Schrödinger Links Up with BioTeam to Form Mobile IT Squad for Pharma Compuchem

October 31, 2008
By Vivien Marx

Schrödinger, a computational chemistry software developer, and BioTeam, an IT-oriented consulting company in the life sciences, last week signed an agreement linking their expertise in a new collaborative effort to help drug discovery clients get complex computational chemistry software up and running in their existing IT environments.

One driver for the partnership is a new computationally intensive molecular dynamics platform that Schrödinger launched called WaterMap that will bring the need for high-performance computing services "to the forefront," Ramy Farid, Schrödinger's president, told *BioInform* in an interview.

Pharma companies such as ARIAD, Abbott, AstraZeneca, Boehringer Ingelheim, Bristol-Myers Squibb, Exelixis, Johnson & Johnson, Millennium, Novartis, Pfizer, Sanofi-Aventis, Vertex, and Wyeth are currently evaluating WaterMap and have been "very excited" about the offering, said Farid. The rub is that on many occasions, once customers installed the software on their machines, "it wouldn't work," he admitted. In one case, it took a customer a month to get the software running. "Imagine how much is lost in that time frame," he said.

According to the collaborative agreement, Schrödinger can now bundle BioTeam's high-performance computing services with its products, Stan Gloss, BioTeam's founding partner and managing director, told *BioInform*.

Instead of being "bogged down" with IT issues, Schrödinger can concentrate on new algorithms and new scientific methodologies, Farid said. When IT problems crop up, BioTeam will be called in. "They can fix the problem so much more efficiently than we can," he said.

"There are always IT issues with our software because of the heterogeneous [IT] environments out there," Farid said.

The company's chemical simulation software includes molecular modeling and statistics packages to explore structure-property relationships, predict protein structure prediction, and study ligand-receptor docking. WaterMap, along with the protein prediction platform Prime and docking software Glide, are "compute-intensive calculations, requiring multiple processors," he said.

Gloss said that BioTeam has been doing work off and on for Schrödinger since 2005. "The difference [to now] is it hasn't been coordinated," he said. "We are very closely aligned as a team," he said, highlighting that his staff is not going to perform computational chemistry research but rather get the compuchem software running for Schrödinger's customers.

Farid said that BioTeam will mainly be working with a job control layer that is common to all of Schrödinger's tools and serves as the link between the applications and the customer's computing environment.

Go Away, IT

“What we are asked to do is to make IT and computing issues go away,” Gloss said. “Everybody has a different computing system; there is no one standardized system.”

Gloss added that this heterogeneity is the BioTeam’s “bread and butter.”

Under the terms of the non-exclusive partnership, Schrödinger will address any customer concerns first. “We can immediately determine if it’s something very trivial that we can fix,” Farid said. “If by the end of the day, they are not running, we bring in the BioTeam.”

Schrödinger has offices in San Diego; New York; Portland, Ore.; the UK, and Germany. Its work with BioTeam will initially be limited to the continental US or through remote access, but on a case-by-case basis the company’s consultants are willing to address issues anywhere, said Gloss.

Schrödinger is technically a reseller of BioTeam’s services, which should help expand the consultancy’s presence in the pharma market, Gloss said. Pharma customers find it “inconvenient” to add new vendors, he said, but under the deal with Schrödinger, “we have a BioTeam services part number in the Schrödinger price list.”

BioTeam’s consultants have been trained on Schrödinger’s software. “We have to know cold how to run their software,” Gloss said. “How does the scientist submit the job to a high-performance computing environment; how does that computing environment handle it and how does it return the results?”

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Gloss said that his staff might need to work with IT specialists as well as end-user researchers at Schrödinger’s customer sites. “In a lot of companies the person in charge of installing the software, in charge of the IT system in the modeling group, is a modeler,” Farid said.

Companies want their scientists to benefit from scientific software, but often they do not wish to hire permanent IT staff for intermittent IT problems, said Gloss, particularly not in a climate in which many pharmaceutical firms are cutting research budgets and shedding R&D personnel.

Although budgets for computational molecular modeling in pharma “are relatively small relative to total R&D spending,” Farid said, companies looking to cut costs might see a benefit in reducing the number of vendors they work with.

A few years ago Schrödinger developed a graphical interface to make its software more user-friendly, but was not in a position to address the high-performance computing issues, Farid said. “We are certainly the best in terms of science and now with BioTeam we are going to be the best with respect to robustness, which we’re not right now,” he said.

“Schrödinger was a smaller player back then,” he said, and customers “didn’t expect that much from us.” Now, he said, “we have become their core provider [and] they’re relying much more heavily on us.” Farid declined to elaborate on specifics of the privately held firm’s growth rate but said that the firm began to see “double digit” growth in revenue around five years ago.

“As of this year, every single pharmaceutical company is using our software,” he said. said. “That was definitely not the case 5 years ago,”

With that, he added, comes a distinct demand for robustness. “It’s a nice problem to have.”

Schrödinger could theoretically create its own “IT SWAT team,” but that would mean a cultural shift in the company, Farid said. “It’s a science company, not an IT company.”

Under the agreement with BioTeam, they can “come in, configure the queuing system, figure out what the problem is, recommend how to run things; they might write a snippet of code that wraps certain things … They do whatever needs to be done,” Farid said.

“It’s a nice model: let us focus on one thing. Instead of doing two things halfway, we do one thing really well, they do their thing really well,” said Farid.

Finding Unhappy Water

The algorithm for Schrödinger's new WaterMap software was developed at Columbia University by chemists Richard Friesner and Bruce Berne who are on the company's scientific advisory board. The firm licensed the software and validated it internally, Farid explained, and he hopes it will help expedite drug discovery.

Once researchers generate a protein-ligand structure with the help of Schrödinger tools such as Prime and Glide, they want to predict whether that compound, as Farid said, is "a tight binder or not," so whether it stands a chance of becoming a drug.

WaterMap predicts the location of water molecules in the crevices of protein-binding sites and the energies associated with those waters, showing the difference between a weak-binding ligand, which is not a potential drug candidate, and a tight-binding ligand, which should probably be moved down the pipeline.

It's important to know where an "unhappy," or chemically unstable water molecule, is, Farid said, because it gives chemists drug design hints. "If you displace an unstable water, you have made a more stable compound … a more tight-binding ligand," he said.

Determining the location and energies of the waters is computationally complex. "We have very sophisticated engines that get at the energies of those waters, but the location of the water comes from explicit solvent molecular dynamic simulation," said Farid. In studies done jointly at Columbia and at Schrödinger, researchers have been able to "calculate the free energies of the waters, the happiness and the unhappiness," he said.

However, he noted, "WaterMap is very complicated from the point of view of IT." One complicating factor is that it is a parallel program that is typically run on eight or more processors.

"Parallel programs are notoriously complicated because they require extremely robust communication between processors or cores," he said. The other source of computational difficulty is that WaterMap is a workflow consisting of nine separate stages. "The first eight are molecular dynamics simulations and the ninth is the analysis of the MD trajectories that produces the energies."

In his opinion, a key technology transition in drug discovery lies with scientific advances in structure-based drug design, in "understanding the physics behind protein-ligand interactions," and "translating that into tools [to] design novel compounds," he said.

As the Protein Data Bank continues to fill up with structures, it is enabling computer-based homology modeling and induced fit modeling, he said, helping drug discovery researchers when no crystal of a protein of interest is available.

Farid said that it is still an uphill battle to assure the pharma industry that computational chemistry software is as essential as, say, instruments for combinatorial chemistry. "The problem is people devalue software, saying, 'Somebody else has something else that is free and there are 15 other products that do the same thing.'"

"That has to change," he said, and when it does, "you will see the technology transition" toward tools that will allow for less waste and more of a focus on drug discovery, he said.

A Cloud Doesn't Thud

New computational environments are accompanying these changes in computational chemistry. "A pharmaceutical company may run a cluster, but might also buy specialty appliances, such as Google's Search Appliance or use cloud computing," Gloss said.

Farid said that Schrödinger enabled all of its software to run on Amazon's Elastic Compute Cloud, or EC2, just a few weeks ago. Customers can submit jobs there, much like they submit jobs to an off-site cluster. "It's clear now we [Schrödinger and BioTeam] will be working to bring that solution to our customers," he said.

"We are sort of blown away by how useful [cloud computing] is," Farid said. In fact, he said that Schrödinger, which was previously thinking about creating its own in-house data center, has put those plans on hold in favor of cloud computing.

Let others worry about the "unbelievably difficult task of keeping a huge number of computers up and running all the time," said Farid. "This is an interesting trend that, clearly, pharmaceutical companies have latched on to."

While the main hurdle for cloud computing has been security, Farid said that anecdotal evidence suggests that "some of the pharmaceutical companies have gotten completely comfortable with the level of security and are willing to submit their proprietary work onto the cloud." For example, Christine Van Marter, Lilly Research Laboratories' manager of communications, confirmed in an e-mail to *BioInform* that the company is experimenting with Amazon's EC2.