

NEW COMPUTER PROGRAMS COULD HELP ACCELERATE DRUG DISCOVERY

University Of Maryland School of Medicine Researchers Develop Approach to Identify Key Features Determining Protein Function

Baltimore, Md., January 16, 2018 – Many drugs work by inhibiting protein enzymes associated with a particular disease. Unfortunately, the same drugs can inhibit protein enzymes unrelated to the disease, resulting in harmful side effects. One potential solution is to better identify structural features that determine a protein enzyme's function.

Now, a team headed by a computational biologist at the University of Maryland School of Medicine (UMSOM) has developed a suite of computer programs that cull through data on structure and genomic sequencing to identify the features that distinguish one enzyme from similar enzymes. This research has the potential to significantly improve drug discovery, allowing scientists to develop more effective drugs, more quickly.

“This new approach allows proteins to be analyzed at a much deeper, more specific level,” says **Andrew F. Neuwald**, PhD, Professor of Biochemistry & Molecular Biology, a senior scientist at the Institute for Genome Sciences (IGS) at UMSOM, and the lead author of the paper describing the new method. ***“This method provides clues regarding sequence and structural features responsible for a protein's specific biological function.”***

The paper was published this week in the journal *eLife*. Dr. Neuwald collaborated on the work with L. Aravind, PhD, and Stephen F. Altschul, PhD, two senior investigators at the National Center for Biotechnology Information at the National Institutes of Health.

In the paper, the investigators used this approach to identify the key features of various enzymes: N-acetyltransferases, P-loop GTPases, RNA helicases, synaptojanin-superfamily phosphatases and nucleases, and thymine/uracil DNA glycosylases. The results revealed striking and previously overlooked structural features likely associated with each protein's function. This has the potential to lead researchers to new ways of designing drugs that have fewer unintended, harmful side effects.

The two main programs are BPPS (Bayesian Partitioning with Pattern Selection), and SIPRIS (Structurally Interacting Pattern Residues' Inferred Significance). The programs and source code are freely available and require only a minimal knowledge of Linux, thereby making this approach widely accessible to other researchers. This approach will also be useful for protein engineering and for understanding the molecular basis of many human diseases.

The three researchers each brought something different to the work. Dr. Neuwald, who has worked on protein analysis for years, has a varied background, with experience in molecular biology, computer science and Bayesian statistics. Dr. Aravind is a well-known computational biologist with a broad knowledge of protein structure and function. Dr. Altschul, whose formal training is in mathematics, was the first author on two landmark publications describing the popular sequence database search programs BLAST and PSI-BLAST.



“This work combines some of the most fertile and dynamic areas in current science: protein analysis and big data,” said **E. Albert Reece, MD, PhD, MBA**, University Executive Vice President for Medical Affairs and the John Z. and Akiko K. Bowers Distinguished Professor and Dean, University of Maryland School of Medicine. *“In its creative linkage of analytics, statistics and genetics, this work points the way forward for a number of significant fields. This is exciting work, and it clearly has clinical potential.”*

More information:

Learn more about the [programs](#).

The paper is [online here](#).

About the Institute for Genome Sciences

The Institute for Genome Sciences, founded in 2007, is an international research center within the University of Maryland School of Medicine. Comprised of an interdisciplinary, multidepartment team of investigators, the Institute uses the powerful tools of genomics and bioinformatics to understand genome function in health and disease, to study molecular and cellular networks in a variety of model systems, and to generate data and bioinformatics resources of value to the international scientific community.
igs.umaryland.edu

About the University of Maryland School of Medicine

Commemorating its 210th Anniversary, the University of Maryland School of Medicine was chartered in 1807 as the first public medical school in the United States. It continues today as one of the fastest growing, top-tier biomedical research enterprises in the world -- with 43 academic departments, centers, institutes, and programs; and a faculty of more than 3,000 physicians, scientists, and allied health professionals, including members of the National Academy of Medicine and the National Academy of Sciences, and a distinguished recipient of the Albert E. Lasker Award in Medical Research. With an operating budget of more than \$1 billion, the School of Medicine works closely in partnership with the University of Maryland Medical Center and Medical System to provide research-intensive, academic and clinically-based care for more than 1.2 million patients each year. The School has over 2,500 students, residents, and fellows, and nearly \$450 million in extramural funding, with most of its academic departments highly ranked among all medical schools in the nation in research funding. As one of the seven professional schools that make up the University of Maryland Baltimore campus, the School of Medicine has a total workforce of nearly 7,000 individuals. The combined School and Medical System (“University of Maryland Medicine”) has an annual budget of nearly \$6 billion and an economic impact in excess of \$15 billion on the state and local community. The School of Medicine faculty, which ranks as the 8th-highest public medical school in research productivity, is an innovator in translational medicine, with 600 active patents and 24 start-up companies. The School works locally, nationally, and globally, with research and treatment facilities in 36 countries around the world. Visit medschool.umaryland.edu/



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