Simbios (http://simbios.stanford.edu) is the National Center for Physics-Based Simulation of Biological Structures at Stanford.

BY KATHARINE MILLER

A Balanced Approach to Designing Force Fields

When simulating the movements of large molecules on a computer, researchers typically rely on an approximation of the force fields at play. That's because a truly correct simulation of those forces would require complex quantum mechanics calculations that would take years to simulate.

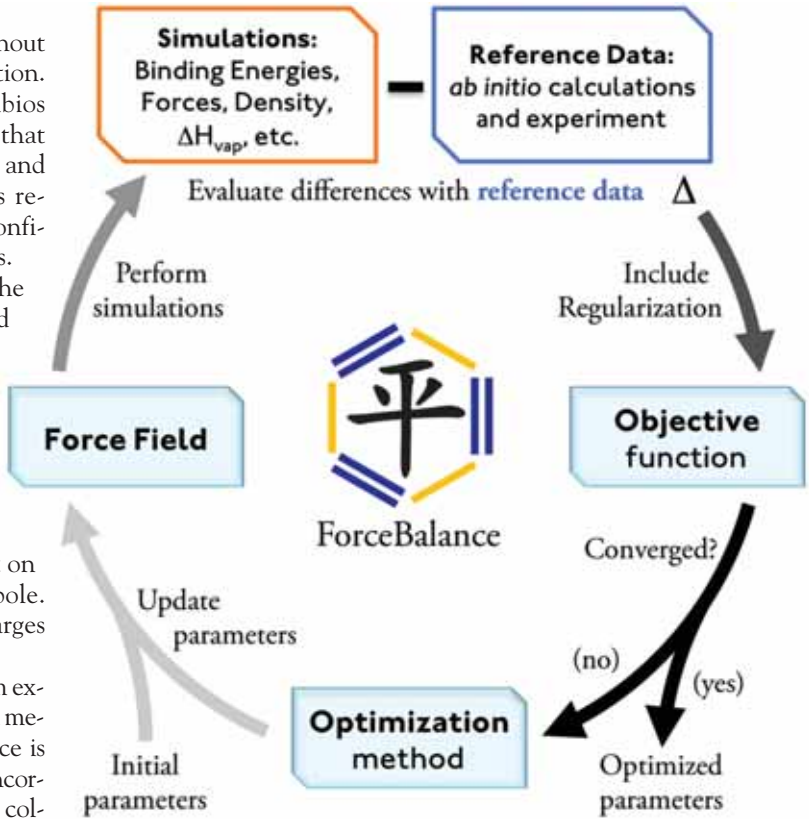
Many researchers use off-the-shelf force fields without knowing whether they are optimal for a specific situation. To address this issue, **Lee-Ping Wang, PhD**, a Simbios postdoc, created ForceBalance, a software program that makes it easier for researchers to efficiently develop and optimize their own force fields. "ForceBalance lets researchers pursue a scientific problem with greater confidence that their force fields are accurate," Wang says.

Force field design depends on three ingredients: The functional form of the forces—essentially a simplified description of the cloud of electrons; data representing the pieces of reality the force field should reproduce; and a method for optimizing parameters.

ForceBalance allows researchers a good deal of flexibility with respect to each of these three ingredients. For the functional form, for example, researchers have the freedom to represent the electrostatics as one positive and one negative point on each atom (a monopole), or as a dipole or multipole. Among other things, they can also model the charges moving around (induction or polarization).

In addition, the data for ForceBalance can come from experiments, theory (based on a small number of quantum mechanics calculations) or both combined. "ForceBalance is the only force-field software that can simultaneously incorporate multiple types of data," Wang says. He and his colleagues used this capability to generate an extremely accurate model of water molecules that was published in November 2012 in the *Journal of Chemical Theory and Computation*.

ForceBalance users can also choose among three different optimization techniques: grid scan (which tests all the possible parameters); simulated annealing (which tries random jumps, honing in on the best parameters); and the Newton-Raphson method (a derivative-based approach).



ForceBalance fully automates the force field optimization process.

Despite offering three methods, Wang says, it's the Newton-Raphson approach that routinely finds the best solution in the least amount of time (taking only about 10 iterations to converge on the optimal parameters).

"With ForceBalance," says **Pengyu Ren, PhD**, associate professor of biomedical engineering at the University of Texas at Austin, who collaborates with Wang, "you can quickly evaluate or compare a number of different physical models to observables and determine what physics are more important to what." Researchers can in turn test more models for accuracy. "ForceBalance will accelerate improvements in models and make things more accurate," Ren says. □

DETAILS

ForceBalance is described in Lee-Ping Wang, Teresa Head-Gordon, Jay Ponder, Pengyu Ren, John Chodera, Peter Eastman, Todd J. Martinez, and Vijay Pande, et al., "Systematic Improvement of a Classical Molecular Model of Water", *J. Phys. Chem. B* 117:9956-9972 (2013), and can be freely downloaded from http://simtk.org/home/forcebalance.

In Other Simbios News...

The Duke's Choice Awards from Oracle and the Java community honor organizations and developers for their creative and innovative uses of Java technology. Ayman Habib accepted the award on behalf of the OpenSim team at the recent JavaOne conference, attended by 60,000 people in San Francisco from September 22-26. □