Can Phase Change Droplets Deliver New Materials?

Omar Saleh's lab dives into the potentially big conductivity of tiny drops

In a recent paper, materials professor and department chair, **Omar Saleh,** and lead author, **Sam Wilken,** a postdoctoral researcher in his lab, described experiments they performed on a test system of engineered DNA molecules to develop fundamental understanding of dynamics related to liquid-liquid phase separation (LLPS), a subject whose relevance to biology has gained notice in recent years. LLPS occurs when an initially low-density homogeneous solution — one having uniform compositional properties throughout — undergoes a phase separation in which macromolecules such as proteins or nucleic acids condense into dense liquid droplets.

Even more recently, cellular bioengineers have discovered that LLPS may play an important role in how a cell functions. “The big idea is that LLPS inside, say, the nucleolus of a cell can modulate its function,” says Wilken. “How exactly cells function remains a large open question in biology, and this recent discovery indicates that physical processes are at work. But understanding cellular function is difficult in living systems, which are complex and hard to control, so we are investigating a model system and trying to identify what are the important parameters at play in this kind of process.”

In a distinct area of research, theoretical physicists recently discovered a new way to classify material structure: *hyperuniformity*. “The word *hyperuniform* indicates that there are not large variations in material structure in different locations,” Saleh explains.

Crystals, such as those in semiconductor materials, are said to exhibit hyperuniformity, because their constituent atoms are arranged in highly ordered lattices. Such materials are very good at transporting light or electrons in a straight line along the lattice grid of their connected atoms, but they are also *anisotropic,* meaning that if electrons are transported at a different angle of, say, 45 degrees off that line, the semiconductor’s properties will change, limiting microcircuit design possibilities.

While the transport properties of crystals have long been known, new materials are being discovered that display something called *disordered* hyperuniformity. “In a crystal, you’ll find an atom at every lattice site, but such a periodic arrangement does not exist in a liquid, where you might have a bit of structure around a particular atom, but if you look far enough away from that atom, the structure appears to be disordered, or random,” Wilken explains.

“A special system that displays both types of order — local randomness and long-range order — is described as disordered hyperuniform, combining essentially the best of both worlds: local isotropy [exhibiting the same disordered material properties in all directions] but, over longer distances, an ordered structure reminiscent of crystals,” he continues. “Systems displaying disordered hyperuniformity offer potentially extraordinary technological value. They could, for instance, enable the fabrication of new materials having transport properties superior to those of crystalline structures, and correspondingly fewer limitations in terms of the types of materials that could, in turn, be made from them.”

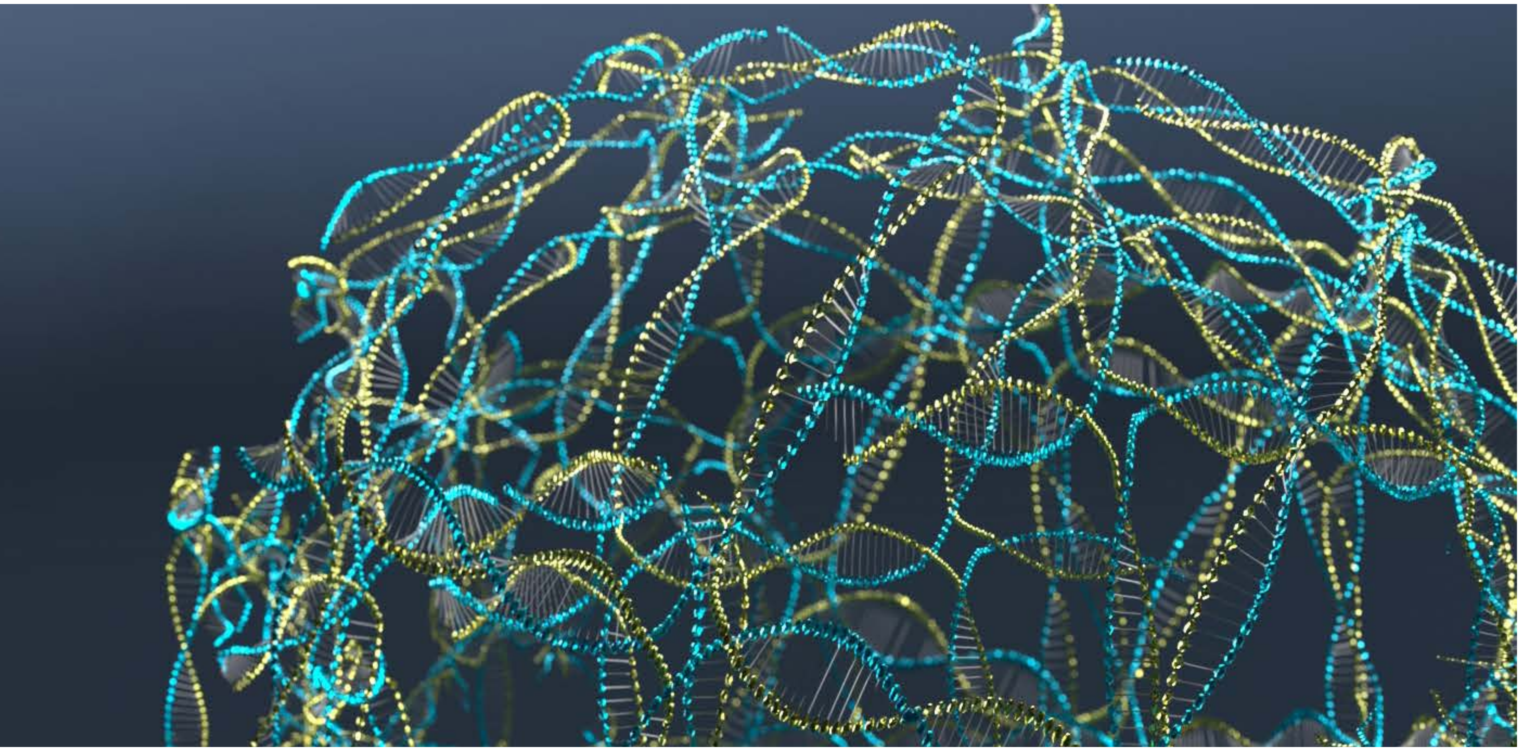
In their paper, titled “Spatial organization of phase-separated DNA droplets” and published in August in the journal *Physical Review X,* Saleh and Wilken report a “clear and surprising experimental result: a droplet structure that is both disordered *and* hyperuniform.”

Wilken notes that, while a handful of hyperuniform experimental systems have been described previously, “The new thing here is that we understand exactly *how it becomes* hyperuniform, as well as the characteristics of its hyperuniformity and what they tell us about how the system organizes itself. We describe systems that appear at first glance to be randomly distributed but that, upon analysis, display a hidden order over long length scales — hyperuniformity.”

The project involved performing experiments to uncover fundamentals relevant to the mechanisms underlying disordered hyperuniformity, which is pervasive in physics, chemistry, astronomy, and biology, and, accordingly, has applications in diverse systems in many areas of study.

In their experiments, Saleh and Wilken used synthetic engineered DNA nanostars, so-called because of their shape, an approach, Wilken says, that is “very powerful, because we can precisely control the shape, the size, and the interactions of the DNA system.”

They induced phase separation of the solution containing the nanostars, causing the initially free solution (of unbound nanostars) to condense and form, at the nanoscale, a dense, dynamic mesh of bound DNA nanostars — liquid



Artist's concept illustration (left) depicts twisted helixes of engineered DNA nanostars that form uniquely ordered patterns of liquid droplets. Described as "disordered hyper uniform," they are characterized by local randomness (as in a liquid) and long-range order reminiscent of a crystal's lattice of atoms.

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droplets, which are measured in microns, and hyperuniform ordered structures consisting of many droplets.

"It's an interesting multiscale problem," Wilken notes. "We have the DNA particle, on the order of nanometers; the droplet, on the order of microns, a hundred times larger; and then a scale one hundred times larger than that to determine the organization over many droplets. You go from essentially random liquid at the droplet scale to being very ordered on the long scale."

The researchers were also able to see the same hyperuniform structures develop in a dissimilar system in which the microstructure and the mechanisms that drove phase separation were very different from those in the nanostar solution. The identical long-range hyperuniform structure in different systems confirms that phase separation itself, not any particular characteristics of the DNA nanostar, is what drives the formation of hyperuniform structures.

Wilken notes another important discovery that came out of the research. They learned that sequence engineering of DNA allows for the creation of two separate species of DNA particles, with no cross-species binding of the two. When testing this design, Wilken found that both species phase-separate simultaneously but result in separate droplets of DNA. "This is a powerful ability," Wilken says. "DNA's design flexibility makes it possible to tune microscopic interactions between DNA particles in order to fabricate a composite material from distinct droplet species."

Saleh adds to that, saying, "One can imagine using this ability to create a novel type of 'soft alloy' that would act as an artificial tissue, with different types of droplets taking on specific arrangements in space and imbuing the material with novel functions."

Additionally, Saleh notes, "The surprising thing about the two-species experiment was that hyperuniformity was preserved within each droplet species, but was destroyed when combining the two species, indicating that the structure of this composite material is exceedingly sensitive to small changes in the structure of the constituent DNA particles."

Wilken sees multiple possible application areas for the findings, relating both to investigating the fundamental operation of the cell, and to fabricating devices that manipulate light in new ways.

"We investigated structures undergoing well-understood equilibrium dynamics, i.e., those of dead or inanimate objects," Wilken says. "What's not clearly understood are the impacts on material structure of non-equilibrium dynamics, which are integral to biology, as living systems constantly consume and expend energy to stay alive. We expect, however, that we could use nanostars to probe the fluctuations that occur in living systems, because nanostars are composed of naturally occurring nucleic acids, which, we know, are compatible with biological systems."

A material composed of disordered hyperuniform DNA droplets might also have technological applications, for instance, as an engineered transport material in photonic devices. As mentioned above, the transport properties of crystals are limited by their anisotropy, such that electrons or, in a photonic device, photons, can travel on only path along the crystal lattice. Interestingly, the isotropic structures that Wilken and Saleh investigated are composed of droplets approximately one micron in size, the same length of a wave of visible light. That suggests, Wilken says, that materials comprising droplets arranged on a square lattice might be capable of transporting light in any direction in a photonic device, thus opening up new possibilities for chip architecture and materials that manipulate light in novel ways.

Hyperuniform materials might very well find their way into the photonic materials that will, eventually, generate quantum bits in quantum computers, ushering in an entirely new way to solve difficult problems associated with, but not limited to, encryption, semiconductor manufacturing, and drug design.