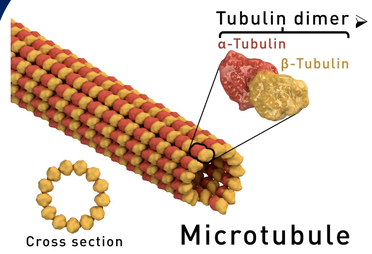
MODELING AND PROPERTY EVALUATION OF SELF-ASSEMBLED NANO-TUBES

NSF GRANT - CMMI-1610812

Ning Liu, JongWon Kim, Xianqiao Wang (co-PI) and Ramana Pidaparti (PI)

College of Engineering, University of Georgia, Athens, GA 30602, USA

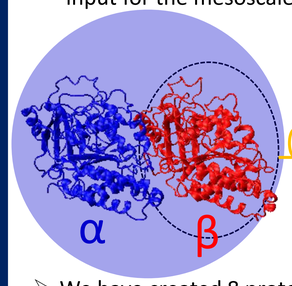
INTRODUCTION



- Microtubules (MTs), the essential structural element of cells, are long filamentous hollow cylinders whose surfaces form lattice structures of αβ-tubulin heterodimers. MTs undergo frequent polymerization and depolymerization processes, during which the binding strengths between and inside heterodimers play an very important role.
- Molecular dynamics (MD) simulations can serve as an very important tool to capture sub-nanometer details of microtubules which can be very hard and expensive when one want to do it experimentally. On the other hand, finite element analysis model enables a large spatial and temporal scale which is hard and expensive for MD simulations. Combining those two methods pave the way for a better understanding of the static and dynamic properties of microtubules.
- Thus, we carry out a variety of full atomistic simulations to investigate the interaction properties, such as adhesion energy, tensile strength, and shear strength between pairs of α and β tubulins. Those data are then used as input for the MD-based FEA model.

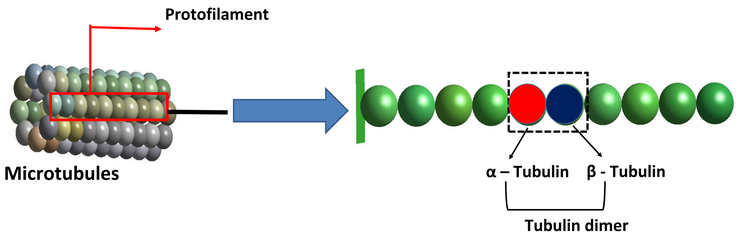
METHODS

- In this work, MD simulations have been adopted to study the intra-dimer binding strength between α and β tubulins. Resultant data will be used as input for the mesoscale FEM model.



Schematic plot of the tensile test for an αβ heterodimer .
The whole tubulin heterodimer is immersed in to a water sphere. The backbone of α tubulin is fixed and the backbone of β tubulin is attached to a virtual spring.

- We have created 8 protofilaments along the circumferential direction, and each protofilament was made with 10 spherical tubulins, and α-tubulin and β-tubulin composes a dimer as shown in the figure below. Each tubulin is created in 6 nm diameter. Inner diameter and outer diameter of microtubule are 12 nm and 24 nm respectively in this study. Microtubule is generated using ANSYS Design Moduler and each tubulin is connected with spring which represents MT protein elasticity.



Schematic plot of the FEA model

MD simulations

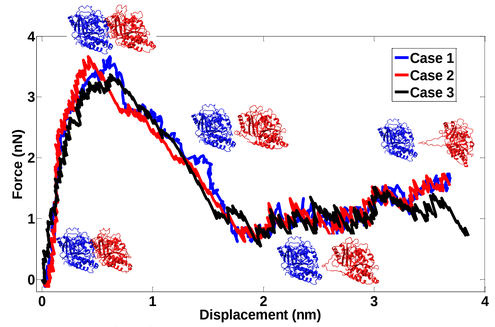


Figure 1: Force- displacement responses upon testing αβ heterodimer binding strength

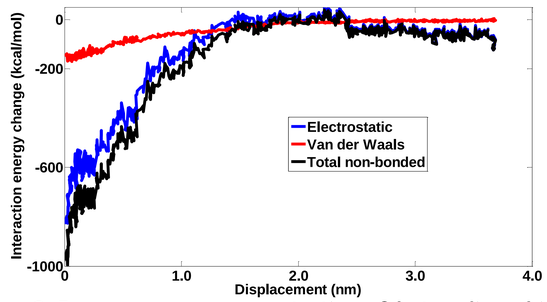


Figure 2: Energy responses upon testing αβ heterodimer binding strength

FEA simulations

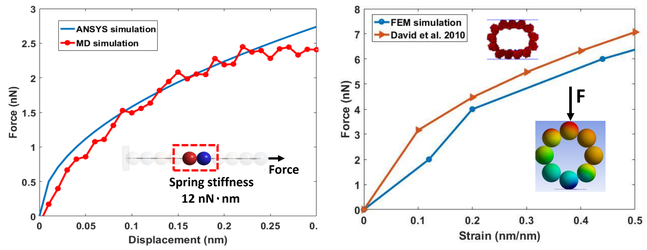


Figure 3: Comparison between FEA results and MD results

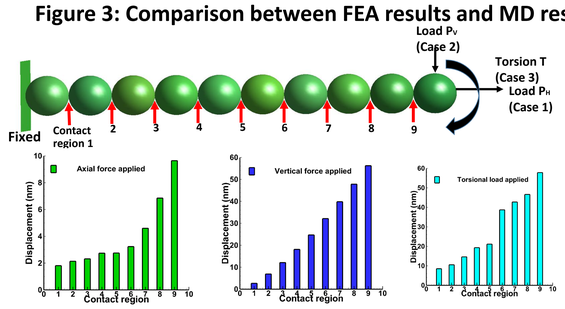


Figure 4. Mechanical testing of protofilament. The force applied in 10 nN for case 1 and 2, and 200 nN · nn for case 3.

Point Mutation and Stiffness (MD)

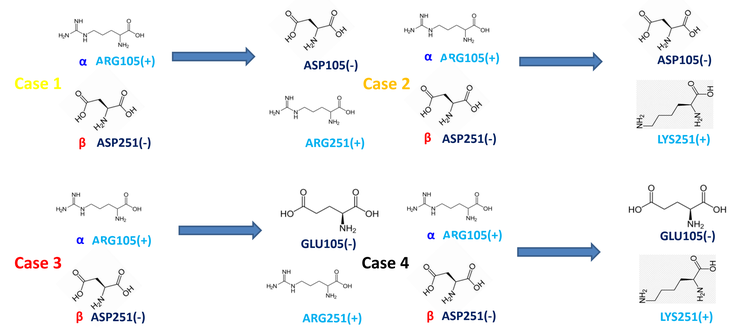


Figure 4: Mutation plan

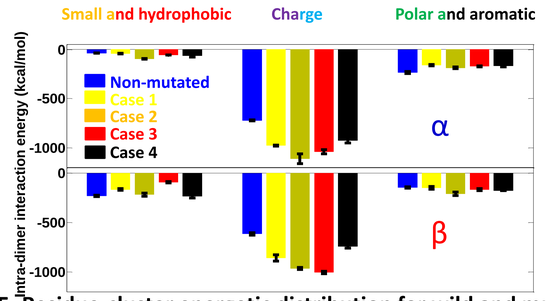


Figure 5: Residue-cluster energetic distribution for wild and mutated species

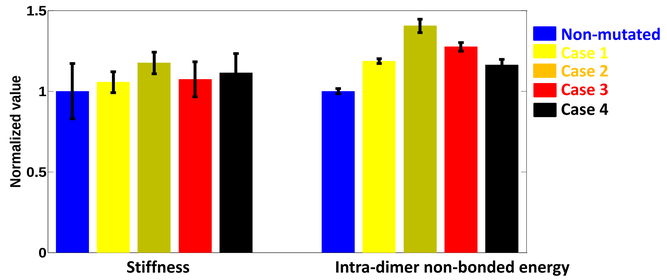


Figure 6: Stiffness and non-boned interaction comparison for wild and mutated species

CONCLUSIONS

- ✓ In our MD simulations, through comparison between wild and mutated species regarding stiffness and non-bonded interaction, we can conclude that the intra-dimer binding strength can be tuned via mutations of residues belonging to charged residue clusters.
- ✓ We have also established a MD-based FEA model, validated by comparison of FEA results with MD results. This FEA model can be further extended to advancing our understanding about the static and dynamic properties of microtubule.

Acknowledgement

This work was supported by supported by a grant from National Science Foundation(Grant No. 1610812).All the simulations were done on the SAPELO cluster from Georgia Advanced Computing Resource Center(GACRC).