DNA crystals are a bacterium's best friend

For many bacteria, when the going gets tough, the tough stop growing. Faced with a lack of nutrients, microbes may shut down many of their cellular activities, such as replication, and simply wait for better days.

During this so-called stationary phase, some bacteria shield their DNA from degradation by embedding the genetic material within crystals of a protein called Dps, Abraham Minsky of the Weizmann Institute of Science in Rehovot, Israel, and his colleagues report in the July 1 NATURE.

"It's an amazing possibility. This could represent a new paradigm for how cells protect themselves in situations of starvation, dryness, or whatever," says microbiologist John R. Battista of Louisiana State University in Baton Rouge.

The story of Dps begins in 1992, when a research team led by Roberto Kolter of Harvard Medical School in Boston described the novel DNA-binding protein produced by nutrient-deprived colonies of the bacterium *Escherichia coli*. "In stationary phase, Dps is one of the most abundant proteins in the bacteria," notes Steven E. Finkel, a Harvard colleague of Kolter.

Kolter's team subsequently found that the protein protects the DNA from highly reactive oxygen-containing molecules called free radicals. Because many bacteria other than *E. coli* also make proteins resembling Dps, Kolter and his colleagues speculated that they had found a common bacterial strategy to safeguard DNA.

Left unresolved was the question of how Dps exerts its protection. In 1997, the team deduced the shape of Dps and concluded that 12 copies of the protein normally aggregate to form a hollow, spherical complex. Since the structure of Dps resembles that of an iron-binding protein called ferritin, the scientists suggested that the Dps complex sequesters iron within it, preventing the metal from helping to produce DNA-damaging free radicals.

The new work reveals another explanation for Dps' protective talents, one not incompatible with the iron-sequestering theory. Minsky and his colleagues, working with Kolter's group, found that when they added DNA to a solution of Dps, the protein spheres aggregated and quickly formed crystals.

Microscopic analysis revealed that the Dps crystals had incorporated the DNA within their structure. This biocrystallization appears to offer an effective method of preserving DNA integrity, says Minsky.

He and his colleagues next studied an *E. coli* strain genetically engineered to overproduce the Dps protein. Under normal growth conditions, no Dps crystals formed within the bacteria. When starved, however, the microbes created large Dps crystals like those observed in the test-tube experiments. Similar, though smaller, crystals arose in normal *E. coli* deprived of nutrients.

The starvation-induced crystallization reverses without damaging the microorganisms. "Once nutrients are supplied, [the crystals] disappear within a very short timescale, and the bacteria are viable and growing," says Minsky.

While the Dps spheres appear to crystallize by packing together like oranges in a crate, how bacterial DNA integrates itself into the crystals remains unclear. "We believe DNA wraps around the outside of the [Dps] protein complexes," says Finkel, noting that such a scenario would allow Dps to separate DNA from any iron within the spheres.

Since actively growing bacteria have free-floating Dps complexes, Minsky's group has begun to look for molecules within starved bacteria that trigger the unusual crystallization.

Why haven't scientists taken note of this process in their decades of research with *E. coli*? Perhaps because investigators tend to study growing bacteria. "The stationary phase of the bacterial life cycle has not really been appreciated until recently," notes Finkel. —*J. Travis*

A pitch for decoding frequency more simply

The music of Mozart is surely inspiring. However, one seldom hears even the most avid music enthusiast exclaim, "Ah, the 800-hertz fundamental in those violins is spectacular!"

One reason is that the human brain translates the numerical frequency of a sound into a qualitative characteristic called pitch—middle C, for example. How and where this handy translation takes place has long been murky. Now, researchers in Spain and Italy have proposed a new explanation for the brain's ability to sort out complex sounds—those that contain tones of different frequencies—such as music or voices. If the theory takes hold, it may challenge scientists' basic understanding of how the brain organizes hearing.

The aspect of a complex sound that largely defines its pitch is its lowest-frequency tone, or fundamental. Yet, people easily perceive a sound's pitch from the overtones when its fundamental is missing, as sometimes happens, for example, when they listen to a small radio.

Since the 1960s, researchers have developed several models to account for pitch perception, but all have shared the idea that the brain sorts through incoming overtones one by one until it has enough information to infer a missing fundamental. This process demands a lot of resources, and scientists believe it could only take place in the auditory cortex, the final and most powerful part of the brain's hearing system.

In the June 28 PHYSICAL REVIEW LETTERS, physicist Julyan H.E. Cartwright of the Higher Council for Scientific Research in Granada, Spain, and his colleagues propose an alternative theory, in which pitch perception could occur earlier in the auditory process.

The team suggests that somewhere in the hearing system, two or more incoming overtones of different frequencies stimulate a specialized bundle of nerve cells called an oscillator, similar to structures found elsewhere in the brain. The oscillator then resonates at a frequency derived from the incoming tones. The researchers theorize that the brain uses that resonance frequency to determine the missing fundamental.

So far, Cartwright says, the theory appears to explain studies of how people perceive shifts in pitch as well as more elaborate models do. The new model, however, hasn't yet been applied to other data, some of which may provide tougher tests of the theory, he notes.

The researchers believe that if further data support the theory, the new model may lead to medical applications, such as better hearing aids. "The more we know about how we process sound, the more we can do to correct things when defects occur in the auditory system," Cartwright says.

Some scientists are skeptical of the theory, however. William M. Hartmann of Michigan State University in East Lansing observes that the model requires interaction between overtones. In experiments, though, researchers have observed that people perceive missing fundamentals best when the accompanying overtones travel through the auditory system along separate channels.

Study coauthor Diego L. González of the Lamel Institute in Bologna, Italy, however, notes that signals that travel along separate nerve pathways through most of the auditory system may still converge and mingle at specialized sites along the way.

Acoustic psychologist Frederic L. Wightman of the University of Wisconsin-Madison argues that the new model doesn't explain how representations of musical tones could interact in this way in the neural depths of the auditory system, where signals operate not as waves but as all-or-nothing electrical spikes.

Cartwright responds that the visual, olfactory, and memory systems use neural oscillators to emit pulses at varying frequencies. "It's not saying anything outrageous to say these nerve cells would oscillate in response to incoming auditory signals," he says. —*S. Carpenter*