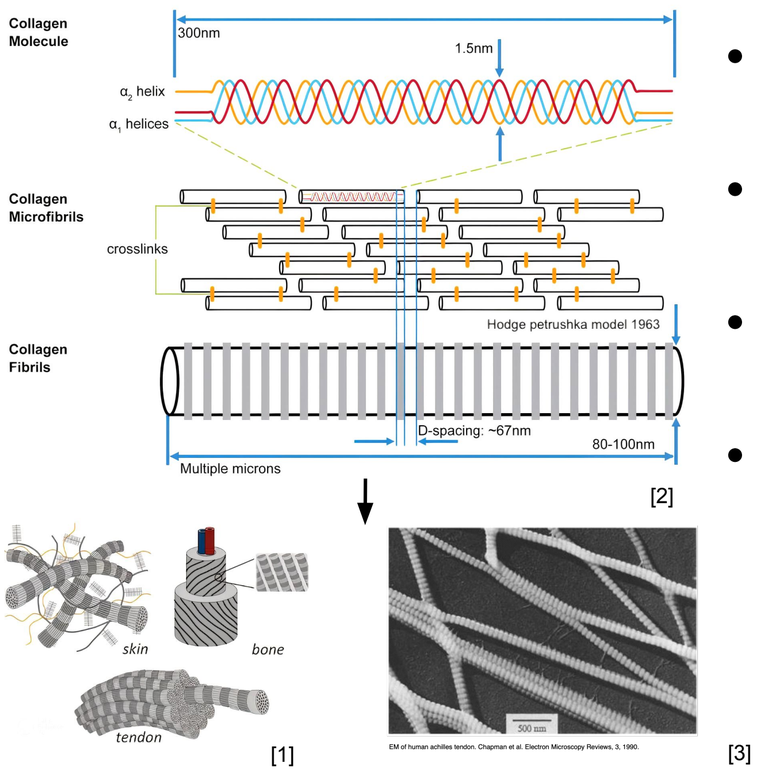
Understanding Collagen Assembly

Smriti Chhibber*+, Kevin Klein+, Anđela Šarić+

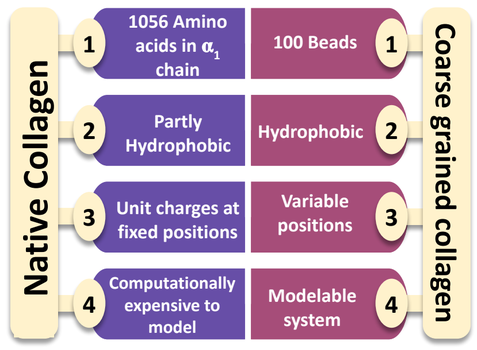
Institute of Science and Technology, Austria+ | Indian Institute of Science Education and Research, Mohali, India*

Introduction and Motivation



- Collagen is the most abundant structural protein in animals
- Famous for its strained periodic pattern with periodicity of 67 nm
- How individual molecules assemble into this pattern is not fully understood
- Aim : To develop an in silico model that mimics the behavior of collagen and understand the factors affecting periodicity

Simulation Protocol

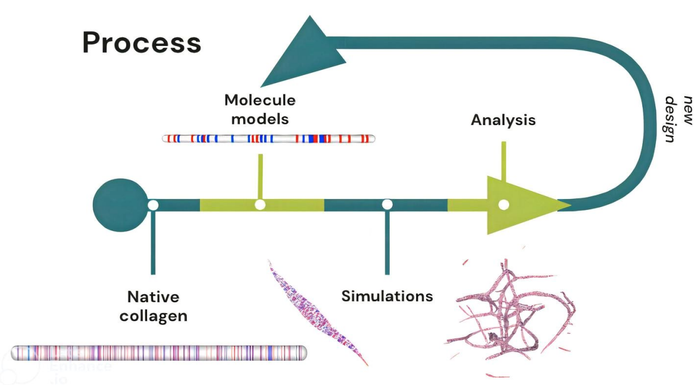


Hydrophobic Interactions

$$E_{LJ} = \begin{cases} 4\varepsilon_{LJ}\left[\left(\frac{\sigma}{x}\right)^{12} - \left(\frac{\sigma}{x}\right)^{6}\right] + E_{\mathrm{LJ}}^{\mathrm{shift}} & \text{for } x \le x_{\mathrm{cutoff}} \\ 0 & \text{for } x > x_{\mathrm{cutoff}} \end{cases}$$

Electrostatic Interactions

$$E_{\mathrm{CD}} = \begin{cases} C\frac{q_i q_j}{\varepsilon_{\mathrm{CD}} \cdot x} e^{-\kappa x} + E_{\mathrm{CD}}^{\mathrm{shift}} & \text{for } x \le x_{\mathrm{cutoff}}, \\ 0 & \text{for } x > x_{\mathrm{cutoff}}, \end{cases}$$



- Molecules interact via two types of interactions
- Implementation of simulations is done in LAMMPS using modified Velocity Verlet algorithm

Molecule Models

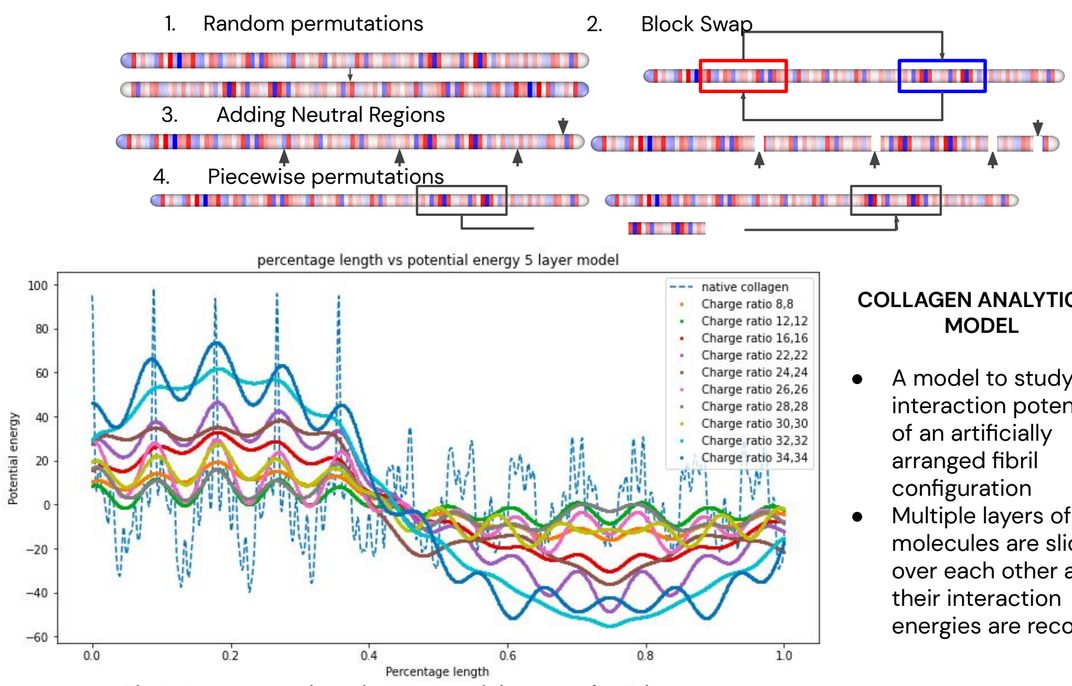
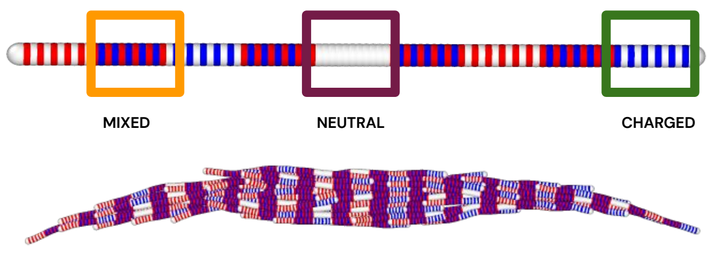


Fig 1 : Percentage length vs potential energy for 5 layers

COLLAGEN ANALYTICAL MODEL

- A model to study the interaction potentials of an artificially arranged fibril configuration
- Multiple layers of molecules are slid over each other and their interaction energies are recorded

Artificial molecule model



Formula for estimating periodicity = (gap+overlap)x(length of a bead = 0.285)x(scaling factor)

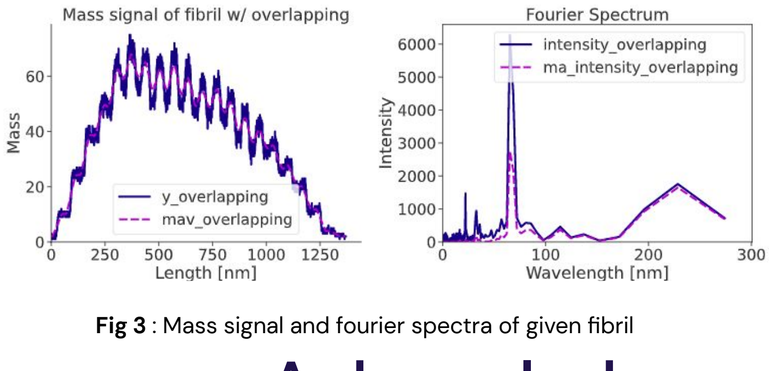


Fig 3 : Mass signal and fourier spectra of given fibril

- New model for simulating artificial fibrils of any periodicity
- Molecule can be divided into three regions and period can be controlled by changing length of each region

Predicted periodicity = 62.7
Observed periodicity = 65.2

Observations and Results

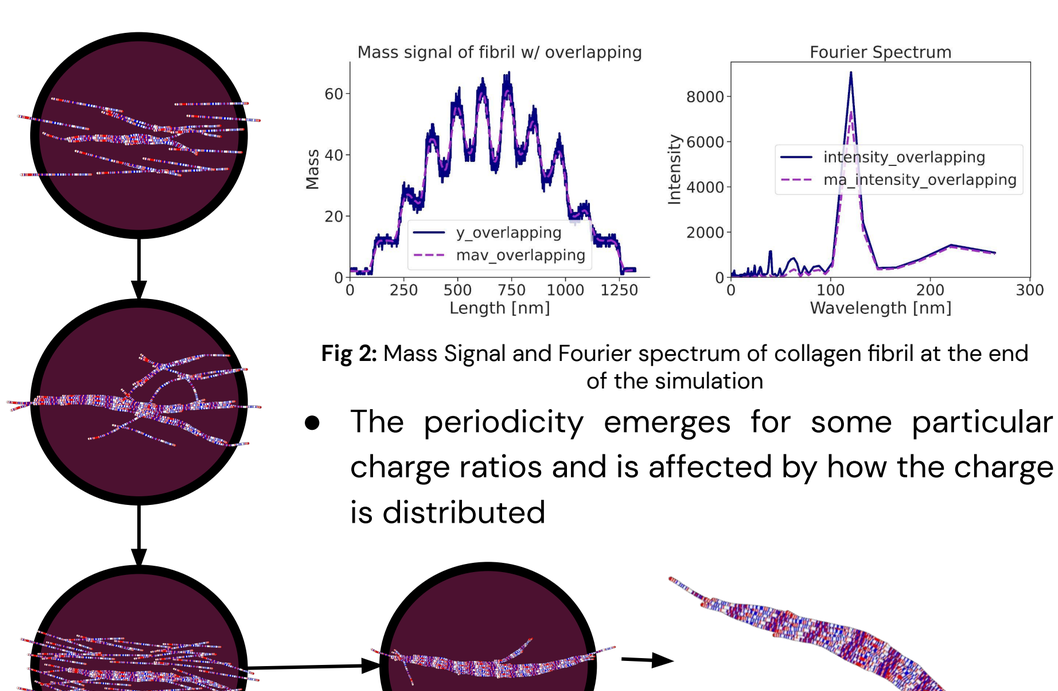


Fig 2: Mass Signal and Fourier spectrum of collagen fibril at the end of the simulation

- The periodicity emerges for some particular charge ratios and is affected by how the charge is distributed

Inter-Chain Comparison

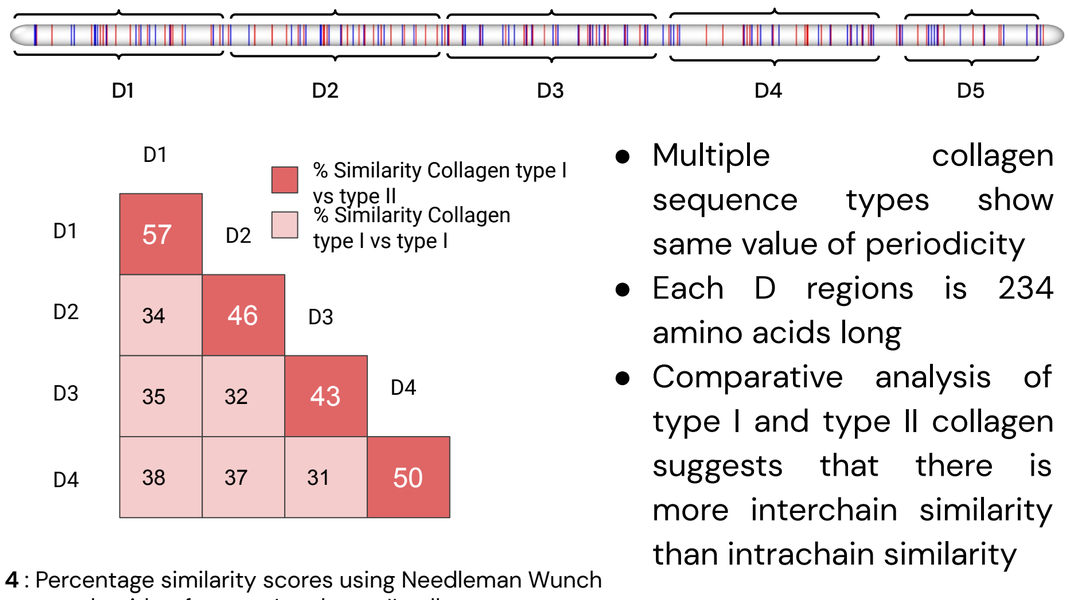


Fig 4 : Percentage similarity scores using Needleman Wunch algorithm for type I and type II collagen

- Multiple collagen sequence types show same value of periodicity
- Each D regions is 234 amino acids long
- Comparative analysis of type I and type II collagen suggests that there is more interchain similarity than intrachain similarity

Acknowledgements

- Thanks to OeAD and the ISTernship program for giving me the opportunity and funding my expenses during my stay, Kevin Klein and Prof. Andela for very fruitful discussions and members of the Šarić lab for the constant support
- Thanks to committee members Prof. Tripta Bhatia, Prof. Abhishek Chaudhari and Prof. Kavita Dorai for constructive feedback

References

- Hodge, A.J. and Petruska, J.A. (1963) In: Ramachandran, G.N., Ed., Aspects of Protein Structure, Academic Press, New York, 289-300
- Image credits : [1] Schwarcz et. al. (2017). The Ultrastructure of Bone and Its Relevance to Mechanical Properties ; [2] Salvatore Luca et. at. Mimicking the Hierarchical Organization of Natural Collagen ; [3] Chapmen et. at. Electron microscopy reviews 1990

Contact : ms18142@iisermohali.ac.in