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How DNA Can Take on the Properties of Sand or Toothpaste

When does DNA behave like sand or toothpaste?

When the genetic material is so densely packed within a virus, it can behave like grains of sand or toothpaste in a tube.

That's essentially what biophysicists at UC San Diego discovered when they began closely examining the physical properties of DNA jammed inside viruses.

Cutaway views of an empty virus shell (left) and one filled with DNA (right). Researchers found DNA can undergo a jamming transition during packaging like that occurring with granular materials such as sand. Image by Jinghua Tang and Timothy Baker, UC San Diego

"We found that under certain conditions, DNA behaves like toothpaste or sand, or like LEGO pieces when you try to put them back into the box and they don't seem to all fit," said Douglas Smith, a professor of physics at UC San Diego who headed a team that published its unusual discovery this week in the journal *Nature Physics*. "Strands of DNA not only contain genetic information, but can behave like 'granular' materials composed of randomly arranged particles (in this case, segments of the DNA string) that undergo what physicists call 'jamming' and 'unjamming' transitions, resulting in either solid-like or fluid-like behavior," he explained. "Sand pours out of a cup like a fluid, but comes to rest in a solid pile on the ground where the sand grains are jammed together. Toothpaste doesn't flow out of the tube until you squeeze it because it is contains tightly packed particles that are jammed but un-jam when you apply force so that the toothpaste can flow out.

Many viruses use a tiny "nanomotor" to pack DNA into their viral shells. But during this process, strands of DNA sometimes become jammed and the motor is unable to complete its job.

To better understand this process, Smith's team of researchers, which included molecular virologists at the University of Minnesota, cleverly applied the research of other physicists who characterized the processes of jamming (and un-jamming) a diverse set of materials consisting of randomly arranged particles—such as sand, pastes, foams and emulsions—to determine exactly what was happening to the viral DNA on a nanometer scale.

The researchers found to their surprise that DNA segments frequently become jammed within the virus when they are "sticky," or more attractive, a condition that physicists had previously predicted would make it easier to pack the DNA.

"On the contrary, we found that this condition inhibits packaging," said Smith. "We also found to our surprise that it is easier to pack the DNA in conditions where segments of the DNA string repel each other. Our measurements suggest this is because when the DNA is sticky to itself, it becomes packed in a very disordered, or messy, way which causes the DNA segments to become jammed. Repulsive interactions appear to help the DNA pack in a more ordered state where it does not become jammed."

DNA packaging is an essential step in the life cycles of many kinds of viruses, including adenoviruses, pox viruses and herpes viruses that infect humans. So could this discovery be used to inhibit DNA packaging and keep dangerous viruses from replicating and infecting us?

Possibly. The scientists found that addition of polyamines—small, positively charged molecules—causes viral DNA to become jammed and halt its packaging process.

"However, we did this in a test tube, not inside infected cells," said Smith. "For a chemical to be useful as a drug one also has to get it into cells and make sure that it doesn't interfere with normal healthy processes. But the basic idea of blocking viral assembly by causing the viral DNA to become jammed may be feasible. One could imagine that a special chemical could be developed that would specifically jam the viral DNA without affecting other processes in the cell. Such an approach would differ from ones currently used to combat viral infections, such as vaccines, which act by spurring one's immune system to attack viruses by recognizing their exterior shell, as opposed to targeting the packaging of the DNA."

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