Statement of Research Interests:
Out of equilibrium dynamical systems, the path from A to B.

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Summary

Increasingly, statistical physics has had to grapple with scientific questions in which techniques of classical, equilibrium thermodynamics have to be stretched in order to apply to inherently slow and often driven systems. As these systems are out-of-equilibrium, it does not suffice to simply study ensembles of configurations. Instead, we are forced to examine dynamical ensembles of trajectories. One such problem is the glass transition. Reconciling the apparent disparity between the microscopic, disordered nature of glass and its macroscopic rigidity has confounded physicists for years. However, we have recently shown how studying a simple model in trajectory space can shed light on the true nature and universality of molecular glassformers. While these simple models have given us new insights into glasses, they are not the complete picture. I am particularly interested in investigating the effects of probe particles on supercooled liquids. Specifically, I seek to understand to what extent probe particles are recorders of the dynamics of the host. Using techniques developed to study dynamical systems (eg. transition path sampling), which I have already applied to simple models, I believe it would be instructive to study other out of equilibrium processes such as motion in a crowded intracellular environment and clot formation in sickle-cell anemia. Beyond these applications, I am intrigued by the development of new dynamical sampling methods. One such example would be investigating new ways to perform parallel tempering in trajectory space which could help improve sampling efficiency in path ensembles. Moreover, I am fascinated by protocols for designing novel materials by optimizing model parameters to create an ideal process for observing a desired effect (say, self assembly). In effect, such a method would shift the focus from studying a set of trajectories given particular parameters, to studying a model with adjustable nobs which could be tuned to obtain a desired effect. Inverting the question would allow us to not only learn more about the physical world we live in but also to gain new ways to engineer models and novel materials to perform desired behaviors.

1 The Glass Transition

Supercooled liquids and the glass transition are a much debated, poorly understood physical phenomenon. The nature of supercooled liquids is inherently out of equilibrium as the equilibrium state (crystal) is avoided by a cooling protocol that frustrates the previously in-equilibrium liquid. In recent work, we have shown how to take a wide range of experimental data for molecular glassformer transport properties and collapse them onto a single curve. Much of the data taken on supercooled liquids originates from measurements that involve probe particles – guest particles that are used as 'thermometers' for their host material, acting as recorders of transport properties. To what extent these probes can record useful information about the material in which they are embedded is unknown. Probe particles are generally designed to be as "inconspicuous" as possible to best mimic the behavior of the host. However, this passivity is often taken *a priori* and unverified. I believe this unverified claim to be of utmost importance to our understanding of glassy measurements. For example, would swelling the probe size tell us something about inherent length scales? Once the probe size is of the order of the typical distance between dynamic heterogeneities (a hallmark of 'glassy' dynamics), would the mean field behavior of an average liquid be recovered? In this regime, would the diffusion constant and the relaxation time be coupled as per the Stokes-Einstein equation, even while the host supercooled liquid exhibits decoupling? I believe that Monte-Carlo and molecular dynamics simulations would be excellent tools for studying the effects of probe particles on host liquids. Through these studies, it would be understood to what extent the probe particle can be used as a molecular thermometer for the host and, moreover, to what extent and in what regime does the probe disturb the normal dynamics of the host liquid. These insights would be useful to experimentalists who often assume that the probe acts only as an ideal 'passive' recorder. As these ideas are a logical next step

of work I have already begun pursuing, it would make an ideal project for a beginning graduate student seeking to learn glassy phenomenology and simulation techniques.

2 Crowded Environments

Recently, many have touted the analogy between crowded cellular environments and the colloidal glass transition. By changing the osmotic pressure, experimenters were able to 'jam' the interior environment, just as they would a dense colloidal or granular material. While this pressure was applied in a laboratory, this change in pressure is similar to the pressure change during tumor formation as cells become more and more densely packed due to rapidly dividing cells. Since cells are crowded, out of equilibrium environments they share many features with supercooled liquids – also dense packings of molecules – only on a different scale. Recent numerical and simulation technique advances have been used to shed light on elementary motions in such supercooled environments. By exploiting the similarity, large molecular simulations of a dense cellular system coupled with new techniques can be used to study basic motion of small proteins as they diffuse in such a crowded environment. These simulations could use techniques of transition path sampling, which I am familiar with based on my studies of glassformers, to characterize the ensemble of possible moves as a protein escapes its environment by exiting its macromolecular cage. I would be especially interested in discussing these topics with biologists and biophysicists. I believe that their biological expertise coupled with my familiarity with work in dense, glassy systems would help shed new insights into crowded cellular environments. Moreover, I believe that collaborative, interdisciplinary research will be the best way to enhance our understanding of the world in which we live. Through such a collaboration, we would be able to answer questions about motion within a cell. We can also compare these motions to the facilitated motions in granular and colloidal materials. This information would lead to a better physical understanding of such a complex, crowded environment.

Beyond intracellular material, analogies with jammed materials are also observed when examining *extra*-cellular materials. Recent work in microfluidic devices have shown how sickle-cell anemia manifests itself when cells change their shape and form clots is narrow veins. The geometry of the cells as they "sickle" has been shown to play an important role in the disease. Understanding elementary processes about how clots form and dissolve can be of use to create new treatments for the disease. It has already been shown that a (toxic) chemical inhibitor that binds to red blood cells can alleviate clot formation. Alternatively, another treatment might be to add an intruder that frustrates the formation of such clots geometrically, rather than chemically. The elementary steps of formation and destruction of such clots can be studied using techniques of transition path sampling. These simulations would add insights about this physical phenomenon that has devastating medical consequences. Moreover, this knowledge might inform what size and shape molecules would be best for treatment, perhaps offering a non-toxic alternative to chemical binding. Again, here I would seek collaborations with biologists to combine my physical understanding of glasses with their biological knowledge. Such a project would be well suited for a more advanced graduate student as it requires a deeper understanding of simulation techniques and the ability to assimilate new, biological information. Plus, it would allow for the possibility of collaborative, interdisciplinary work ideal for students near the end of their degree.

3 Sampling Methods

The problem of efficient and accurate sampling methods for complex systems is one that continues to challenge researchers even in the face of great technological and algorithmic gains. To that end, in the future it will be necessary to expand methods to improve sampling and design in materials. For example, the development of a new parameter space sampling technique to investigate ensembles of trajectories with increased computational efficiency for dynamical problems will be useful. On the other hand, scientists and engineers are seeking methods which would optimize parameters to select for certain dynamical behaviors. The creation of such methods would allow us to engineer models which strike a balance between thermodynamics and kinetics. Both methods would have applications for studying glassformers, biophysics, and designing novel materials.

To investigate behaviors of rare events, we have used advanced sampling methods developed to study ensembles of trajectories. One of the most significant of these is transition path sampling. This method has

allowed people to probe a diverse set of dynamical problems from supercooled liquid dynamics to biological self-assembly. While current methods can investigate trajectory space for fixed parameters very well, few techniques exist which allow for crossing large barriers in parameter space. Traversing dynamical barriers in trajectory space suffers the same pitfalls as traversing barriers in configuration space: barriers in space-time can prove too high to climb in a given parameter set, meaning that important regions of trajectory space may go unexplored. If this is the case, the transition path ensemble will be poorly converged and may not reflect the true nature of the underlying dynamical free energy landscape. In fact, even with our simple models, straightforward sampling leads to a large number of rejected trajectories.

Parameter space methods for parallel tempering have been mostly limited to swapping static configurations with different parameters by taking into account the relative probabilities of these states. However, recent works have shown that it is possible to extend these methods to include other parameters. I believe it will be possible to extend these methods to mix both dynamical order parameters (which characterize a trajectory) as well as thermodynamic parameters (such as the temperature). In order to make such a trajectory space parallel tempering method fully functional, the path probability for the entire trajectory must be calculated - requiring storing every step of the simulation. This computational demand has only recently become tractable with advances in computing – both in hardware as well as architecture designed to take advantage of the parallel nature of supercomputers. Using such a technique, the path probability could be reconstituted for any arbitrary set of parameters and thus parallel tempering-like swaps could be attempted between two trajectories run with different thermodynamic and dynamical parameters. This work could potentially be expanded to swapping between "protocols" (eg. cooling a liquid toward its glass transition). Take, for example, a trajectory whose temperature changes as a function of time. As long as the path probability of that trajectory can be computed for any arbitrary protocol, swaps can be attempted between these protocols. Such methods would be easily verified on lattice models such as kinetically constrained glassy models (which I have studied extensively) and lattice protein models – both known to exhibit rich dynamic phenomena.

Material Design

In the last twenty years, nanoparticles and their applications have come to the forefront of scientific consciousness. Certain nanoparticles can be used for self-assembly, spontaneously forming complex aggregated structures. The future will hold a variety of uses for particles that can self-assemble such as for targeted drug delivery, in optics, and as surfactants. The final, assembled, structure depends on the interactions between the nanoparticles and how those interactions dictate kinetic pathways to assembly. It has been noted that interactions should be strong but *not too strong*, so that an unassembled system has enough time and energy to bind but also to anneal out defects. Many have tried to design methods to optimize specified assembly pathways (and final structures) at viable conditions. However, a reliable method remains elusive.

Tuning interactions until they produce a desirable effect involves developing a method to allow trajectories to explore parameter space. For specific parameters of interest, one can gain insight into dynamics by sampling this space. This allows us to sample the extreme values of our ensemble distribution along with the average. This information can be used to optimize parameters that select for a particular behavior in a system with two basins, say A and B. For example, in a self-assembly process A could be an unassembled state and B an assembled state. Ideally, we could optimize the probability of seeing a trajectory that goes from A to B given that the trajectory starts in A; that is, optimize, relative to the thermodynamic parameters, the probability of ending in state B given that the system started in state A.

Optimization methods for these kinds of problems have been recently promoted and are known as *maximum likelihood estimators*. These methods can be then used iteratively until an ideal set of parameters is found that increases the probability of going from A to B. This method would act as a maximization method for path probability in parameter space. These results can be informed by real thermodynamic control parameters that experimentalists can tune – such as the interaction strength between particles (say, by changing the host material) or by tuning an external field.

These sampling ideas could form the basis for a graduate thesis or, equally for a postdoctoral project. Moreover, these ideas would be especially well suited for collaborations with material scientists.