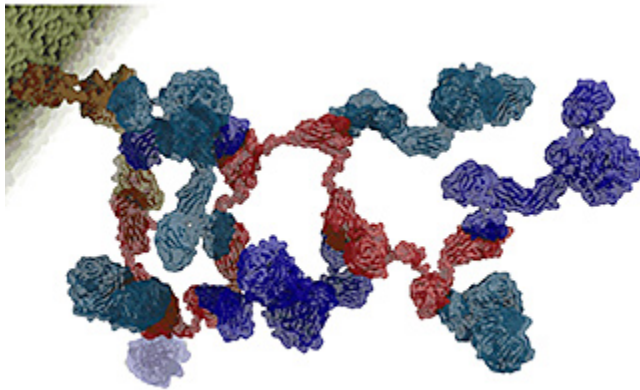


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Cellulosomes: One of Life's Strongest Biomolecular Bonds Discovered with Use of Supercomputers

Linda Barney



Prominent computational biologist Klaus Schulten and his team at the University of Illinois at Urbana-Champaign, working in collaboration with Professor [Hermann Gaub](#) ^[1] and his Single Molecule Physics group at the University of Munich, discovered one of nature's strongest mechanical bonds on a protein network called cellulosomes. The cellulosome network includes bacteria that contain enzymes that can effectively dismantle cellulose and chemically

catalyze it. This discovery was aided by the use of supercomputers to simulate the interactions at the atomic level.

Schulten states, "Our findings are of value for developing catalysts for a second generation of biofuels that can cheaply use agriculture bio-waste and other materials, rather than food resources, to develop a fuel like ethanol. The bacteria and processes we are researching are also of great interest for biology and biomedical use, because they play a key role in human and animal metabolism. There is an increased interest in the natural habitat of these bacteria and how one can optimize the use of bacteria in these processes."

The Cellulosome network

Schulten's group is doing research that looked at how digestion occurs in the rumen (stomach) of a cow and how cellulosome-bacterial enzymes could degrade in modern biofuel production lignocellulosic biomass, which includes plant fibers, such as various plants and wood. The research focused on specialized bacteria that produce multi-component protein networks called cellulosomes.

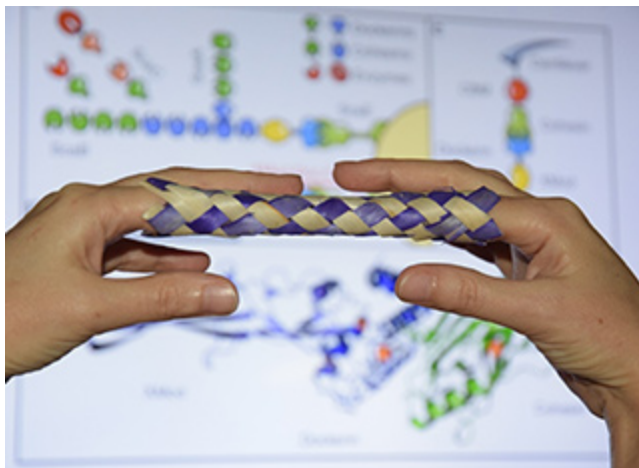
Schulten describes cellulosomes as a complex system that provides a mechanical handle for bacteria acting on the cellulose fibers. The cellulosome system bacteria foothold (anchor) to the cellulose fiber with finger-like protrusions on the surface of the bacterial cell bodies that have enzymes at the tips of the "fingers" that catalyze and digest fibers. There can be hundreds of proteins that build these anchor and finger systems that make up the cellulosomes.

HPC aids in discovery of life's strongest bonds in cellulosome system

The bacterium *Ruminococcus flavefaciens* found in a cow's stomach, uses proteins called Cohesin and Dockerin that make up the mechanical connection points of the cellulosome system. Schulten's team realized that it was crucial to have an easy way to form and break up the Cohesin and Dockerin components but that, under mechanical load, the two components must hold together tightly.

"In our research, we found that, once mechanical stress is applied, the Cohesion/Dockerin bond becomes very strong. This is analogous to an example of the Chinese finger trap. If you put your fingers in both sides of the trap and pull gently, then it is easy to remove your fingers. However, if you pull quickly, your fingers get trapped," indicates Schulten.

• **CONFERENCE AGENDA ANNOUNCED:** The highly-anticipated educational tracks for the 2015 R&D 100 Awards & Technology Conference feature 28 sessions, plus keynote speakers Dean Kamen and Oak Ridge National Laboratory Director Thom Mason. [Learn more](#) [2].



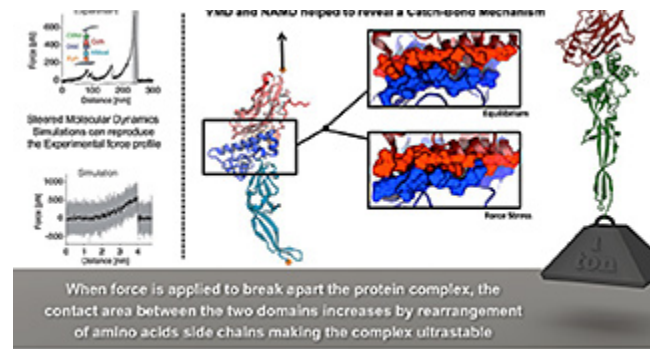
When you apply mechanical force, the surface between Cohesion and Dockerin rearranges geometrically so that they fit together much better, forming a mechanism known as a catch-bond, indicates Schulten. "The research showed that the biomolecular interaction between Cohesin and Dockerin withstands forces of 600-750 piconewtons (pN) [3], making it one of the strongest biomolecular interactions reported, equivalent to half the mechanical

strength of a strong chemical bond," according to the research [findings](#) [4].

Continued research of the bond

Ultrastable Biomass Adhesion Complex

Ed Bayer at the Weizmann Institute in Israel [5], a research pioneer who has been studying the structural details of cellulosomes since the early 1980s, is actively involved in the team's research of the physical mechanisms associated with cellulosomes. Their research has found that cellulosomes adopt a certain hierarchy of organizing themselves with connections to the bacterial cell wall in one layer, additional layers of connection, the anchoring point and tips with enzymes. Schulten and collaborators will continue investigating the physical properties that exist in various parts of the cellulosome to determine why some bonds are stronger and show more of the catch-bond mechanism.



Cellulosome research not possible without supercomputers

The cellulosome research was done mainly using the Stampede supercomputer at the Texas Advanced Computing Center (TACC) [6] — a system based on Intel Xeon Phi Coprocessors — the Blue Waters supercomputer (National Center for Supercomputing Applications (NCSA) [7] at the University of Illinois at Urbana-Champaign), and the Extreme Science and Discovery Environment (XSEDE) [8] virtual system funded by the National Science Foundation (NSF.) This kind of research is not possible without simulation on a supercomputer.

Schulten states, “Today’s high-performance computers are very important for our research, because they allow us to see through simulations what every atom is doing. In addition, the simulations let us see more than a static picture, namely the dynamic processes involved. Computers can be considered a computational microscope with very high resolution. They can work in situations where there is no experimental microscope available.”

Rafael Bernardi (post-doctoral researcher in the Schulten group and the key computational researcher on the cellulosome project) indicates that it takes a huge amount of computer resources to do their cellulosome dynamic simulations. The work involved for the cellulosome biofuel research required between 10 to 20 million supercomputer units (SUs) for computing hours.

“We have found that it is better to use technology-advanced supercomputers, such as the Stampede supercomputer at TACC, because computations can be faster and cheaper than other supercomputers. The Stampede supercomputer processors at TACC are much faster than other those of other supercomputers, because of its efficient network and better processing when we select to run it with software that can take advantage of the Intel Xeon Phi coprocessor. As an

example, I can run 7 nanoseconds (ns)/day of a cellulosome system on Stampede without using code to run on Intel Xeon Phi. When using it, with the same number of nodes, I get 11.2 ns/day. So, the Intel Xeon Phi coprocessor saves about 35 percent of computer time, which provides more than a 50-percent speed up," explains Bernardi.

NAMD and VSD software aid in cellulosome research

Supercomputers are not the only tools required to perform biomolecular research, specialized software is also required. In 1995, Schulten's team at the University of Illinois developed the NANoscale Molecular Dynamics program (NAMD) [9] and the Visual Molecular Dynamics (VMD) programs to help visualize and analyze biomolecular systems. The NAMD and VMD programs are available for free and are used by scientists globally from the richest countries to the poorest nations of the world.

"NAMD is a parallel molecular dynamics code [10] designed for

high-performance simulation of large biomolecular systems. Based on Charm++ parallel objects, NAMD scales to hundreds of cores for typical simulations and beyond 200,000 cores for the largest simulations. NAMD uses the popular molecular graphics program VMD for simulation setup and trajectory analysis."

Schulten's group developed over two decades both NAMD, as well as VMD, and used the programs in their cellulosome research. They achieved faster processing by using NAMD with an Intel compiler and specifying options in the configuration script to take advantage of the Intel Xeon Phi coprocessor and MIC Architecture.

Why HPC matters: What this research means for biofuel production

Previous cellulosome research by other groups compared two bacteria with the same enzymes; one had enzymes attached to cellulosomes, while the other was free. The bacterium that is attached to cellulosomes is approximately 50 times more efficient at breaking down fiber than the one that doesn't have cellulosome attachment. This has major implications for being able to break

TACC Stampede Supercomputer Specifications

The TACC Stampede system is a 10 PFLOPS (PF) Dell Linux Cluster based on 6400+ Dell PowerEdge server nodes, each outfitted with 2 Intel Xeon E5 processors and an Intel Xeon Phi Coprocessor. The aggregate peak performance of the Xeon E5 processors is 2+PF, while the Xeon Phi processors deliver an additional aggregate peak performance of 7+PF. Stampede provides large memory and large data transfer capabilities.

down biomass fibers and will be a major area of research in biofuel development, as well as biomedical applications.

Bernardi states, "There is great interest in this research from companies developing second-generation biofuels, because it is currently very expensive to create biofuels from agricultural waste. If you can use cellulosomes to help breakdown biomass, then the cost of producing biofuels from plant materials can be reduced."

The Future: Applications of cellulosome research for bio-medicine

There are also possible bio-device and biomedical applications for Schulten's cellulosome research. Schulten directs The Center for Biomolecular Modeling at the Beckman Institute which has done National Institute of Health (NIH) research for more than 25 years. Schulten states, "The Center is planning future research on gut bacteria in animals and humans, tissue properties and the role of cellulosomes, bacteria and enzymes activity in digestion and providing nutrition. We will have a major initiative geared toward biomedical applications and will continue work using supercomputers to model and simulate cellular activity."

Research done by Professor Isaac Cann, from [Energy Biosciences Institute at University of Illinois at Urbana-Champaign](#) [11] has focused on bacteria that are common between animals and humans and discovered some of the same enzymes in the human gut that are also found in the cow rumen (second stomach) that help to more efficiently break down food. Research will continue in this area.

"Some possible applications if the research is successful include designing bacteria with these enzymes and adding them to products, such as yogurt, to aid in human digestion. This is a fascinating area of study and could have some wide-range benefits," states Bernardi.

The use of HPC systems, such as the Intel Xeon Phi-based Stampede supercomputer at the [Texas Advanced Computing Center \(TACC\)](#) [6], for investigating cellulosomes is yet another indisputable example of how HPC is transforming the world in which we live.

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Links:

- [1] http://www.biophysik.physik.uni-muenchen.de/personen/group_leader/gaub/index.html?
- [2] <http://rd100awards.com/?cmpid=horizontalcontent>
- [3] <http://www.aqua-calc.com/what-is/force/piconewton>
- [4] <http://www.nature.com/ncomms/2014/141208/ncomms6635/full/ncomms6635.html>
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