Computational medicine enhances way doctors detect, treat disease

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Computational medicine, a fast-growing method of using computer models and sophisticated software to figure out how disease develops—and how to thwart it—has begun to leap off the drawing board and land in the hands of doctors who treat patients for heart ailments, cancer and other illnesses. Using digital tools, researchers have begun to use experimental and clinical data to build models that can unravel complex medical mysteries.

These are some of the conclusions of a new review of the field published in the Oct. 31 issue of the journal *Science Translational Medicine*. The article, "Computational Medicine: Translating Models to Clinical Care," was written by four Johns Hopkins professors affiliated with the university's Institute for Computational Medicine.

The institute was launched in 2005 as collaboration between the university's Whiting School of Engineering and its School of Medicine. The goal was to use powerful computers to analyze and mathematically model disease mechanisms. The results were to be used to help predict who is at risk of developing a disease and to determine how to treat it more effectively.

In recent years, "the field has exploded," institute director Raimond Winslow said. "There is a whole new community of people being trained in mathematics, computer science and engineering, and they are being cross-trained in biology. This allows them to bring a whole new perspective to medical diagnosis and treatment. Engineers traditionally construct models of the systems they are designing. In our case, we're building computational models of what we are trying to study, which is disease."

Looking at disease through the lens of traditional biology is like trying to assemble a very complex jigsaw puzzle with a huge number of pieces, he said. The result can be a very incomplete picture.

"Computational medicine can help you see how the pieces of the puzzle fit together to give a more holistic picture," Winslow said. "We may never have all of the missing pieces, but we'll wind up with a much clearer view of what causes disease and how to treat it."

Biology in both health and disease is very complex, Winslow added. It involves the feed-forward flow of information from the level of the gene to protein, networks, cells, organs and organ systems. This is already complex, he said, and to make matters even more difficult, it also involves feed-back pathways by which, for example, proteins, mechanical forces at the level of tissues and organs, and environmental factors regulate function at lower levels such as the gene.

Computational models, Winslow said, help us to understand these complex interactions, the nature of which is often highly complex and non-intuitive. Models like these allow researchers to understand disease mechanisms, aid in diagnosis, and test the effectiveness of different therapies. By using computer models, he said, potential therapies can be tested "in silico" at high speed. The results can then be used to guide further experiments to gather new data to refine the models until they are highly predictive.

"Our intent in writing this journal article was to open the eyes of physicians and medical researchers who are unfamiliar with the field of computational medicine," said Winslow, who is first author of the

Science Translational Medicine overview. He also wanted to describe examples of computational medicine that are making their way out of research labs and into clinics where patients are being treated. "This transition," he said, "is already under way."

Here are some examples described in the paper:

- Advanced mathematical models are allowing researchers to better understand how networks of molecules are implicated in cancer and then use this knowledge to predict which patients are at risk of developing the disease.
- A discipline called computational physiological medicine is using computer models to look at how biological systems change over time from a healthy to an unhealthy state. This approach is being used to help develop better treatments for cancer, diabetes and heart disease.
- Computational anatomy uses medical images to detect changes, for example, in the shape of various structures in the brain. Researchers have found shape changes that appear to be associated with Alzheimer's disease and neuropsychiatric disorders, such as schizophrenia.
- Computational models of electrical activity in the heart are on their way to being used to guide doctors in preventing sudden cardiac death and in diagnosing and treating those at risk for it.

Winslow said many challenges must still be overcome before computational medicine becomes a routine part of patient care. But, as one example of how quickly the field is being embraced, he points to a new iPad application that uses computational anatomy methods to guide doctors in delivering deep brain stimulation to patients with Parkinson's disease.

"We are poised at an exciting moment in medicine," he writes in the journal article. "Computational medicine will continue to grow as a discipline because it is providing a new quantitative approach to understanding, detecting and treating disease at the level of the individual."

More information: stm.sciencemag.org/content/4/158/158rv11.full

Provided by Johns Hopkins University

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