices, i.e., the slip boundary layer is resolved using atomic level resolution MD simulations, whereas the bulk of fluid is modeled using the N-S equations [11]. This new approach retains many of the desirable features of the two disparate approaches, MD and continuum models, while overcoming the overwhelming computational expense of a full MD simulation. Nevertheless, the main difficulty with applying this hybrid scheme to study the dynamics of fluids in nano-devices is still the relative inefficiency of the molecular dynamics component.

Another exciting application of multiscale MD is in computer–assisted drug design. Medically active drugs typically incorporate small molecules (ligands) that bind to target protein(s) or DNA as tightly as possible. A tight binding leads to a more effective conformational change of the target protein or DNA. This is referred to as binding affinity. For example, in the treatment of breast cancer, the Tomaxifen or Raloxifen molecule binds to the estrogen receptor (ER) tightly so that estrogen molecules can no longer bind to ER, thus preventing cancer cells from proliferating. There may be hundreds or even thousands of candidates for such a drug, however, the binding affinity can only be computed reliably by efficient sampling using very long MD simulations [57].

The investigator plans to continue his research program developing more efficient time stepping algorithms for MD and novel multiscale modeling approaches. These will be applied to two specific problems: modeling the the slip boundary condition in nano-fluid dynamics (for which the proposer

will also develop effective and efficient interfacing techniques), as well as obtaining binding affinity predictions in computer–assisted drug design. Part of the latter study includes developing effective and efficient coarsening techniques for biological systems. This plan builds on a base of prior research in time stepping algorithm development for multiscale molecular modeling and molecular dynamics [36, 34, 24, 37, 33, 35]. The deliverables of this research will include more advanced algorithmic techniques for multiscale molecular modeling and software and toolkits developed for employing these new techniques.

Evaluation of novel molecular dynamics algorithms is very compute-intensive, especially when the dimension of the system becomes large, which is the case for the simulation of the boundary layer in nano-fluidic systems. A MD simulation of a medium size system on a modern workstation usually runs for days only to achieve a simulated time scale of a few nanoseconds. Parallel computing is sorely needed to help this research, which partially justifies the need for the computer cluster we are proposing. Excellent parallel MD codes exist, such as NAMD developed at the University of Illinois at Urbana-Champaign [26], and ProtoMol developed with the aid of the proposer at the University of Notre Dame [37, 38]. NAMD is the best scalable parallel MD code existing today, whereas ProtoMol is easily extensible due to its modular design. Both codes runs efficiently in a parallel environment such as the Linux cluster we are proposing. In the proposed study, we will use both codes for algorithms development and verification.

Computations and Processing by the Visual Cortical Neuronal Network

Louis Tao

The primary visual cortex (V1) is the first area along the visual pathway where individual neurons are sensitive to elementary features of the visual scene (for instance, a pattern's orientation or its spatial location). Selectivity is revealed in electrode measurements of activity in individual neurons: An anesthetized animal is shown a simple visual pattern, such as a bar or a grating, and the dependence on the pattern's orientation (or location, contrast, size, etc.) is measured. Individual V1 neurons show *preference*, in terms of higher firing rates, to certain orientations. It is properties similar to this "orientation selectivity" that likely underly important higher-level processing such as "contour completion" and "edge detection". V1 computes within a complex architecture that is characterized by a layered structure, with intralayer connections locally isotropic [15, 32, 9, 8] while specific feedforward and feedback pathways run between layers. The network activity of feature selectivity is likewise complex and spans multiple space- and time-scales. While the precise mechanisms underlying the basis of visual perception are beginning to be understood, some of these same mechanisms are likely to be operating in any computation involving pattern detection and recognition.

Despite much research, there does not yet exist a comprehensive mathematical model that accounts for the observed selectivity and the response diversity of V1, while remaining consistent with known anatomical and physiological studies. However, because of recent developments [49, 53, 1, 39, 55], the proposer believes that a detailed model is emerging and that the understanding and mathematical description of some of V1's elementary functions now appear to be within reach. Recently, the investigator and collaborators have developed a numerical model of the primary input layer (4Cα) of macaque V1. This model consisted of a large number ($> 16,000$) of coupled excitatory and inhibitory integrate-and-fire (I&F) point neurons representing a small, $1mm^2$ cortical area. The model cortex rationalized many aspects of the available experimental data and led to distinctive predictions of population response measures [51] with the qualitative structure seen in recent experimental measurements [46].

Analytical studies and numerical simulations of neuronal networks help form the basis for our current theoretical understanding of the properties of large, interacting neuronal systems. Issues include the stability of these dynamical systems and the dependencies of the system dynamics on the synaptic couplings. A major challenge is to develop reduced descriptions to simulate and understand the larger, multi-layered models. Using a kinetic theory approach, we have been developing, in several directions, a coarse-grained description of neuronal network dynamics that is effective and efficient for representing the firing rates of a neuronal population that is sufficiently small so that the cortical architecture does not change appreciably across it, and yet sufficiently large to contain hundreds of neurons [7].

A typical simulation of $1mm^2$ of layer 4Cα with $16,000$ neurons responding to 60 seconds of a visual pattern takes over a day on a single processor on the fastest currently available workstation. While a parallel implementation will reduce simulation time, to understand the functional consequences of the complex architecture of V1 requires a major extension of the local patch model. In the current model neurons in $1mm^2$ "see" less than 1° of visual space (1° is about the size of a dime held at an arm's length). To capture interesting cortical processing such as "edge detection" and "contour completion", we must consider a much larger region of cortex, include longer range ($> 1mm$) interactions, involve non-local anisotropic connections, and increase the number of

model layers. A realistic model requires at least three layers: an input layer (4Cα), an output layer (4B) and a feedback layer (6). The computational requirements then increase 100-fold, which goes beyond current capabilities, but which is within reach of the proposed parallel cluster. With the further development of coarse-grained representations, new numerical methods, and the access to a state-of-the-art computing cluster, simulation of an extended cortical model is within reach.

Dynamics of dense granular materials

Lou Kondic

Collective systems that are far from equilibrium present some of the most important challenges within statistical physics. One of the most intensively scrutinized systems at the current time is that of granular materials. On the one hand, these materials—collections of particles interacting via classical mechanics— bear a great resemblance to non-quantum molecular systems. For instance, they exhibit fluctuations and random behavior that is highly suggestive of classical thermal systems. On the other hand, granular interactions are dissipative due to friction and to collisional (restitutional) energy losses. In order to sustain any state other than a totally static situation, there must be a continuous input of energy. Thus, despite a strong resemblance to molecular systems, granular materials are always out of equilibrium in any dynamical state.

Substantial progress in understanding of granular systems has been reached for systems that are sufficiently dilute and energetic that all interactions can be characterized by binary short-lived collisions [25, 47]. However, for dense granular systems, this assumption does not apply and there is still no generally accepted theory. One particular characteristic of granular systems, *jamming*, introduces additional complications, because of nonuniform (in space and time) system response to external driving [30]. Jamming occurs not not only in granular systems, but also in sheared foams [13, 28] and colloidal suspensions [10, 31]. Moreover, it appears to be closely related to the glass transition in supercooled liquids [19]. Although these systems are significantly different from the granular ones, the numerous similarities offer a tantalizing possibility that all of these systems could be explained by extensions of the same (still unknown) underlying theory.

The proposer has already performed extensive simulations of various granular systems [27, 40, 52]. These are so-called soft sphere simulations which have a potential to realistically describe contact dynamics between granular particles. These simulations effectively integrate through the collision process, and therefore require rather short time steps. Additional simulations are currently being performed under the investigators guidance by a postdoctoral associate at NJIT, Oleh Baran (supported by NASA).

The proposed research involves developing and performing large scale discrete element simulations of sheared granular systems. This project will be carried out in close collaboration with the experimental efforts at Duke University, under the guidance of Robert P. Behringer. The simulations will also serve as a guidance for the flight experiment of sheared granular systems in zero gravity, which is planned to be performed at Space Station during 2008 (supported by NASA).

The simulations will concentrate on 3D sheared granular system in a Couette geometry. An experiment in 2D [22] has recovered the phase transition as the volume fraction of a granular sample is increased. The main issue which will be addressed in the proposed simulations is to obtain an understanding of the phase transition in 3D systems, with and without gravity. These simulations will help us understand the flow properties of sheared granular systems (in particular, shear-banding) and identify the spatial and temporal characteristics of the stress distribution in granular systems close to jamming. Additionally, this work will lead to better insight into statistical properties of granular systems, including computational verification of a newly proposed statistical theory of granular matter [14] The simulations will also provide significant guidance to the experiments currently being performed at Duke.

Behringer's experiments, as well as the proposed space experiments, utilize a large number of particles, on the order of $10^6 - 10^7$. The simulations currently being performed at NJIT use up to 10^4

particles. While these simulations already provide a significant insight into the granular sample, it is necessary to increase the number of particles in the simulations in order to (i) improve the statistics of the obtained results; (ii) understand more precisely the influence of various system parameters, such as frictional properties of the physical boundaries; (iii) understand the scaling properties of the granular systems; and (iv) analyze the features, such as force chains, that propagate throughout the granular sample.

The current simulations are being performed in a serial mode, and individual runs in parameter studies use up to a day of computing time. We expect that an improvement of our computational methods and the increased speed and memory of the proposed state-of-the-art multi-processor machine will allow us to increase the number of particles by an order of magnitude. Further increases in the size of the system are expected to require development of the parallel version of our computational routines. Discrete element simulations naturally scale with the size of the system, and a significant increase in the speed of computations can be reached by performing simulations in a parallel computing environment. This particular aspect of the proposed research is expected to be performed as a part of research training of a graduate student, which would lead to research results appropriate for a PhD dissertation. For this purpose, it will be very useful to have available (parallelizable) computational resources DMS. A cluster with a large number of CPU's will be the most appropriate for this kind of computations.

Mesoscopic Simulation for Surface Processes

David Horntrop

Surface processes are multiscale problems in which proper incorporation of small scale behavior is essential to understand large scale phenomena. The main approaches traditionally used to study surface processes have included a macroscopic approach and a microscopic or molecular approach. The macroscopic approach typically involves partial differential equations and does not incorporate interactions at the molecular level in a direct fashion. On the other hand, the microscopic approach directly models the molecular interaction by considering individual molecules. A typical numerical study based on such micromechanisms follows many particles undergoing such processes and is referred to as a molecular dynamics or Monte Carlo simulation. Not surprisingly, these calculations are quite demanding of computer resources for systems with large numbers of particles for which long time results are needed.

The approach here is to use mesoscopic (or local mean field) models to bridge the gap between scales. Mesoscopic models lie between microscopic models and macroscopic models while incorporating many features of both of these approaches. Mesoscopic models can be derived through a coarse graining of the underlying microscopic system in a rigorous fashion in which the effect of small scale phenomena is described as stochastic forcing on larger scales. These stochastic terms naturally arise and are derived without the introduction of any artificial cutoffs. A typical mesoscopic model equation is a stochastic partial integrodifferential equation which incorporates the (potentially long range) molecular interactions explicitly through convolutions.

One important surface process which can be modeled mesoscopically is colloidal gold labeling of proteins in a biomaterial. A knowledge of both the location and pattern of proteins is very important in many biological applications including the development of biomaterials which are compatible with blood and the determination of the structure of subcellular components and organelles [3-4]. In colloidal gold labeling, a suspension of colloidal gold particles covered with ligands that bind only to the desired protein receptor sites is placed above the biomaterial to be labeled. The system is allowed to equilibrate thus "staining" the locations of the protein on the surface. The attachment of the gold particle to the protein on the surface is an adsorption process which occurs rapidly. However, the presence of a gold particle above a given location of the biomaterial surface depends on the much longer time scale of transport within the suspension. A quantity of importance to biophysicists which can be determined from the time evolution of the model is the time required for complete staining of the surface. Other important issues to understand include the selection of a flow in the colloidal suspension and other physical parameters such as the concentration and size of the gold particles in the suspension so as to minimize the amount of time required to stain the biomaterial.

Colloidal gold labeling of proteins is an ideal problem in which to use mesoscopic models due to the relatively simple molecular behavior at the surface of the biomaterial; this equation will be coupled with a transport equation for the colloidal suspension to model the complete system. Given that a typical system can involve 10^{15} gold particles, it is clearly impractical to use a molecular dynamics simulation approach. The success of the mesoscopic modeling approach to this problem depends crucially on the existence of computationally efficient and accurate schemes. Recently developed spectral schemes for stochastic partial differential equations [5] are especially well-suited for studying mesoscopic models. The enhanced efficiency of spectral calculation makes possible much longer time simulations than would be possible using existing finite difference schemes; how-

ever, even with the spectral method, a mesoscopic simulation of a two dimensional surface without external coupling can require a week of computational time to obtain only about 100 realizations using a single processor. Given the physical importance of the equilibrium staining pattern of the biomaterial, longer time simulations for each realization are necessary for the study of a two dimensional surface coupled with a transport equation. The greatest amount of computational time required by the overall spectral algorithm is spent taking FFT's and generating random variates. These computations are well-suited for a parallel machine for many reasons. Given the necessity of calculating thousands of realizations in these stochastic simulations, the availability of a parallel machine with a large number of processors will greatly facilitate the completion of the necessary simulations.

Calculations of Surface Motion for Crystalline Materials

Michael Siegel

It is well known that stress effects play a large role in the surface morphology of growing crystals. For example, elastic stress causes a flat surface bounding a material solid to be unstable to small amplitude shape perturbations (the Asaro-Tiller-Grinfeld instability [3]). This instability is now recognized to be an important mechanism for the formation of "islands"' on thin material films as well as the appearance of cracks and defects in solids. Another important factor in the evolution of material surfaces is the anisotropy of physical quantities, such as surface energy, that occurs due to the crystalline nature of materials. The presence of large anisotropy, for example, is associated with the formation of corners on an interface, as dictated by the well known Wulff construction.

The PI proposes to continue his research program (supported by NSF) investigating the effects of stress and large anisotropy on surface evolution using continuum models. Much of the understanding of crystal growth is based on continuum modelling. Generally, the motion of free surfaces in such models is driven by variations in a chemical potential μ along the surface. One component of the chemical potential, denoted by μ_s, is related to the surface energy density γ. For crystals with anisotropic surface energy γ is normally taken to be a function only of the orientation angle θ of the outward surface normal. In this case, the contribution of the anisotropic surface energy to the chemical potential is described by the well-known relation (written in nondimensional form)

$$\mu_s = [\gamma(\theta) + \gamma''(\theta)]\kappa \tag{1}$$

where κ is the interfacial curvature, considered positive for a convex profile, and the prime denotes derivative with respect to θ. A representative (dimensionless) expression for $\gamma(\theta)$ is that for a simple four-fold symmetry $\gamma(\theta) = 1 + \epsilon \cos 4\theta$ where ϵ is a measure of the degree of anisotropy. The θ dependence of μ_s described in (1) leads to severe difficulties for large anisotropy, i.e., for $\epsilon > 1/15$. In that case there exists values of the angle θ for which the expression (1) is less than zero. At these 'unstable' orientations, the coefficient in front of the largest derivative term in the equation governing interfacial evolution is negative, and the initial value problem is ill-posed. Additionally, the equilibrium shapes of unstressed voids subject to large anisotropy have 'missing orientations', i.e., corners corresponding to jumps in θ along the surface. These are the well-known Wulff shapes.

One way to overcome the ill-posedness, proposed by Gurtin [18], is to regularize the evolution equations by incorporating higher order terms in the surface energy. In previous work [48] the proposer has employed such a regularization combined with boundary integral numerical simulation to study the evolution by surface diffusion of two dimensional material voids, in the case of large anisotropy. The emphasis in [48] was on inferring trends in limit of zero regularization ($c \to 0$). It is found that in the presence of elastic stresses the limiting corner angles (as suggested by the numerics) can differ from angles found on the zero-stress Wulff shape. This is an unexpected result. For large elastic stress a new filamenting instability is found.

The proposed project is to extend the above work to higher dimensions, as well as the incorporation of additional (yet critical) physical effects, such as surface stress. Theses computations are numerically intensive. For small regularization, the problem is 'nearly' ill-posed and there are a large number of fast growing modes. This necessitates a large number of surface nodes N as well as small time steps. Serial computations for the 2-D problem (which has complexity $O(N^2)$, reduced to $\mathrm{O}(N \ln N)$ using the Fast Multipole Method) take on the order of days. The complexity rises to

$O(N^4)$ for naive implementations in 3-D. The application of Fast Multipole techniques and parallel computations will be required to make the 3-D calculation feasible.

Finally, we shall explore a way of marrying continuum and atomistic based approaches. A disadvantage of the continuum model studied in [48] is that the assumed curvature dependence of the surface energy density $\gamma(\theta, \kappa)$ is phenomenological and effectively ad hoc. In general, the nonequilibrium surface energy depends on internal energy as well as entropy of a system of atoms, and hence first principles calculation of γ needs to take into account microscopic fluctuations. This requires numerically intensive techniques, such as Kinetic Monte Carlo or Molecular Dynamics (see e.g., [23] for calculations of θ dependence of γ using MD simulations). Further calculations are required to infer the curvature dependence in addition to the angle dependence.

Fourth-Order Schemes for the Maxwell Equations

Peter Petropoulos

Many modern technology applications involve the propagation and scattering of transient electromagnetic signals, e.g., electronic interconnects in semi-conductor circuits. The design and optimization of new systems demands fast and accurate solvers of the time-domain Maxwell equations over complex closed/open domains filled with heterogeneous dielectrics in which metals are embedded. In [56] we derived appropriate difference stencils to implement boundary and dielectric interface conditions in a *fourth-order* accurate staggered scheme for the time-dependent Maxwell equations discretized on a Cartesian grid. We adopted a domain-decomposition point of view and treated dielectric interfaces as boundary points between subdomains in which the spatial derivatives were computed to fourth-order accuracy with boundary data imposed as in the Yee scheme [50] (a 2nd-order accurate scheme popular in the engineering community). In [43] we derived accurate and stable spatial mesh refinement strategies for the fourth-order staggered scheme of [56]. Further, in [44] we considered an approximation in terms of damped exponentials of the impedance boundary condition (IBC). This boundary condition applies at a planar interface separating a homogeneous lossy half-space (of conductivity σ and permittivity ϵ) from free-space, and relates the tangential components of the electric and magnetic field evaluated at the interface. More precisely, the expression used in [44] is

$$E_{tan} = \frac{\eta_0}{\sqrt{\epsilon_r}} H_{tan} + \zeta * H_{tan}, \tag{2}$$

where η_0 is the impedance of free-space, ϵ_r is the relative permittivity of the lossy half-space, $*$ denotes convolution, and $\zeta(t) = \frac{\eta_0}{\sqrt{\epsilon_r}} a e^{at}[I_0(at) + I_1(at)]$ is the time-domain impedance function with I_0 and I_1 being modified Bessel functions. Additional parameters are $a = -\frac{1}{2\tau}$, and $\tau = \frac{\epsilon}{\sigma}$, the dielectric-loss relaxation time. Our approximation of $\zeta(t)$ in terms of N exponential functions is (see [44] for details and an error estimate) $\zeta_N(t) = \frac{\eta_0}{\sqrt{\epsilon_r}} \frac{a}{N} \sum_{k=0}^{N-1} (1 + v_k) e^{at(1+v_k)}$. Consequently, the computationally efficient IBC is $E_{tan} = \frac{\eta_0}{\sqrt{\epsilon_r}} H_{tan} + \zeta_N * H_{tan}$.

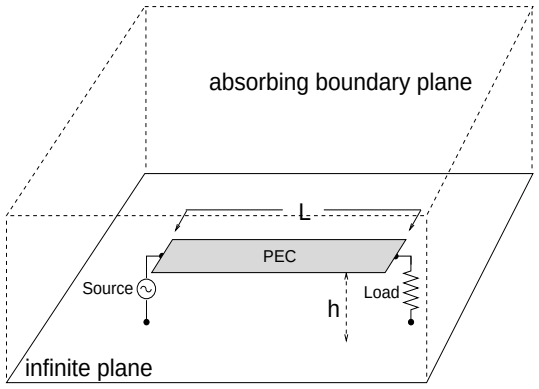

Figure 1: The computational domain. The surrounding walls (around and top) indicate the absorbing layer location.

In this project we intend to derive a fourth-order accurate implementation of the IBC originally used in [56] in order to study wave propagation in certain complex geometries, such as that shown

in Figure 1. It turns out that the presence of the half-space restricts the spatial discretization, however, employing the proposed IBC allows for a larger space step. Furthermore, we propose to combine the results of [43]-[56] with the fourth-order implementation of the IBC to construct a simulation for the problem depicted in Fig. 1. The model problem is one of signal propagation on a metallic microstrip and combines all the previously derived procedures for the implementation of boundary conditions to fourth-order accuracy. Additionally, it requires the use of an absorbing boundary condition on five sides of the computational box; our intent is to implement the long-time stable perfectly matched layer [4] to fourth-order accuracy. The domain-decomposition approach employed in our fourth-order method is ideally suited to parallel computation, and this project will provide us with the opportunity to investigate parallel programming techniques and issues of load balancing on the proposed computer hardware. The resulting algorithms will enable 3D simulations, even with very complicated geometries, and provide a useful tool in the design of microelectronic components. This research is supported by AFOSR.

Stability of Nonlinear Light Pulses Trapped by Defects

Roy Goodman

The investigator's research , supported by NSF, centers on the interactions between solitary waves and localized variations in the media through which they travel. Of particular interest has been the interaction of gap solitons with localized defects in Bragg grating optical fibers. Bragg grating fibers have found increasing application as components of optical communications systems due to their very high dispersion and their ability to filter out light at selected wavelengths. Bragg grating solitons support a family of traveling waves (pulses of light) known as gap solitons which have the intriguing property that they may travel at any speed less than or equal to the speed of light. In particular, the equations predict the existence of light pulses which do not propagate: trapped light! This could have many applications and might serve as the basis for an optical memory. Unfortunately, technical barriers make it extremely difficult to create these zero-velocity pulses.

With Michael Weinstein and Dick Slusher, both at Bell Labs, the proposer has been investigating the trapping of light pulses with specially designed defects in the grating structure, which act as localized potentials. The group has shown in numerical studies that under certain conditions, moving pulses transfer their energy to localized nonlinear modes supported at the defect [16]. They also find from exact analysis that the linearized equations may have several distinct eigenpairs. As the nonlinearity (i. e., the norm of the solution) varies, the eigenfunctions deform, and persist as separate branches of nonlinear defect modes. The stability of these modes is an important open question. Investigation of this problem requires two steps. The first is to numerically determine the nonlinear defect modes, the second is to compute their stability. The first component of this research has been accomplished, and work on the second is ongoing.

The computational tool used for the stability problem is the Evans function$f(\lambda)$, whose roots correspond to eigenvalues of the linearization of the PDE about the numerically computed solutions [5, 6]. Any roots in the right half-plane, then, correspond to growing modes. Typically one computes the winding number of the image of the imaginary axis, and if this exceeds zero, instability is inferred. Thus $f(\lambda)$ must be computed for a large set of λ's on the imaginary axis. Each evaluation of the Evans function requires the numerical solution of ODE's derived from the linearized operator, as well as combinations of those solutions in a way that leads large loss of significance. Therefore, the calculations require numerical schemes of high accuracy. A typical run requires the order of 1000 evaluations of $f(\lambda)$ in order to calculate the winding number accurately. For each branch of solutions, we have computed 10-30 defect modes, and the defects of most importance usually support 3 defect modes. Therefore, finding the stability profile of all the modes supported by a given defect involves the solutions of tens of thousands of ordinary differential equations, and usually takes days on the currently available computers. By computing the stability of multiple modes or branches in parallel, this could easily be reduced to an hour or two, greatly facilitating parameter studies. The proposed cluster provides an ideal environment to further develop these ideas.

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