FOLLOW THE MONEY:
Big Grants in Biomedical Computing

By Kristin Sainani, PhD

Several biomedical computing projects received multi-million dollar funding in the fall of 2011, including efforts to: simulate the cardiac physiology of the rat; build a state-of-the-art DNA simulation toolkit; build an artificial pancreas; and mine data for clues about psychiatric disease. The initiatives will bring together diverse experts, datasets, or models to accomplish ambitious goals.

Modernizing the Lab Rat

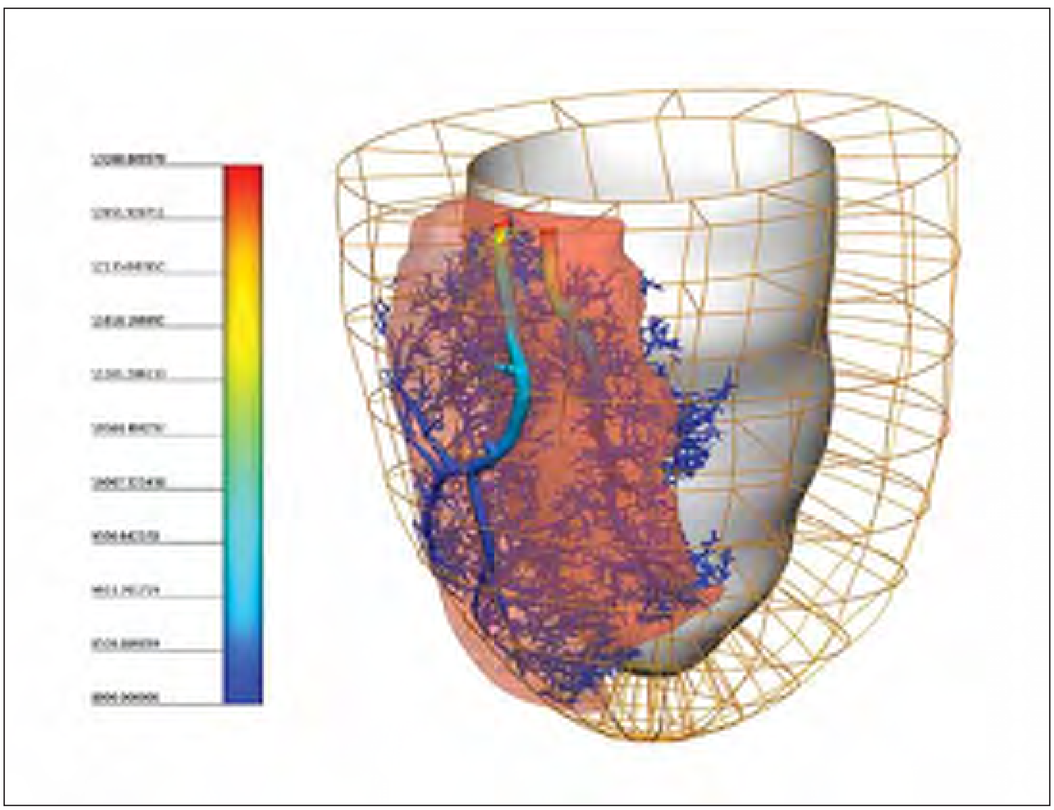
A new type of lab rat—one simulated on a computer—will help scientists tease out the multifactorial causes of cardiovascular disease, thanks to a $13 million grant from the National Institutes of Health. The grant establishes a new National Center for Systems Biology.

"The goal of the Virtual Physiological Rat Project is to understand how high level traits, such as hypertension, arise from multiple inputs at multiple levels, including genetic variation and environmental perturbations," says principal investigator **Daniel A. Beard, PhD**, professor of physiology at the Medical College of Wisconsin.

Beard's team will build detailed computational models of the rat's heart, vasculature, and kidneys. "In some cases, we're drilling down to the individual cells and individual transporters and pumps that are involved in the operation of the organ and integrating all the way up to the whole organ," Beard says. Though sophisticated models already exist for some of the pieces—for example, the heart is the best modeled of all organs—they will have to adapt these models for rats in general and for particular genetic strains of rats.

"The biggest novelty and the biggest challenge is this cycle of making a prediction and then making a rat," Beard says. "We're doing this on an unprecedented scale."

Once the models are refined, Beard's team will breed new strains of rats *in silico* and subject them to different environmental stressors to predict which combinations of genes and environment lead to hypertension, heart failure, kidney failure, and other cardiovascular diseases. Then his team will test the most interesting predictions with experiments in real rats. "The biggest novelty and the biggest challenge is this cycle of making a prediction and then making a rat," Beard says. "We're doing this on an unprecedented scale."



***Virtual Rat Heart:** A computational model of the rat heart that will be incorporated into the Virtual Physiological Rat Project. Courtesy of: Daniel Beard, Medical College of Wisconsin.*

Simulating DNA at All Levels

A new DNA simulation toolkit will be the first to span all levels of resolution. Funded by a $3 million grant from the European Research Council, the toolkit will help scientists gain new insights into how DNA functions, including how genes are regulated and how they interact with the environment (epigenetics).

"The overall goal is to develop a complete theoretical and computational framework to be able to simulate DNA in a multiscale manner, from atomistic to chromatin scale," says principal investigator **Modesto Orozco, PhD**, senior professor and head of IRB Barcelona's Molecular Modeling and Bioinformatics group and director of life sciences at the Barcelona Supercomputing Center. "If we are successful, we will define a unique series of tools covering the entire time and size scale of DNA."

The toolkit will help researchers answer questions about how nucleic acids work "from the point of view of the first principles

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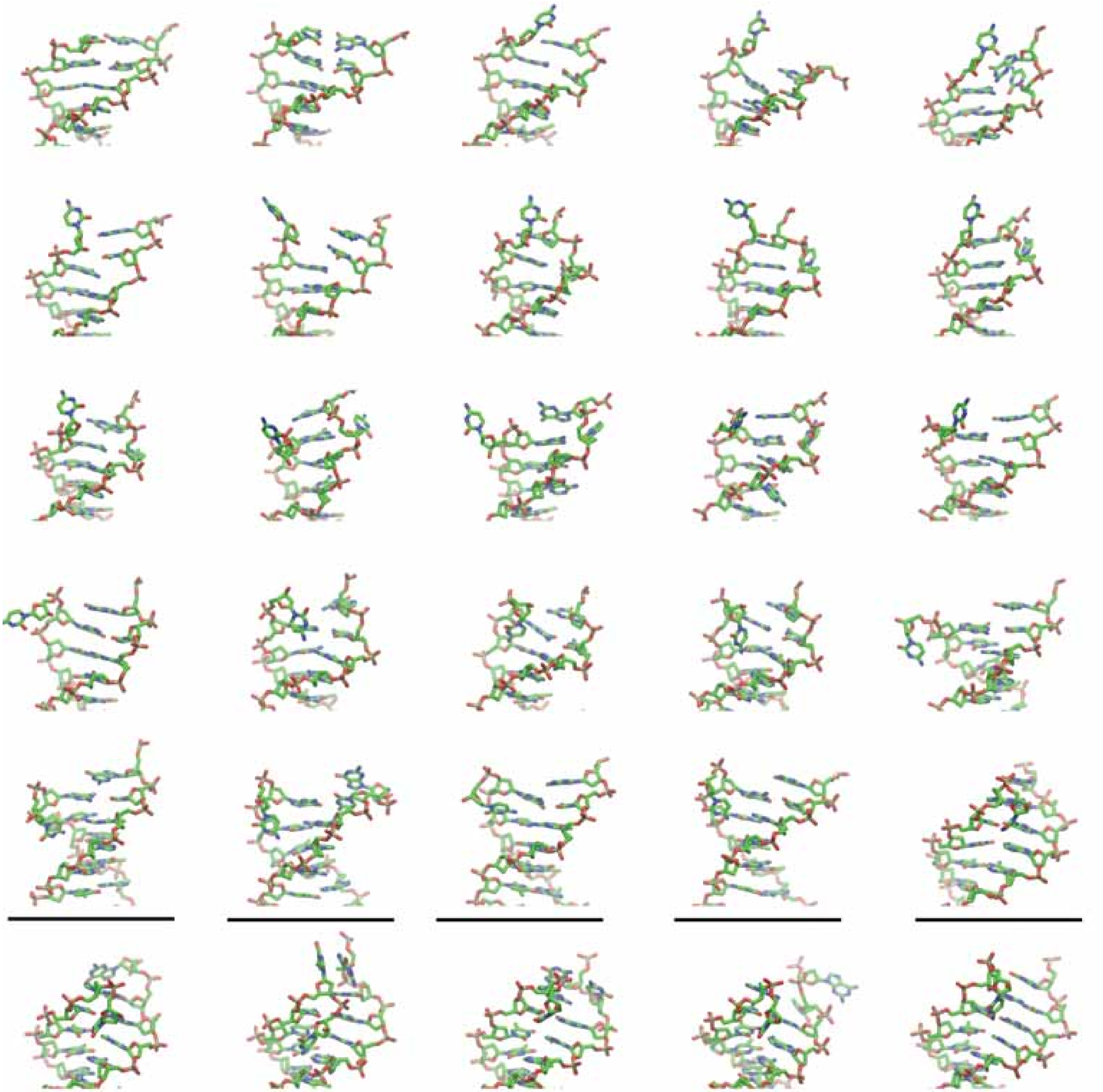

***DNA Unveiled**: This computer simulation (which precedes from left to right and top to bottom) gives insights into the mechanism by which DNA starts to unfold. Courtesy of: A. Pérez, IRB Barcelona.*

of physics"— for example, how the physical properties of chromatin impact DNA regulatory mechanisms. "We will have to overcome major challenges at the frontier between the different simulation levels," Orozco says. "It is a very ambitious project."

Advancing the Artificial Pancreas

A device that mimics the pancreas' job may soon be a reality, thanks in part to a $4.5 million grant from the National Institutes of Diabetes, Digestive, and Kidney Diseases. The device—which features a state-of-the-art control algorithm—would free patients with type I diabetes from their current regimen of manual glucose monitoring and insulin injections.

"We've assembled an international dream team," says principal investigator **Frank Doyle**, **PhD**, professor of chemical engineering and of electrical engineering at the University of California, Santa Barbara. His team includes scientists from Italy, the Mayo Clinic, the University of Virginia, and the Sansum Diabetes Institute. Several groups have prototypic artificial pancreas devices in testing. But Doyle's team aims to bring the first sophisticated device into real-world use. "The exciting part of this grant is the possibility of getting beyond in-clinic prototyping," Doyle says.

The devices consist of an ipod-sized computer, glucose sensor, and insulin pump (which can be attached to the arms, legs, or stomach). A simple version (made by Medtronic) is already on the market in England: the system monitors glucose and shuts off the pump automatically when blood sugar drops too low. But Doyle's team is going beyond such a simple feedback loop, using an advanced algorithm called "model predictive control" (which is also used in aerospace controls). "We forecast and anticipate insulin needs," rather than simply responding to current glucose levels, Doyle says. The algorithm will even adapt to a patients' individual patterns, such as the timing of exercise and meals, as well as to individual variation in insulin metabolism, Doyle says. "It won't be a one-size fits all algorithm; it will be tailored and customized to the individual patient."

Synthesizing Data on Mental Illness

A new center at the University of Chicago will explore the origins of psychiatric disease by integrating existing data from diverse disciplines and across multiple sites. The center is the newest Silvio O. Conte Center for Neurosciences Research and the first with a computational focus. It received $14 million in grants from the National Institutes of Mental Health and the Chicago Biomedical Consortium.

"We have a lot of datasets from different communities that have never been analyzed within the same model before. It's an exciting research opportunity," says principal investigator **Andrey Rzhetsky**, **PhD**, professor of medicine and human genetics at the University of Chicago Medical Center.

Rzhetsky will head a consortium of 15 lead investigators from seven schools that will bring together clinical data, genetic linkage data, gene pathway data, functional data on genes and proteins, drug data, and drug-gene interaction data. "The main premise of the center is to get together wonderful specialists in different disciplines; make them talk to each other; design models that span all datasets; and make predictions that can be tested experimentally."

Rzhetsky's team will attempt to unearth novel connections between genes, environment, and disease phenotypes, as well as between the disorders themselves. For example, Rzhetsky and colleagues have previously shown that autism, schizophrenia and bipolar disorder have considerable genetic overlap. "You can get a lot more from joint analysis of several phenotypes than from a single phenotype," Rzhetsky says. □

LEVERAGING SOCIAL MEDIA: For Biomedical Research

By Katharine Miller

It has become commonplace for people to use social media to share their healthcare stories, seek a community of individuals with the same diseases, and learn about treatment options. All this Internet activity also produces data that can be used for research.

"In the networked world, who cures cancer? We all do," says **Paul Wicks**, **PhD**, director of research and development at PatientsLikeMe, a site where people diagnosed with serious life-changing illnesses can record and share information.

For PatientsLikeMe and a number of other sites, doing biomedical research using data gathered online is part of the business plan. With names such as 23andMe, MedHelp, TUDiabetes, myMicrobes.eu, CureTogether, these sites blend community building with information gathering. They then turn to computational approaches, such as data mining and natural language processing (NLP), to analyze the information gathered.

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This crowd-sourced research often reaches into realms that otherwise wouldn't or couldn't be studied, due to a lack of either appropriate information or financial support. Moreover, with their access to large populations of both cases and controls, these sites are rapidly producing clinical research results. That they function in a landscape of ever-changing and growing data just makes the process that much more interesting.

Doing Research That Others Can't or Won't

On social media healthcare sites such as PatientsLikeMe, people record and share information about their diseases. This self-re-