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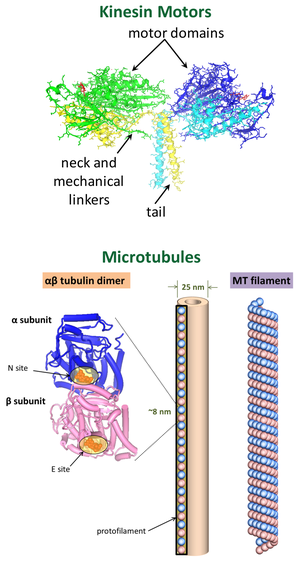
Active Assembly of Dynamic and Adaptable Materials

George D. Bachand (**PI**), *Darryl Sasaki (Co-PI), Erik Spoerke (Co-PI), and Mark Stevens (Co-PI),*
Virginia VanDelinder, Haneen Martinez, Marlene Bachand, Adrienne Greene, Namita Nabar, Walter Paxton,
Sandia National Laboratories, Livermore, CA & Albuquerque, NM

Introduction

Our program, Active Assembly of Dynamic and Adaptable Materials, examines fundamental materials science issues at the intersection of biology, nanomaterials, and hybrid interfaces. The *overall program goal is to understand how nature's biomolecular machines assemble non-equilibrium, multi-scale materials, and to apply these principles and components in hybrid or composite materials whose assembly and organization can be "self-directed" or autonomously responsive to stimuli.* Specifically, we are exploring materials systems that exhibit adaptive behaviors based on energy consuming proteins capable of removing the constraints imposed by diffusion and chemical equilibria.

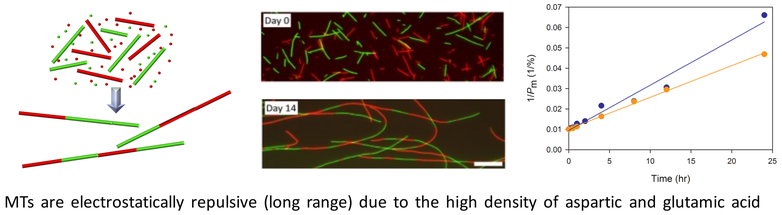
We have focused on the active transport system consisting of microtubules (MTs) and their associated motor proteins. MTs are hollow filaments composed of αβ tubulin dimers that provide structural stability and serve as "train tracks" for the bidirectional transport of macromolecules and organelles. The associated motor proteins kinesin and dynein achieve efficient transport through the conversion of chemical energy into mechanical work. Living organisms use the concerted and dynamic interactions between kinesin and MTs for physiological processes ranging from chromosomal segregation at the cellular level to macroscopic color changing behaviors at the organismal level. Learning to exploit, mimic, and/or translate the role of active proteins in emergent biological behaviors represents an opportunity to dramatically advance nanomaterials assembly.



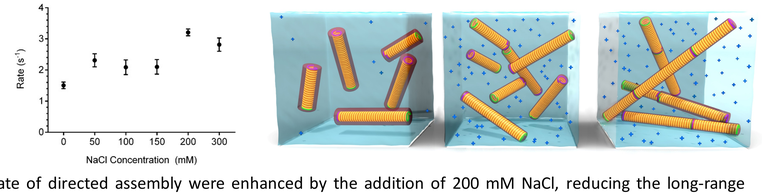
Bachand et al., (2013). *WIREs Nanomed. Nanobiotechnol.* **6**, 163-177

Directed assembly of biological Janus rods

We previously described the directed (head-to-tail) self-assembly of MTS into extended 1D structures, where the growth is diffusion-limited and follows second order rate kinetics.



MTs are electrostatically repulsive (long range) due to the high density of aspartic and glutamic acid residues on the outer surface, which limits lateral interactions and aggregation. The opposing ends, however, exhibit short-range attractive interactions, which enable the polymerization of tubulin. Based on these properties, we hypothesized that the directed self-assembly of MTs is analogous to that of Janus colloids/rods, where the self-assembly can be modulated with the addition of monovalent counterions that screen the electrostatic interactions.



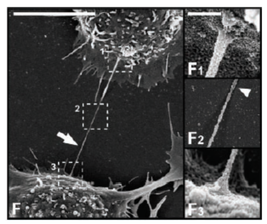
Rate of directed assembly were enhanced by the addition of 200 mM NaCl, reducing the long-range repulsive forces and enhancing the short-range hydrophobic, head-to-tail interactions.

Bachand et al. (2014), *RSC Adv.* **4**, 51641; Greene et al. (2017), *Chem. Comm.* **53**, 4493

Transport systems of lipid tubules and vesicles

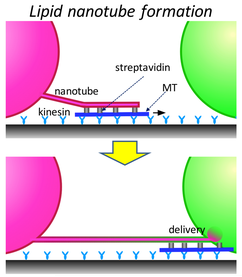
Lipid membrane structures define transport systems between cells and within cells between organelles. Here, we are developing materials and routes towards generating lipid tubules and vesicles via selective interaction between lipid membranes and the pulling activity of the kinesin-microtubule assay.

Intercellular transport

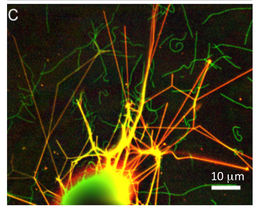


Tunneling nanotube between cells (from Rustom, A. et al., *Science* (**2004**) *303*,1007).

Lipid nanotube formation



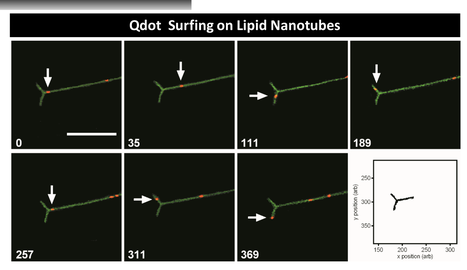
Lipid-Polymer Nanotube Network



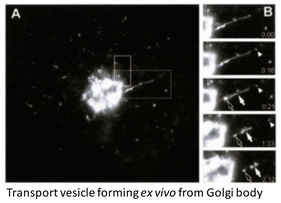
Previously, we have shown that lipid and polymer nanotubes form through the interaction of biotinylated membranes and streptavidin coated microtubules. This potentially enables the formation of fluidic connections between vessels containing different reagents. We demonstrated "surfing" of Qdots attached to lipid nanotubes as a single-file 1D diffusion.

Bouxsein et al. (2013), *Langmuir* **29**, 2992; Paxton et al. (2015). *Nanoscale* **7**(25), 10998-11004

Qdot Surfing on Lipid Nanotubes



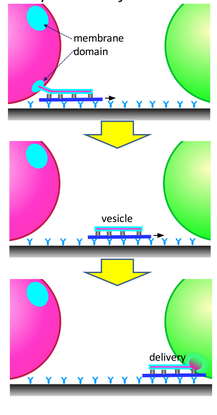
Intracellular transport

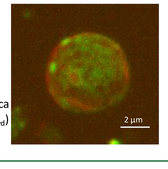


Transport vesicle forming *ex vivo* from Golgi body interacting with kinesin-microtubule. Polishchuk, E. V.; et al. *Molec. Biol. Cell* **2003**, *14*, 4470.

Formation of discreet vesicles from organelle-like assemblies requires selective interaction between the active motor protein and a domain in the membrane. Through recent work we developed new insight for designs of lipid chemistry/structure that imparts selective partitioning to membrane domains. This enables selective interaction and optical monitoring of specific domains with the microtubules.

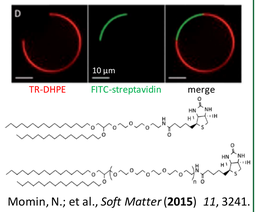
Lipid vesicle formation





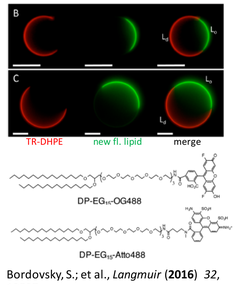
3D projection of membrane coated mesoporous silica particle showing phase separation of liquid-disordered (L_d) (red) and biotinylated liquid-ordered (L_o) (green) phases.

Phase selective biotinylated lipids



Momin, N.; et al., *Soft Matter* (**2015**) *11*, 3241.

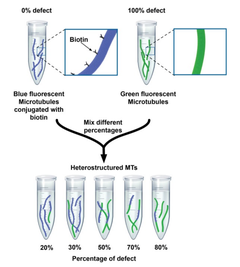
Phase selective fluorescent lipids



Bordovsky, S.; et al., *Langmuir* (**2016**) *32*, 12527.

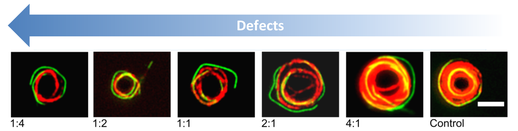
Defects in ring composite assembly

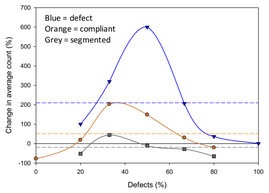
We have previously shown the active (motor-driven) assembly of ring nanocomposites composed of biotinylated MT filaments and streptavidin-coated semiconductor nanocrystals (Qdots). These composites are generally stable despite the presence of a large number of sub-micron defects. To better understanding the role of defects, we developed MT building blocks containing varying levels of "defects," which are defined as non-biotinylated segments (green segments).

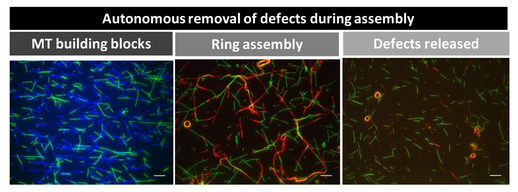


Using these building blocks, we observed that the defect (green, non-biotinylated) segments are selectively removed from the ring composites during the assembly process. Their inability to form biotin-streptavidin bonds to offset the energy associated with MT bending results in cleavage.

Work performed by the motors mechanically shears and releases defect segments at a higher rate than compliant segments.







Liu et al., (2008), *Adv. Mater.* 20, 4476; VanDelinder et al. (2016), *Biomacromolecules* **17**, 1048; Martinez et al., (2017), *Nat. Nanotech* (in prep)

Future plans

MT assembly dynamics

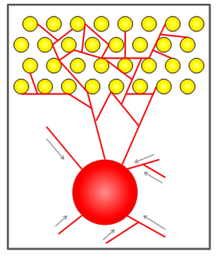
- Understanding metastability of MT *ex vivo* through combined experimental work and MD simulations

Nanotube Networks

- Use of "molecular rewards" to regulate the spatial, morphological, and temporal dynamics of lipid nanotube networks

Ring Nanocomposites

- Introduce additional non-covalent/covalent chemistries to direct (instruct) the assembly of composite rings with defined structure (e.g., layer-by-layer growth)



Acknowledgments

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