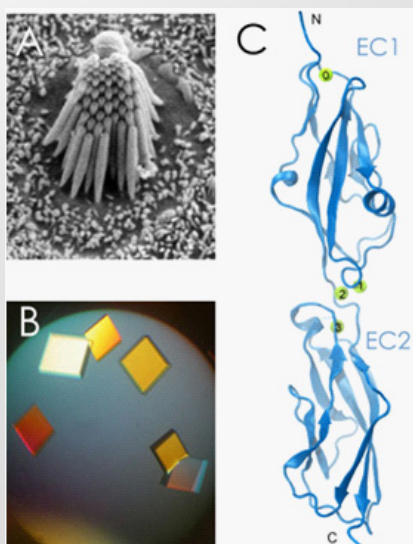


Sound Science

Simulations at TACC and NCSA show how subtle mutations cause deafness



Three views of the cadherin-23 protein involved in sound transduction. (A) a scanning electron micrograph image of a hair bundle (bullfrog sacculus). (B) Crystals of cadherin-23, and (C) a structural model of cadherin-23 obtained through X-ray crystallography.

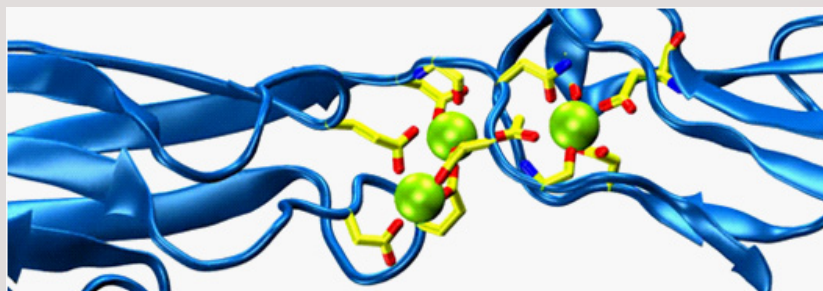
The ear is a mysterious instrument. Tiny machinery in the cochlea transform sound waves in a process called “transduction,” which the brain recognizes as our name or a ringing telephone.

Scientists at Harvard Medical School have produced the first x-ray crystallographic structure of a main protein in the hearing process: cadherin-23. This protein opens the hair cells so ions can pass through the membrane. Importantly, cadherin-23 is known to malfunction in some individuals with hereditary deafness.

The Harvard research team used the Ranger supercomputer at the Texas Advanced Computing Center to determine the 3D structure of cadherin-23. They also simulated the behavior of each atom in the protein as it reacted to sound waves.

“Using Ranger, we were able to see where calcium is bound, how it’s bound to the protein, and how calcium modulates the elasticity of the protein,” said Marcos Sotomayor, a research fellow in the Neurobiology Department at Harvard Medical School. “That’s something that cannot be done with any other technique.”

According to Sotomayor, the simulations showed how mutations to the protein change the way it binds calcium, making it weak. When the weakened proteins snap, it causes deafness in some individuals. The results of the computational experiments are being validated through laboratory experiments, and the knowledge will help doctors test and treat certain types of hereditary deafness.



Harvard researchers used X-ray crystallography to determine the molecular structure of cadherin-23, an important protein involved in hearing, with and without a mutation causing deafness.

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