Denise Myshko

Making *Data* Meaningful

Advancing knowledge in science and medicine requires new tools and skill sets for managing and analyzing data.

The genomics revolution has led to an explosion of biological data. But using these data to discover and develop new medicines requires newer, more sophisticated tools. Bioinformatics is a growing field, and industry experts expect pharma companies to continue to invest in tools to manage the vast amounts of data being generated.

One of the challenges of developing new medicines is understanding the data that already exist, says Rudy Potenzone, Ph.D., VP of product strategy informatics, at PerkinElmer.

"In the area of gene expression, we have to begin to understand what parts of the genome are being turned on and off during the disease and try to relate the information back to actual patient profiling," he says. "We then will be able to identify biomarkers, address pathway analysis, and know how to better understand how this all fits together in terms of the biological system and the mechanisms of action for both the normal state and the disease state."

New bioinformatics tools can definitely help scientists understand how medicines help patients, Dr. Potenzone says.

"Scientists can look at all of the different pieces of information in a structured, logical form and look for patterns and changes," he says. "This is difficult because of the amount and the complexity of the data, which makes it hard to see the relevant changes over the course of a treatment. Newer tools give us the opportunity to look at a lot of different variables at the same time to try to pick out the key changes happening and determine the changes at the patient level."

This level of understanding of how a disease works and how medicines can impact a disease is leading to new scientific discoveries.

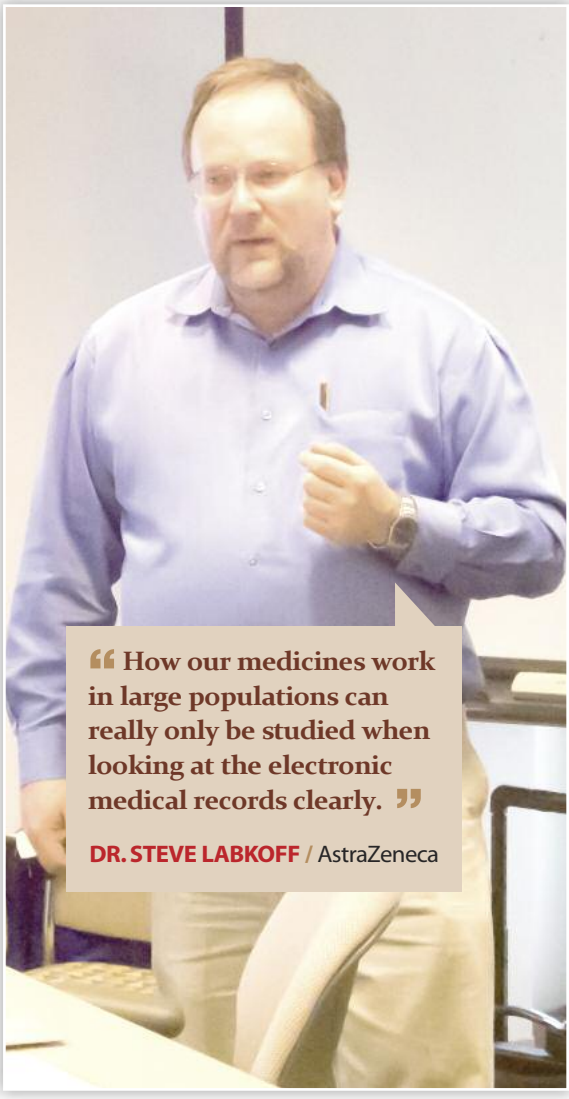
"Until now, we have not had the level of visibility into how the human body works and how the different pathways come together," Dr. Potenzone says. "Bioinformatics is absolutely pushing the boundaries of science."

The adoption of technology has been dramatic, particularly with whole genome sequencing, which has the potential to revolutionize the "omics" field, says Jonathan Sheldon, Ph.D., global senior director, translational medicine at Oracle.

"Whole genome sequencing is a very powerful tool that allows us to look at all the variances in the genome," he says. "Pharma companies are starting to invest in technology that looks at, for example, copy number and methylation and large structural variation."

But, he says, it's easy to be seduced by the power of genomics technology.

"Unless we have accurate, high-quality, standardized, clean clinical data, the 'omics' data are of little value," Dr. Sheldon says. "Clinical data need to accurately characterize the phenotype and assess the outcomes. That is the output that we want to model. Within pharma, the boom area over the last year or two has been the adoption of real-world evi-



> "How our medicines work in large populations can really only be studied when looking at the electronic medical records clearly."
>
> **DR. STEVE LABKOFF** / AstraZeneca

dence groups that are focused on bringing together clinical trial and clinical practice data."

Outcomes-based groups would be a clear beneficiary of the types of data that bioinformatics tools can potentially uncover.

But Dr. Potenzone says understanding diseases and medicines brought about by bioinformatics tools requires new skill sets, new types of studies, and investments in new types of technologies.

"Pharmaceutical companies will have to partner with smaller companies that are pioneering particular types of capabilities rather than the good old days where they just brought that technology in-house and trained a new group of scientists," he says. "With the type of science and the skills that are needed and with companies under such cost and time pressures, they can't afford to have huge staffs and investments in new technologies. Companies are looking for new ways to bring in the help they need to do the project."

The global bioinformatics market is forecast to reach $6.8 billion by 2017, according to a recent report by Global Industry Analysts. Driving market growth are significant developments in genomics and its application in the research and development processes; breakthrough technologies in drug discovery initiatives; and the entry of new market players. One of the key growth areas of bioinformatics is systems biology modeling, which would be driven by large-scale integration across various stages of drug discovery.

> "Tools are becoming more sophisticated for developing novel biologics, and tools are becoming more sophisticated about measuring how test subjects are responding to disease and the administration of a therapeutic."
>
> **DR. CLIFFORD BARON** / Accelrys

What is Bioinformatics?

Bioinformatics is the research, development, or application of computational tools and approaches for expanding the use of biological, medical, behavioral or health data, including those to acquire, store, organize, archive, analyze, or visualize such data. Bioinformatics applies principles of information sciences and technologies to make the vast, diverse, and complex life-sciences data more understandable and useful.

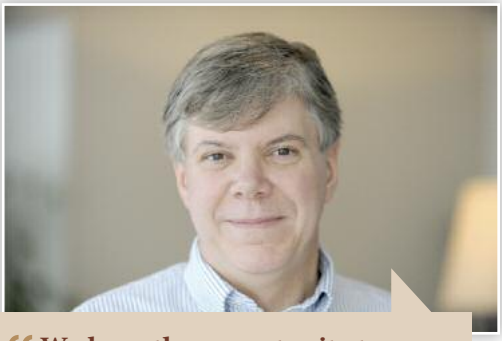
Source: National Institutes of Health

Dr. Sheldon says in the future, growth will be in the area of solutions that enable integration and analysis of cross-platform "omics" data.

"We need solutions that enable analysis of the data that are generated internally by the organization as well as in the broader context of the public domain," he says.

Discovery/Early Phase

There is a convergence of traditional chemistry-based small molecule discovery and the



> **"We have the opportunity to revolutionize the way we conduct clinical trials, helping us to quickly and efficiently bring critical new medicines to patients."**
>
> **TIMOTHY WRIGHT** / Novartis

application of medicinal and structural chemistry tools to develop more sophisticated biologics substances, says Clifford Baron, Ph.D., director of biology product marketing at Accelrys.

"We are now seeing the application of many tools for medicinal and synthetic chemistry to biologic substances," he says. "We're developing better tools for predicting the biophysical properties of large molecules. It used to be that predictive models were only good for relatively small chemical molecules that were potential therapeutics. With great increases in computing power, as well as improvements in the algorithms, we are finding that we can better predict properties such as separation and viscosity and aggregation propensity much earlier in the discovery process. We are essentially able to computationally screen out many potential therapeutics that wouldn't make very good drugs because they couldn't be properly formulated into a form that could be easily administered."

Dr. Baron says one example of where this has led to a new medicine is Genentech's Herceptin-based antibody drug conjugate, Kadcyla, which received FDA approval in February. An antibody-drug conjugate is a relatively new type of targeted cancer medicine that can attach to certain types of cancer cells and deliver chemotherapy directly to them. Kadcyla is the first FDA-approved ADC for treating HER2-positive metastatic breast cancer.

Dr. Baron says pharma companies are using these chemical conjugate technologies more and more effectively to identify and target cell surface proteins or particular genes that might be candidates for intervention with a therapeutic.

Another area he says where bioinformatics is proving useful is in the next-generation application of genomics and other technologies for identifying biomarkers in the context of translational research.

"People are looking at the genome not just as a static entity but as an extremely dynamic system," he says. "Though the genome itself is fixed throughout an organism's lifespan, the way that the genome is expressed and regulated dynamically is becoming more accessible to evaluate through techniques such as RNA-seq experiments. RNA-seq experiments use the same technology as next-generation sequencing to evaluate the response of the genome to specific conditions and interventions, whether diseases or the application of drugs."

Dr. Baron says many of these genomic and related technologies use bioinformatics to try to identify subsegments of a potentially relevant therapeutic population who are either going to respond poorly to a drug with some nasty side effects or who are going to respond favorably because the drug only targets a particular protein mutation or aberrant pathway cell.

"Being able to identify which patients will respond, which one won't respond at all, and which ones may respond but have nasty side effects is an important application of these biomarker technologies and bioinformatics tools that help assess those correlations," he says.

"Translational research is becoming the standard model in the pharma industry," Dr. Baron adds. "This means translating results from simpler systems, such as tumor cell lines, into results that are relevant to patients in the clinic. Better bioinformatics, especially for managing and interpreting complex genomic data, is a key to enabling translational research."

Dr. Baron says the advantage to using these tools is shorter R&D cycles.

"The candidates that companies bring into Phase II and Phase III trials will be more likely to succeed," he says. "If the translational correlations are done correctly there is far less chance of bringing a poor candidate into a clinical trial and incurring all of the expense that goes along with this."

Late-Phase Development

Dr. Sheldon points out that while bioinformatics tools initially were used in discovery and early development, they are becoming increasingly important throughout the continuum of development.

"Pharma now wants to access clinical practice data that comes from an EHR and not just clinical trial data that comes from an EDC system," he says. "Researchers want to be able to look at both types of data. It's going to be increasingly important that we have systems and solutions that enable that real-world evidence view of the effectiveness of drugs."

Integrated data from electronic medical records and other data sources will be where bioinformatics will grow in the future, says Steve Labkoff, M.D., head of strategic programs, R&D information, at AstraZeneca.

"There needs to be algorithms to match patient records to different sources and come up with probabilistic matching of patients in claims and health records," he says. "The real magic happens when we can marry the two to get a longitudinal look at both the claims and the EMR data to be able to draw deeper conclusions."

EMR data, Dr. Labkoff says, can be used postlaunch and prelaunch, as well as for clinical trials.

"If we can create an EMR alerting system that a doctor can use in conjunction with his or her routine work flow, a patient's record can be matched against clinical trial inclusion and exclusion criteria," he says. "If there is a match, the EMR can alert the doctor in the moment to talk to the patient about enrolling directly into the trial. This will allow pharmaceutical and biotechnology companies to recruit patients for clinical trials easier and faster. This is great for patients also because many times they find it difficult in some situations, such as in an oncology setting, to connect with the latest trials."

AstraZeneca has made a commitment to studying real-world data. In 2011, the company and HealthCore, the health outcomes subsidiary of WellPoint, began a collaboration to conduct prospective and retrospective observational studies on disease states as well as comparative effectiveness research.

"We are trying to marry EHR data with claims data to figure what medicines are doing in large patient populations," Dr. Labkoff says.

At Novartis, Timothy Wright, global head of development, says the company is leveraging some of the newest technologies in pharmaceuticals via its Trials of the Future initiative, which aims to revolutionize the way it conducts clinical trials, improve operational efficiency, and reduce the time to recruit without compromising quality or patient safety.

"We believe these technologies will ultimately help us develop more targeted data, reach more patients, and provide new drug development with streamlined timelines and lower costs," he says.

Mr. Wright says mobile technology can improve coordination and quality of clinical studies, while also enhancing R&D productivity.

"Electronic sensors that capture clinical data have the potential to remotely help patients manage their participation in studies from anywhere, increasing convenience for patients while at the same time reducing costs," he says. PV

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