Some Ideas For Statistical Mechanics

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What don’t we know?

Special Section

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Protein Folding Problem

We argue that great headway has been made, both theoretical and experimental, and that the central problems of principle, and even key problems of implementation and practice, have already been solved. – Ken A. Dill (2007)
“I wouldn’t have told them about a great solution I had developed, and they wouldn’t tell me their solution.”
— Klaus Schulten

POWER PLAY
A German physicist and a hedge-fund magnate are competing to push protein simulations into the realm of the millisecond. Brendan Borrell finds out what is at stake.
The deepest and most interesting unsolved problem in solid state theory is probably the theory of the nature of glass and the glass transition. This could be the next breakthrough in the coming decade. The solution of the problem of spin glass in the late 1970s had broad implications in unexpected fields like neural networks, computer algorithms, evolution, and computational complexity. The solution of the more important and puzzling glass problem may also have a substantial intellectual spin-off. Whether it will help make better glass is questionable.

P. W. Anderson
Joseph Henry Laboratories of Physics
Princeton University

Science, 1995

What is the nature of the glassy state? Molecules in a glass are arranged much like those in liquids but are more tightly packed. Where and why does liquid end and glass begin?

Science, 2005
Dr. Reichman said of Dr. Wolynes’s theory, “I think a lot of the elements in it are correct,” but he said it was not a complete picture. Theorists are drawn to the problem, Dr. Reichman said, “because we think it’s not solved yet — except for Peter [Wolynes] maybe.”

David A. Weitz, a physics professor at Harvard, joked, “There are more theories of the glass transition than there are theorists who propose them.”
Water!

**What is the structure of water?**
Researchers continue to tussle over how many bonds each H₂O molecule makes with its nearest neighbors.

**Insights into Phases of Liquid Water from Study of Its Unusual Glass-Forming Properties**
C. Austen Angell

**Interfaces and the driving force of hydrophobic assembly**
David Chandler
Granular Materials/Packing Problems

Can we develop a general theory of the dynamics of turbulent flows and the motion of granular materials?
So far, such “nonequilibrium systems” defy the tool kit of statistical mechanics, and the failure leaves a gaping hole in physics.

Science, 2005

A phase diagram for jammed matter

Chaoming Song, Ping Wang & Hernán A. Makse

Vol 453 | 29 May 2008 | doi:10.1038/nature06981

LETTERS
Most physical scientists nowadays focus on uncovering nature's mysteries, chemists build things. There is no synthetic astronomy or synthetic physics, at least for now. But chemists thrive on finding creative new ways to assemble molecules. For the last 100 years, they have done that mostly by making and breaking the strong covalent bonds that form when atoms share electrons. Using that trick, they have learned to combine as many as 1000 atoms into essentially any molecular configuration they please.

Impressive as it is, this level of complexity pales in comparison to what nature flaunts all around us. Everything from cells to cedar trees is knit together using a myriad of weaker links between small molecules. These weak interactions, such as hydrogen bonds, van der Waals forces, and 

\[ \pi-\pi \] interactions, govern the assembly of everything from DNA to its famous double helix to the bonding of \( \text{H}_2\text{O} \) molecules in liquid water. More than just riding herd on molecules, such subtle forces make it possible for structures to assemble themselves into an ever more complex hierarchy. Lipids coalesce to form cell membranes. Cells organize to form tissues. Tissues combine to create organisms.

Today, chemists can't approach the complexity of what nature makes look routine. Will they ever learn to make complex structures that self-assemble?

Well, they've made a start. Over the past 3 decades, chemists have made key strides in learning the fundamental rules of noncovalent bonding. Among these rules:

- **Like prefers like.** We see this in hydrophobic and hydrophilic interactions that propel lipid molecules in water to corral together to form two-layer membranes that serve as the coatings surrounding cells. They bunch their oily tails together to avoid any interaction with water and leave their more polar head groups facing out into the liquid. Another rule: **Self-assembly is governed by energetically favorable reactions.** Leave the right component molecules alone, and they will assemble themselves into complex ordered structures.

But the need for increased complexity is growing, driven by the miniaturization of computer circuitry and the rise of nanotechnology. As features on computer chips continue to shrink, the cost of manufacturing these ever-smaller components is skyrocketing. Right now, companies make them by whittling materials down to the desired size. At some point, however, it will become cheaper to design and build them chemically from the bottom up.

Self-assembly is also the only practical approach for building a wide variety of nanostructures. Making sure the components assemble themselves correctly, however, is not an easy task. Because the forces at work are so small, self-assembling molecules get trapped in undesirable conformations, making defects all but impossible to avoid. Any new system that relies on self-assembly must be able either to tolerate those defects or repair them. Again, biology offers an example in DNA. When enzymes copy DNA strands dur-

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**How Far Can We Push Chemical Self-Assembly?**

Chemists have learned to take advantage of these and other rules to design self-assembling systems with a modest degree of complexity. Drug-carrying liposomes, made with lipid bilayers resembling those in cells, are used commercially to ferry drugs to cancerous tissues in patients. And self-assembled molecules called rotaxanes, which can act as molecular switches that oscillate back and forth between two stable states, hold promise as switches in future molecular-based computers.

In many ways, these early attempts at self-assembly parallel the embryonic development of an organism. In the beginning, the parts are simple and the connections are few. But as the system grows, the interactions multiply and the parts form into something more complex.

As the cell division, they invariably make mistakes—occasionally inserting an \( \text{A} \) when they should have inserted a \( \text{T} \), for example. Some of those mistakes get by, but most are caught by DNA repair enzymes that scan the newly synthesized strands and correct copying errors.

Strategies like that won't be easy for chemists to emulate. But if they want to make complex, ordered structures from the ground up, they'll have to get used to thinking a bit more like nature.

—Robert F. Service
Self-Assembly of Colloidal Particles

Dijkstra, 2008
DNA-based Self-Assembly

LETTERS

DNA-guided crystallization of colloidal nanoparticles

Dmytro Nykypanchuk, Mathew M. Maye, Daniel van der Lelie & Oleg Gang

Programming DNA Tube Circumferences

Peng Yin, Rizal F. Hariadi, Sudheer Sahu, Harry M. T. Choi, Sung Ha Park, Thomas H. LaBean, John H. Reif

Synthesizing molecular tubes with monodisperse, programmable circumferences is an important goal shared by nanotechnology, materials science, and supermolecular chemistry. We program molecular tube circumferences by specifying the complementarity relationships between modular domains in a 42-base single-stranded DNA motif. Single-step annealing results in the self-assembly of long tubes displaying monodisperse circumferences of 4, 5, 6, 7, 8, 10, or 20 DNA helices.
Membrane Organization and Mediation

Smit, 2008
The cell is a viscoelastic material with highly unusual properties. Measurements of the mechanical behavior of cells are beginning to probe the contribution of constituent components to cell mechanics.
Stochastic Biological Signaling

Fluctuations in Genetic Networks: a Computational Study

Marco Morelli