WIRES WITHIN WIRES: A MULTISCALE MODEL FOR COMPUTATIONAL INVESTIGATION OF BIOELECTRONIC PROTEIN DESIGN

Rachael Mansbach, University of Illinois at Urbana-Champaign
2017–2018 Graduate Fellow

EXECUTIVE SUMMARY

Certain proteins containing aromatic groups can assemble under appropriate conditions to form fluorescent mini-"wires" that can be used for electronic applications such as photovoltaic cells, light-emitting diodes, or pH sensors. Such organic electronics are desirable due to their ease of manufacture and nontoxicity. In order to produce rational principles for the design of such proteins, it is of great importance to understand their assembly on a molecular scale. Using Blue Waters, we employed coarse-grained molecular dynamics to study how changing the chemical properties of a series of proteins containing aromatic centers changes the properties of their amorphous aggregation. We illuminated generic properties of aggregation and identified five potential chemistries for further study. In the future, this work could help lead to the production of new biocompatible electronic devices.

RESEARCH CHALLENGE

The DXXX series is a group of small rod-like proteins with central aromatic cores possessing the ability to aggregate under acidic conditions into fluorescing semiconductive nanostructures [1]. However, the fluorescent properties of the nanostructures are limited by the extent to which the aromatic cores overlap. This overlap, in turn, is controlled by multiple factors, including the chemistry of the amino acid side chains and the kinetics under which aggregation occurs. The study of such protein aggregation at a molecular level is hindered by the comparatively large length scales and long time scales on which such aggregation occurs. Understanding the key determinants governing assembly is crucial in providing rational precepts for molecular design and engineering.

METHODS & CODES

In order to understand the effects of side chain chemistry on the aggregation of the DXXX series and to identify specific candidates with desirable optical properties, we created a simple model of the DXXX series, in which a single monomer was represented as a set of rigidly constrained beads. By changing the interactions of the different beads, we modeled changing the chemistries of the aromatic cores and the side chains. Using this inexpensive model to reach previously inaccessible length and time scales, we conducted Langevin dynamics in the HOOMD 2.1.7 simulation suite [2,3]. We performed five independent simulations of systems of 10,000 peptide monomers for 660 microseconds each using sixty different sets of model interaction parameters and analyzed the resulting properties of aggregation.

RESULTS & IMPACT

From our analysis of the simulations of large-scale aggregation, we identified the most salient interaction characteristic controlling the formation of aggregates likely to possess desirable optical properties. This characteristic is the overall "stickiness" of the amino acid side chains, represented in the model by the interactivity of the beads that represent the side chains. When the magnitude of the interactivity of the side chain beads becomes smaller than that of the beads representing the aromatic cores, desirable aggregation strongly increases because core—core interactions become more favorable than side chain—side chain interactions.

Our work also showed that the size of the side chains controls the small-scale morphology of the aggregates. At small scales (~10 nm), increasing the radius changes the aggregates from flat ribbons to twisted fibers, but at large scales (>30 nm), due to the intrinsic peptide geometry, all systems generically form a porous, branched network.

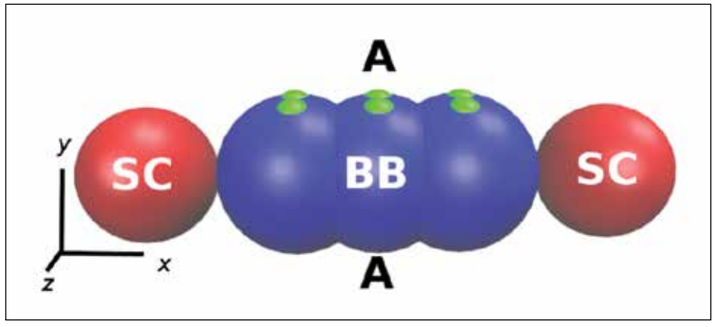

Figure 1: Visualization of a rigid body, patchy model of a DXXX peptide. The small, green *A* beads represent cofacial aromatic interactions; the large, red *SC* beads represent side chain interactions; and the large, blue *BB* beads represent noncofacial aromatic interactions.

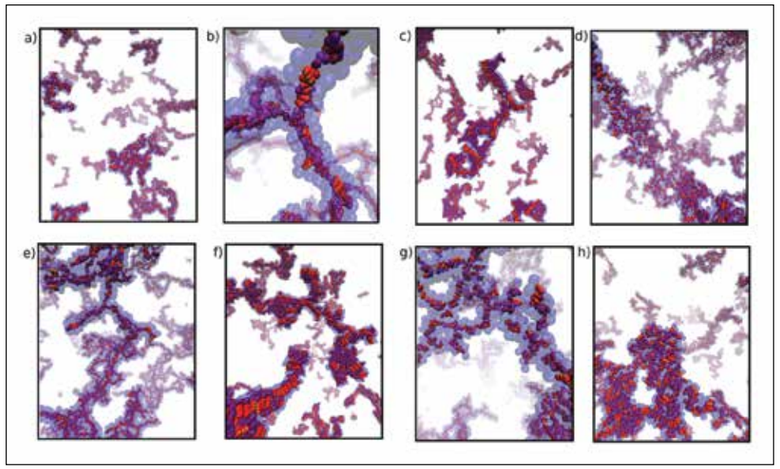

Figure 2: Snapshots of the assembled morphologies for selected parameter settings (a–h). Side chain beads (*SC*) are transparent and blue, noncofacial aromatic core beads (*BB*) are red, and cofacial core beads (*A*) are green. The small-scale morphology depends on the specific parameters, but all molecules form porous branched networks at large scales.

We defined two metrics by which to measure the quality of the assembled aggregates: (1) the rate at which "optical clusters"—aggregates expected to possess fluorescent properties—grow, and (2) the degree of one-dimensional order of the resulting aggregates that form. Using these measures, we performed a multiparameter optimization over the space of the sixty parameters to identify six model molecules expected to display the best aggregate properties. From these six parameter sets, we employed a mapping to identify the five peptide sequences corresponding to these optimal parameters. These five chemistries are expected to display rapid aggregation into thin wires with desirable optical properties.

Overall, this work characterizes the interactions and assembly of the DXXX series from the microscopic to the mesoscopic level, thus providing new fundamental understanding of the important molecular determinants of assembly behavior. This understanding enables rapid screening over molecular parameter space and the identification of chemistries predicted to favor assembly of large, linear aggregates with desirable optical properties. It also provides new rational design principles by which to engineer self-assembling peptides to fabricate large assemblies for bioelectronic applications. Further, it forms the coarsest level in a hierarchy of models of varying resolutions by which to perform high-throughput virtual screening of molecular space to efficiently discover and engineer these molecules and guide and accelerate experimental synthesis and characterization.

WHY BLUE WATERS

Performing molecular dynamics simulations, even at coarse-grained resolution, over sixty different parameter sets would have been prohibitively expensive without access to the computational resources provided by Blue Waters. Access to multiple XK GPU nodes enabled us to generate the necessary simulation data. In addition, the generous storage space on Blue Waters made it much easier to run in parallel by eliminating concerns tied to the fact that each of the 60 × 5 = 300 simulation runs generated between 10 and 20 gigabytes of data. Furthermore, the close support of the project staff, in particular our point of contact, was invaluable in enabling us to get up and running quickly. Finally, access to a larger big data community is particularly important for a highly interdisciplinary application such as ours, providing a pool of expertise we might otherwise have been unable to access.

PUBLICATIONS & DATA SETS

Mansbach, R., and A. Ferguson, A Minimal Patchy Particle Model for a Family of Self-assembling π-conjugated Optoelectronic Peptides. (To be submitted, 2018.)

Sixth-year PhD candidate Rachael Mansbach received her degree in physics in August 2018 from the University of Illinois at Urbana-Champaign, where she worked under the direction of Andrew L. Ferguson.