Molecular Dynamics Study of Collagen Fibrils: Relation between Mechanical Properties and Molecular Chirality

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Collagen (Tropocollagen): As a new biology-oriented substance, tropocollagen(TC) molecules are now attracting much interests of researchers in many research fields.[1)]

Aim of this study:

- ✓ Constructing atomic-level computation model of TC fibril (bundle of TC molecules)
- ✓ Evaluating mechanical properties and functions (Flexibility, rigidity and shape-memory) in collagen
- ✓ Discussing change of chirality originated by triple-helix in TC molecules during deformation

To realizing a new material:
Mechanical properties, functions (flexibility, rigidity, shape-memory) are needed

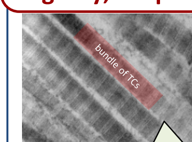
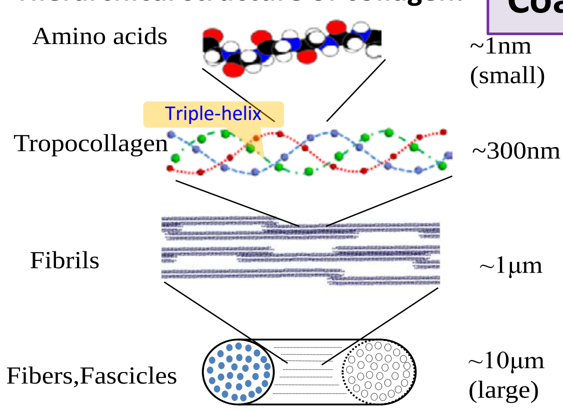


Photo: Type-I collagen (Wikipedia)

Composite structure → A new material including "collagen"

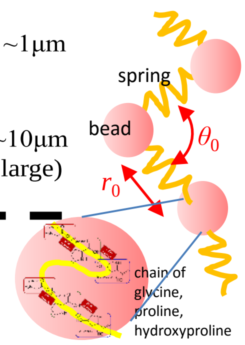
Future Applications:
- ✓ Regenerative medicine
- ✓ Functional material for structural use
- ✓ Fiber reinforced mater.

Hierarchical structure of collagen:



Coarse-grained molecular dynamics (CGMD) modeling

Beads-Springs MD model for tropocollagen(TC) and TC fibrils:
- Six consecutive peptide chain of Gly (glycine), Pro (proline) and Hypro (hydroxyproline) is treated as coarse-grained one particle (one bead).
- Study of Buehler[2)] is used as a reference model.



Intramolecular interactions:	A) Stretching and contracting (for pairs) B) Angular change (for triplets)
Intermolecular interactions:	C) Intermolecular interaction(VDW etc.) (L-J potential) D) Cross-link bond (CL) between molecules

A)	$\Phi_{str} = \frac{1}{2}k_{str}(r-r_0)^2$
B)	$\Phi_{bend} = \frac{1}{2}k_{bend}(\theta_{ijk}-\theta_0)^2$
C)	$\Phi_{LJ} = 4\varepsilon\left(\left[\frac{\sigma}{r}\right]^{12}-\left[\frac{\sigma}{r}\right]^{6}\right)$
D)	$\Phi_{CL} = \beta\Phi_{LJ}$

Computation model

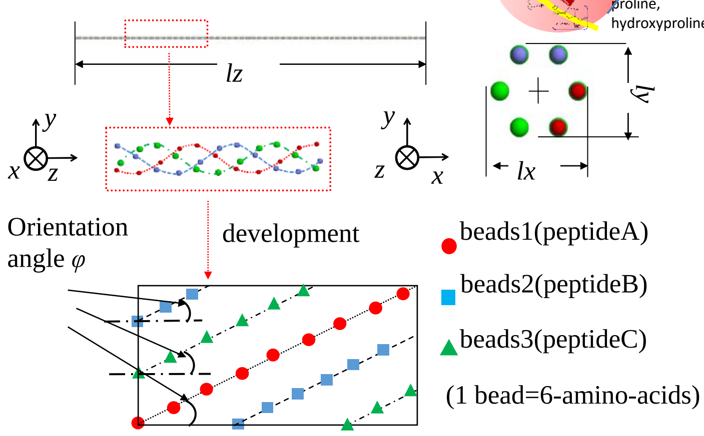


Fig. MD simulation model of single tropocollagen(TC) and definition of intermolecular orientation angle φ

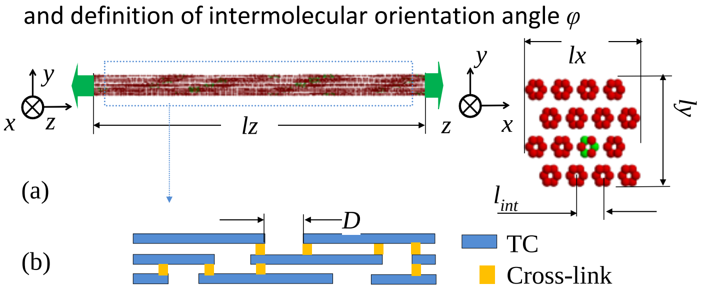
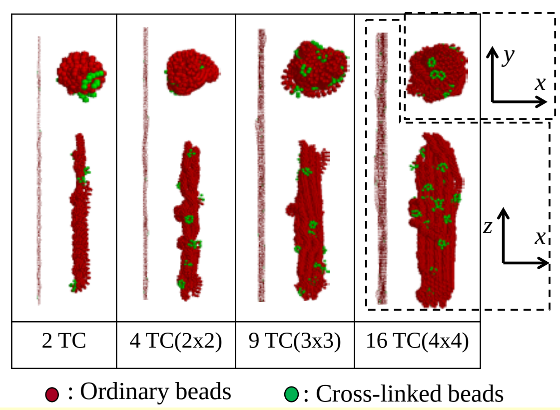


Fig. (a)MD simulation model of a "Fibril of tropocollagen (FTC)" model (case of 4x4=16TC) (b)Schematic of cross-link modeling

Table 1 Calculation condition	
The number of particles (beads) [-]	1554 ~ 12432
The number of TCs [-]	2~16
Length of single TC l_z [nm]	299
Length of TC fibril l_z [nm]	366 ~ 1304
Intermolecular distance l_{int} [nm]	2.97
Longitudinal gap D [nm]	6.7
Cross-link factor β [-]	12.5
Tensile/compressive strain rate [1/s]	±5 × 10^7
Temperature T [K]	10,100,200,300
Orientation angle φ [deg]	0 ~ 35
Time increment Δt [fs]	1.0

Results and discussion (Tensile simulation)

※Compression test is also performed and buckling occurs [3)]. Details can be found in the conference paper.



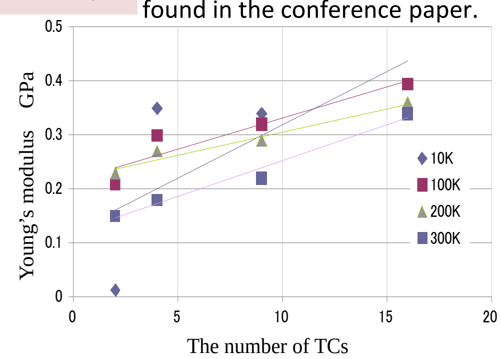


Fig. Comparison of Young's moduli for different size of FTC and for system temperature

Geometrical change (curvature & torsion) for various orientation angles

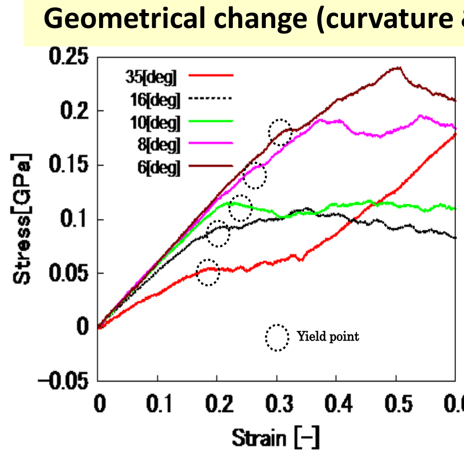
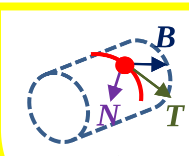


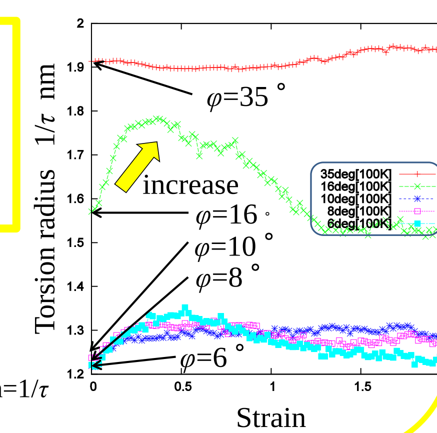
Fig. Stress-strain curves obtained by tensile test of orientation-FTC (OFTC) model (T = 100 K) and evaluation of yield points

$$\frac{d\mathbf{N}}{ds} = -\kappa\mathbf{T} + \tau\mathbf{B},\quad \frac{d\mathbf{T}}{ds} = \kappa\mathbf{N},\quad \frac{d\mathbf{B}}{ds} = -\tau\mathbf{N}$$

Frenet-Serret formulas
- N: normal vector
- T: tangential vector
- B: binormal vector
- κ: curvature
- τ: torsion

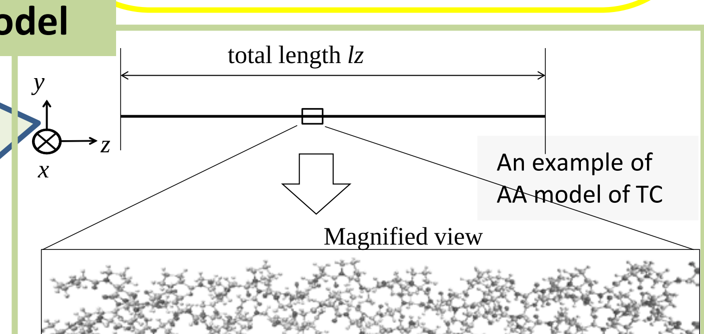


Radius of torsion=$1/\tau$



Development to all-atom (AA) model

- ◆ ***NAMD***(conventional MD software package)
- ◆ In ***PDB*** (Protein Data bank), a structure of short collagen molecule(1CAG.pdb) is found.
- ◆ Polymerizing up to 300 nm-length, including internal rotation angle (internal twist) is added.
- ◆ **TODO**: Fibrillar structure (bundle of TCs). Simulation of mechanical testing



Summary: In this study, mechanical properties of collagen is atomically investigated. Tropocollagen (TC) fiber and its fibril structures are analyzed by using coarse-grained framework of molecular dynamics (MD) simulations. It is recognized that chirality (twist, torsion) of fiber constituents is related to mechanical state of TC fibers. We also found that there is a deep relationship between molecular chirality and mechanical properties.

References:
1. H. Gao, *et al.*, *PNAS*, **100**-10, 5597–5600 (2003).
2. M.J. Buehler, *J.Mech.Behav.Biomed.Mater.*, **1**, 59-67 (2008).
3. T.Shirahana, Master's thesis, Graduate school, Kansai University (2015).