From ribbon to scroll: Gaining shape control by electrostatics

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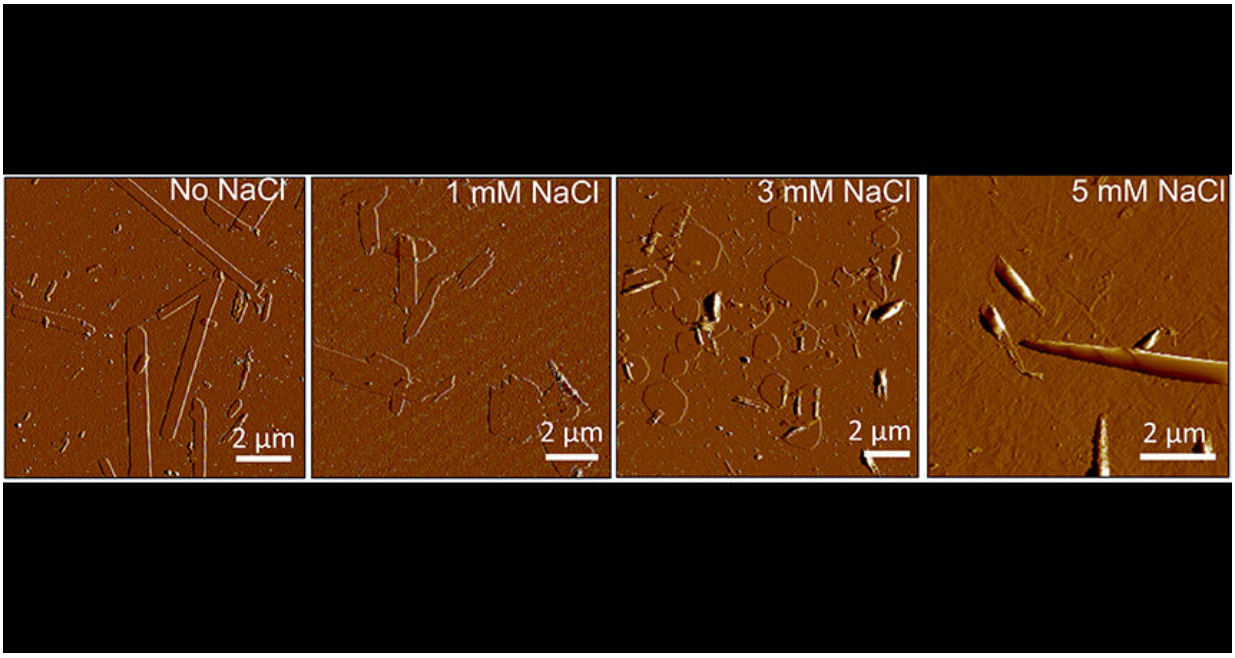

C16-K1 assembly images showing high aspect transformations to cochleate with increasing salt concentration. Credit: Northwestern University

Northwestern Engineering materials science researchers have uncovered new insights into how electrostatic interactions can be regulated to attain and control scroll-like cochleate structures, which could inform how to capture and release macromolecules in a size-selective manner as part of future drug-delivery strategies.

Charged molecules, such as DNA and proteins, are present throughout biological systems. Membranes, a bilayer of these charged lipid molecules, are used to compartmentalize matter in a variety of structural forms, from spherical vesicles to helical nanoribbons to cochleates.

"In biology, molecules take the form of many coexisting shapes. Some are decided based on the variations placed upon them, such as concentrations of pH or salt," said Monica Olvera de la Cruz, Lawyer Taylor Professor of Materials Science and Engineering at the McCormick School of Engineering.

"Using a simple charged biomolecule, we have shown how the interplay between electrostatic, elastic, and interfacial energies can lead to structural polymorphism, or coexistence of multiple shapes. While cochleate structures have been observed in other systems, the entire pathway for their formation had not been explained," she added.

The team's findings were published in a paper, titled "Electrostatic Shape Control of a Charged Molecular Membrane from Ribbon to Scroll," on October 14 in *Proceedings of the National Academy of Sciences*. Olvera de la Cruz was the study's co-corresponding author along with Michael Bedzyk, professor of materials science and engineering.

Using a combination of microscopy techniques and small- and wide-angle X-ray scattering, the team studied changes to the membrane shape of a charged amphiphilic molecule called C16-K1, composed of a hydrophilic single amino acid headgroup and a 16-carbon-long hydrophobic tail. A salt-based solution screened the charge of the headgroup of the membrane, allowing researchers to control the range of electrostatic interactions.

"We repeated the C16-K1 molecules in a crystalline 2-D way, and each

molecule carried particular left or right chirality—or geometric orientation," Bedzyk said. "If the ionic strength was strong enough, it caused the membrane to go from a flat ribbon with a large length-to-width ratio to an even aspect ratio. As we increased the salt concentration further, the bilayers transformed to sheets and rolled themselves to form this cochlear structure."

The team then turned to theoretical modeling to validate their experiments. They found that the membrane's transformation to a cochleate could be credited to two factors: the electrostatic interactions and the elastic energy, which includes bending caused by the molecules' chirality and tilt, leading to a natural curvature to the bilayer.

"Crystalline arrangements for molecules like these have a natural bending to their shape. We wanted to learn how the molecular tilt aligns with the rolling direction of the cochleate structure," Olvera de la Cruz said. "It's similar to if you place two screws next to each other, they would need to be tilted to have the grooves of one go into the other. If you have a large number of them in a crystalline arrangement, the best way to do that is to roll the whole membrane."

The team was able to match the theoretical analysis with these experimental observations. "The spacing in these scroll-like structures has a very defined relationship with salt, which allows for control over the distance separating the bilayers," said Sumit Kewalramani, a research assistant professor in materials science and engineering and a co-first author on the study.

The ability to control and adjust the separation between the bilayers of these molecules could pave the way for the controlled capture and release of macromolecules and nanoparticles for drug-delivery applications.

"By controlling how the membranes are spaced, we may be able to trap specific molecules," Kewalramani said. "That functionality and control could be used for trapping and releasing molecules for drug delivery. Depending on the salt concentration, we could trap particular types of molecules or release them somewhere else."

The team's work could also inform future studies that further explore the relationship between the shape of biomolecular assemblies and molecular properties, like charge and chirality, which could inspire more detailed theoretical models for studying morphological transformations in crystalline assemblies.

"While these molecules are all assembling into different shapes, they all coexist and relate to each other by first-order phase transitions," Bedzyk said. "Understanding the transition mechanisms will allow for greater control over forms—and thus the function—of self-assembled structures."

More information: Changrui Gao et al, Electrostatic shape control of a charged molecular membrane from ribbon to scroll, *Proceedings of the National Academy of Sciences* (2019). DOI: 10.1073/pnas.1913632116

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