1. Introduction

Polymer thin films employing nanotubes as pores are highly desirable as an environmentally friendly and efficient selective transport system for potential applications in CO\textsubscript{2} separation, energy storage and desalination. However, solution-based fabrication of polymeric membranes with (i) monodisperse subnanometer pore size and length, (ii) vertical pore alignment to membrane surfaces, and (iii) tunable pore interior chemistry remains elusive. Cyclic peptide nanotubes (CPNs) are self-assembled supramolecular structures that exhibit outstanding mechanical stiffness and transport properties that match those of biological transmembrane proteins having an alluring potential as synthetic nanopores in membranes for applications such as carbon capture or low energy water desalination. CPNs offer precise control of the pore diameter and the possibility to tailor the inner and outer surfaces of the nanotube, providing an alternative to inorganic nanotubes with the advantage of being fully reversible.

The PI’s collaborators Ting Xu (UC Berkeley) and Brett Helms (LBNL) have recently developed a synthesis method for flexible polymer membranes with vertically aligned subnanometer pores (Fig. 1(a)). The pores consist of cyclic peptide nanotubes (CPNs) – polypeptides that form circular loops that self-assemble into tubes via inter-ring hydrogen bonding. CPN ring sidechains are conjugated with polymers that mediate co-assembly of subunits into nanotubes within a block copolymer matrix, leading to a thin film with hexagonally packed subnanometer diameter pores aligned continuously across the film. Gas selectivity tests on these membranes have shown size-selective transport of CO\textsubscript{2} over neopentane at rates that exceed continuum approximations by Knudsen diffusion (Xu et al., ACS Nano, 5(2), 2011). More interestingly, Helms and Xu’s groups have demonstrated the capability of introducing mutations to CPN rings to insert functional groups into the pore (Fig 1(b)). Molecular Dynamics (MD) simulations by the PI have identified this single mutation as a minimal design that simultaneously achieves selective transport and thermomechanical stability, which was not observed with multiple mutations (Hourani et al., JACS, 133(39), 2011). The PI’s group has also carried out the first study on the mechanics of individual CPNs under deformation scenarios relevant to pressurized thin film stress conditions (Ruiz & Keten, IJAM, 3(4), 2011). These investigations have revealed failure mechanisms of CPNs in extreme environments, thereby providing guiding insight into tough membrane design through formation of hydrogen bonded hard phases that are analogous to beta sheet nanocrystals in spider silk and amyloids (Keten et al., Nature Materials, 9, 2010, APL, 96, 2010).

Our research aimed to explain how the basic building blocks of organic nanotube membranes should be tailored and hierarchically arranged to achieve thermomechanically stable nanoporous structures with chemically tunable interiors. This objective was pursued through atomistic and coarse-grained simulations that aimed to delineate the stability and assembly of CPNs.
2. Persistence Length and Stochastic Fragmentation of Cyclic Peptide Nanotubes

Tailoring physical properties of CPNs for many of the foreseeable applications requires precise understanding of their elastic behavior and susceptibility to fragmentation. The dynamic character of supramolecular assemblies, arising from the weak nature of the stabilizing forces under thermal fluctuations, poses an important challenge on the assessment of their mechanical response using basic structural analysis concepts that cannot readily account for progressive probabilistic failure. Our work under ISEN funding has focused on unraveling the mechanical response of these super stiff supramolecular nanotubes using atomistic simulations coupled with probabilistic strength theories.

![Figure 1](image1.png)

*Figure 1.* Simulations of CPNs, where mechanical deformations under uniform shear load can be utilized to compute the persistence length and fragmentation probability of CPNs as a function of stress states.

In a recent study (Ruiz et al. *Nanotechnology, 24, 2013*), we quantified for the first time the CPNs’ bending rigidity and dynamical fragmentation, establishing the theoretical basis to generate rectilinear structures with controlled aspect ratio and rigidity. Molecular dynamics simulations of CPN under mechanical load (Figure 1a), together with TEM image analysis (Figure 1b) were employed to characterize CPNs’ persistence length (rigidity), showing good agreement between simulations (0.46 µm) and experiments (0.6 µm). This result suggests that CPNs are exceptionally stiff despite their small diameter, and hence may serve suitably as rectilinear pores in nanoporous membranes. The role of dynamic loading on the fragmentation and localization of the failure along the nanotube was also studied using a theoretical framework and numerical simulations. An exponential dependence of force and failure times was observed, with higher loads leading to stiffer responses and well-defined failure locations (Figure 1c). This result opens the possibility of controlling the polydispersity and length of the CPNs or other supramolecular assemblies by tuning the shear forces applied during fragmentation-coupled self-assembly.

In a separate study, we further studied the dynamic fragmentation mechanisms of peptide
assemblies under shock deformation using an atomistically informed anharmonic lattice model (Sullivan et al. J. Applied Mechanics, 2013). We found that fragmentation mechanisms strongly on the relative magnitude of the shock front radius to the fibril length and the ratio of the impact energy to the fibril cohesive energy. The competition between size scaling of curvature and impact energy leads to a mechanism change at a critical impact velocity, developing a stark contrast in the size scaling of fragmentation at low and high strain rates. Thus, we have shown that the fragmentation mechanisms can reliably be classified on the basis of the length and time scales of deformation and relaxation to provide new insight into experimental observations on the size-distribution of beta-sheet peptide assemblies such as CPNs and amyloids.

3. CPNs with Tunable Interiors

A key bottleneck in generating biomimetic nanopores similar to transmembrane channels is the difficulty of placing functional groups (polar / nonpolar) in the interior of the pores. CPNs synthesized by our collaborators overcome this barrier by the use of a nonstandard amino acid that presents methyl functionality into the pore interior, thereby changing the interior electrostatic potential landscape and the size of the pores. Our MD simulations illustrated that these pores selectively transport water over THF on the basis of size-selectivity. Our analyses on nanotubes with polar interiors also showed that these tubes assemble readily in a variety of solvents (THF, H$_2$O), which sets the stage for using polar/nonpolar functionalities to generate nanotubes with vertically variable interior polarity. Synthesis efforts are underway to study mixing of these two functionalities and how the stacking order can be controlled in various solvent conditions.

![Figure 1. Amine and methyl functionalized CPs form stable assemblies in solution as characterized by interring H-bonds, paving the way for CPNs with tunable interior polarity.](image)

4. Using Polymer Conjugation to Dictate Spatial Ordering of Functional CPs

Our current work is envisaged towards the use of polymer conjugates to direct the CP self-assembly and control the nanotube sequence to enhance the selective transport properties of the systems. The sequence of a nanotube composed by different types of CPs is determined by the binding energies between the different building blocks. In the case of conjugated-CPs, the self-assembly process, mainly driven by the enthalpic gain of the backbone hydrogen bonding, is hindered by the polymer conjugated arms that introduce a free energy penalty to the binding due to steric confinement effects. We propose using the free energy penalty introduced by the conjugated polymers, and regulated by the degree of conjugation, to control the binding energies and hence the nanotube self-assembled sequence. If successful, this strategy will open novel design routes towards the fabrication of CPN membranes with selective transport capabilities, including those arising from precise stacking ordering of functional groups in the pore interior similar to transmembrane channels.
External Proposals Garnered As a Result of ISEN Funding

Funded Projects (proposals built on preliminary findings from this ISEN project)

Support: Current
Project/Proposal Title: DMREF: Collaborative Research: Simulation-Based Design of Functional Sub-nanometer Porous Membranes (PI)
Source of Support: NSF
Award No: CBET-1234305
Total Award Amount: $225,053
Total Award Period Covered: 09/01/12 – 08/31/15
Location of Project: Northwestern University
Person-Months Per Year Committed to the Project:
Cal: 0.0   Acad: 0.00   Sumr: 1.00

NSF DMREF-CBET, Chemical and Biological Separations Program; Keten as PI: One of the first 14 projects selected as part of the Materials Genome Initiative by the White House.

Support: Current
Project/Proposal Title: Mechanics and self-assembly interplay in polymer-conjugated peptide nanotubes (PI)
Source of Support: ASME Haythornthwaite Award
Award No: Letter 11/9/12 – Check #225
Total Award Amount: $20,000
Total Award Period Covered: 10/01/12 – 09/31/13
Location of Project: Northwestern University
Person-Months Per Year Committed to the Project:
Cal: 0.0   Acad: 0.09   Sumr: 0.00

ASME Applied Mechanics Division (AMD) Haythornthwaite Research Initiation Grant, Keten as PI, awarded to young faculty in the field of mechanics to boost their research activities early in their career. Proposals selected by the AMD executive committee.

Submitted and under consideration:

Support: Pending
Project/Proposal Title: A Unified Predictive Theory for Polymer-Conjugated Peptide Nanotube Design (PI)
Source of Support: Department of Energy
Total Award Amount: $747,905
Total Award Period Covered: 06/01/13 – 05/31/18
Location of Project: Northwestern University
Person-Months Per Year Committed to the Project:
Cal: 0.0   Acad: 0.00   Sumr: 0.25
Publications under ISEN support (* indicates corresponding author)


