NIH Integrated Multiscale Biomaterials Experiment and Modeling Group

Collagen & mineralized collagen modeling

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February 10, 2014
Support: NIH U01

Massachusetts Institute of Technology

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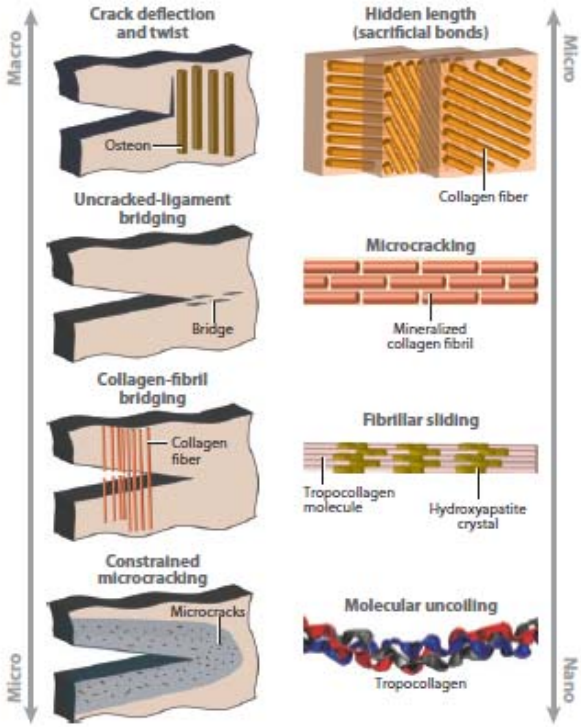
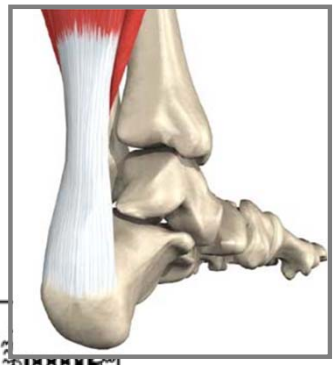
Collagenous tissues – a (t)issue of multiple scales



macro

ïssues (tendon, one)
dimension ≈ cm



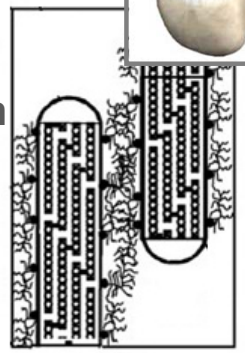
Bone

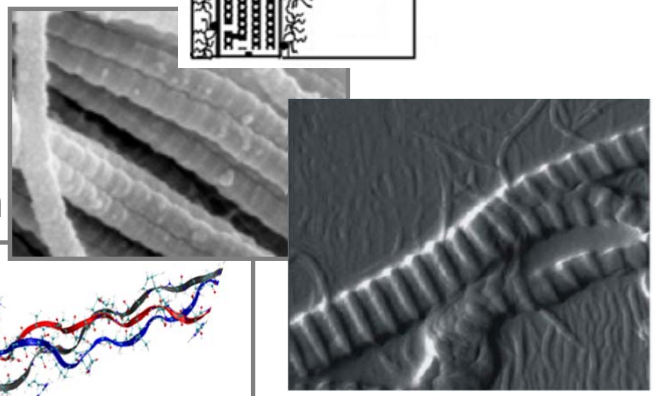
Tendon

Cartilage

Eye's cornea

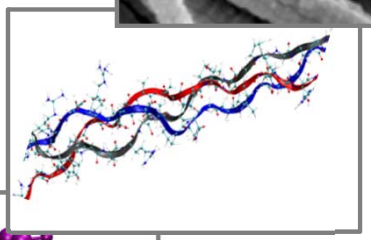
Collagen fiber
length ≈ mm
diameter
≈ 10 μm



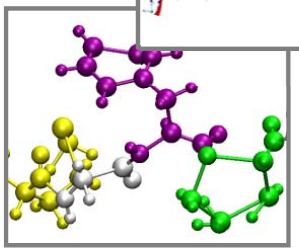


Collagen fibril diameter ≈ 100 nm

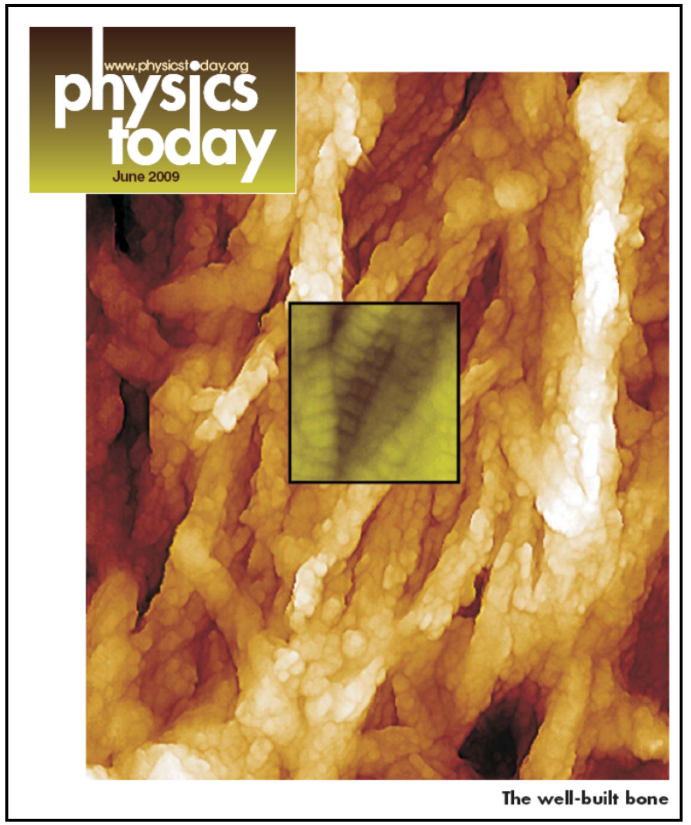
Collagen molecule
length ≈ 300 nm
diameter ≈ 1.6 nm



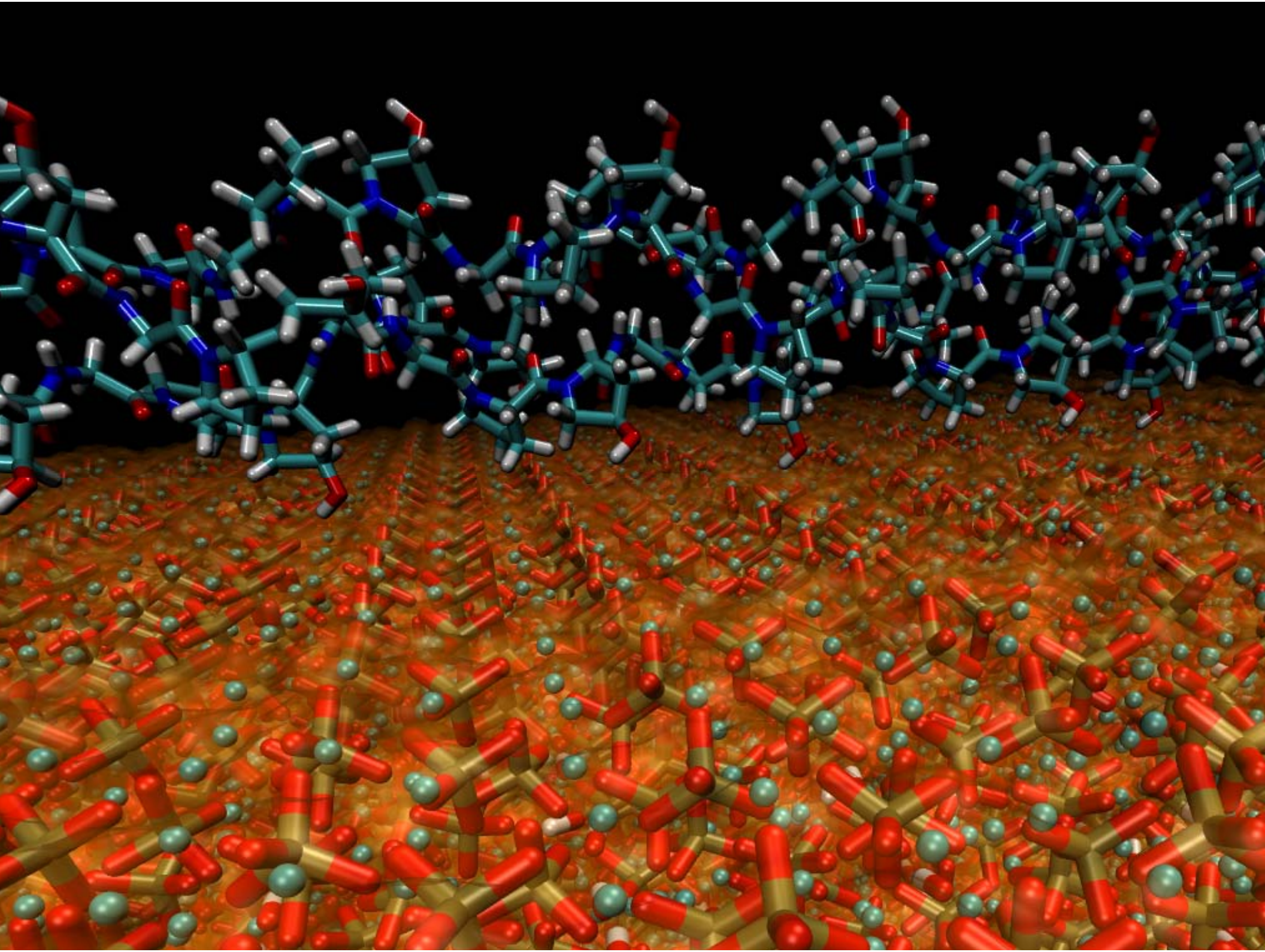
Amino acids
covalent bond ≈1 Å



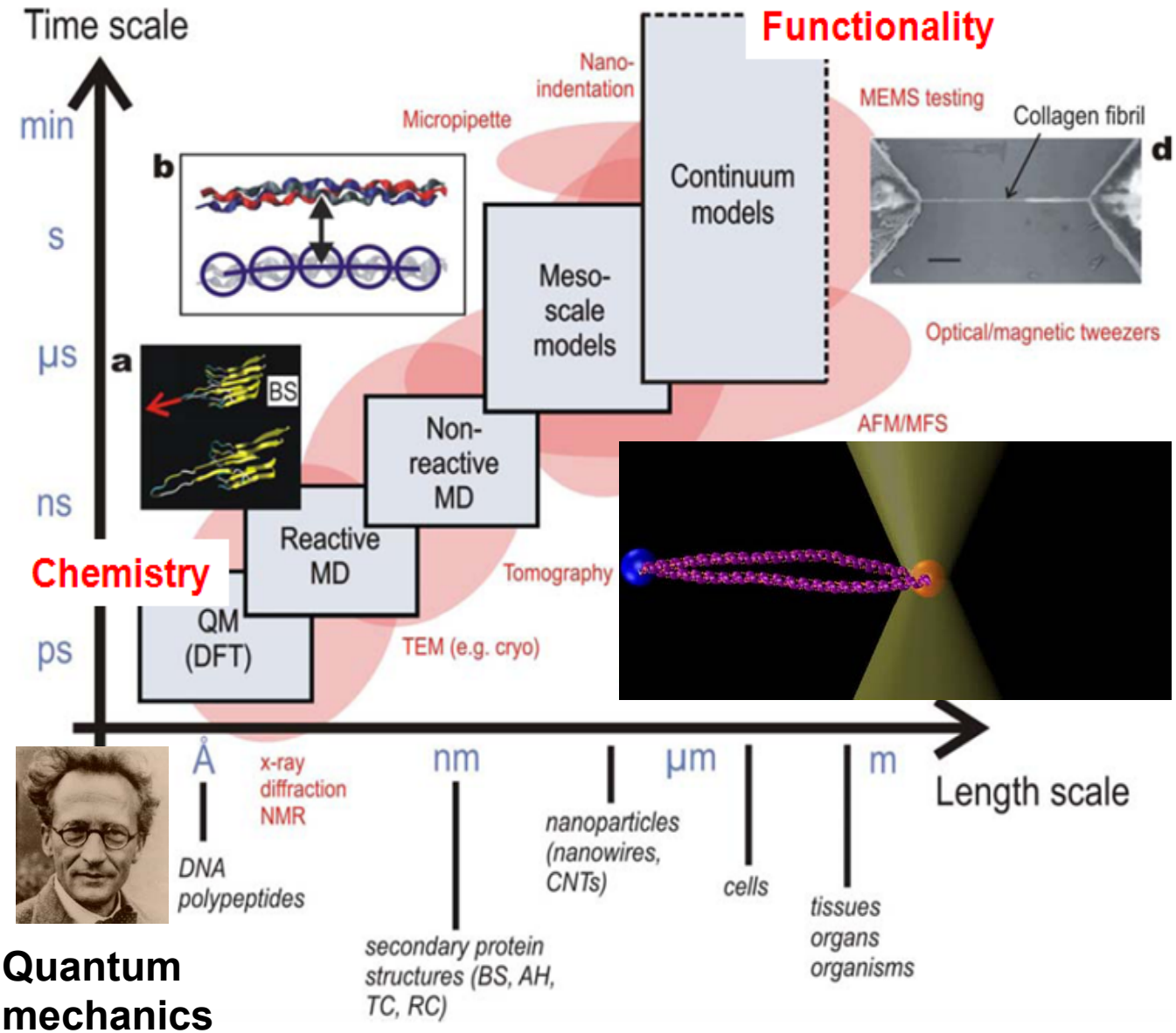
nano



M.J. Buehler, *PNAS,* 2006; R. Ritchie, M. Buehler, P. Hansma, *Physics Today*, 2009; *Ann. Rev. Mat. Sci.*, 2010



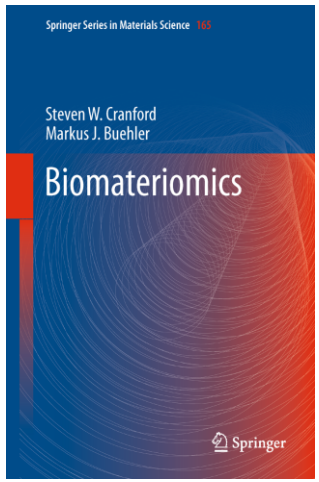
Integration of experiment and computation



Quantum mechanics

Three-pronged research approach: "materiomics"

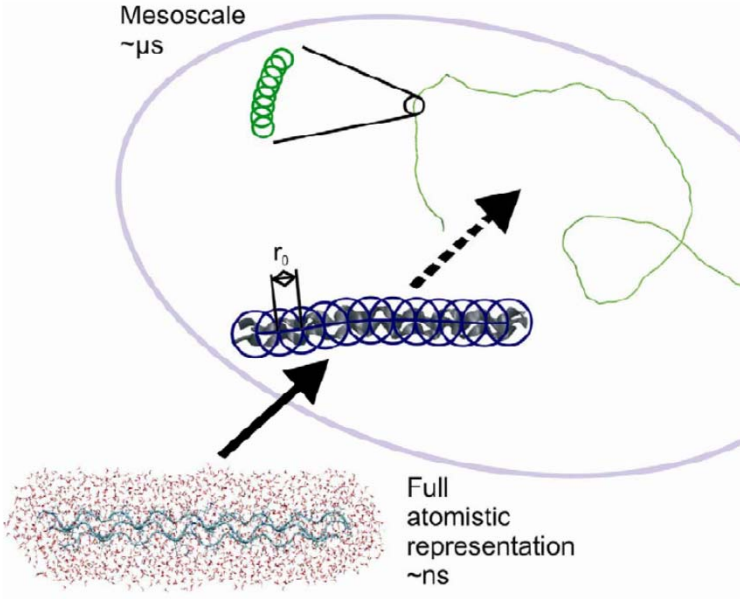
1. **Simulation and experiment of different systems**
2. **Generalize insight through comparative study**
3. **Analytical models, mathematical tools**



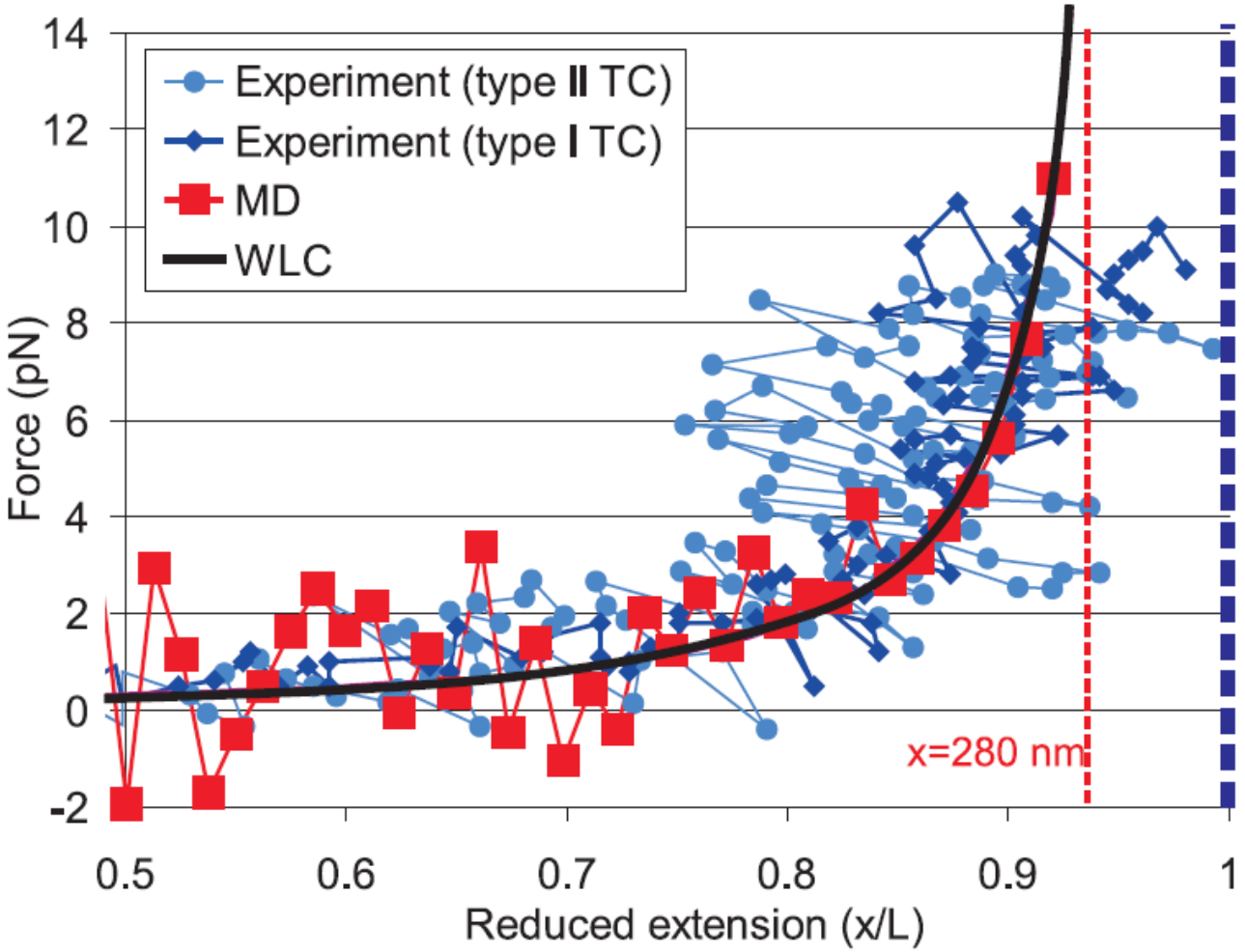
Buehler *et al*., *Nature Materials*, 2009;. Z. Qin *et al*., 2010, 2012

Pulling on a single collagen molecule

Coarse-graining



Mechanism:
Entropic elasticity
(change in configurational entropy)

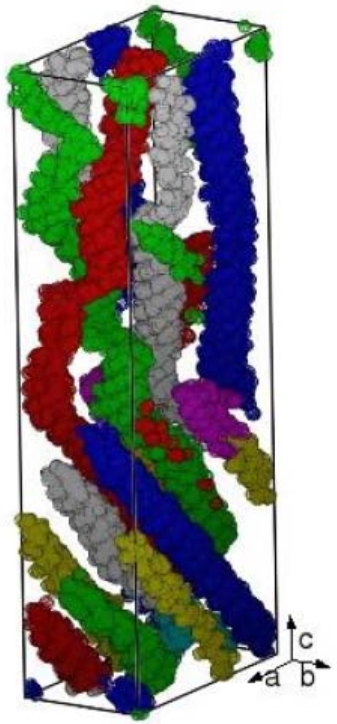


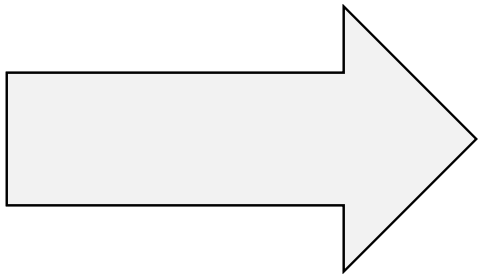
Advancement in experimental equipment:
Have quantitatively confirmed predictions from our simulations

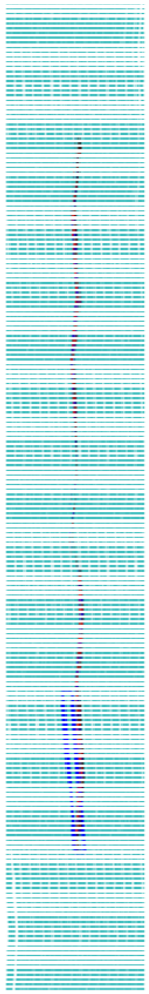
Sun *et al*., *J. Biomechanics*, 2004; Buehler and Wong, *Biophys. J., 2007*

Full-atomistic 3D model of collagen fibril

Orgel collagen fibril structure

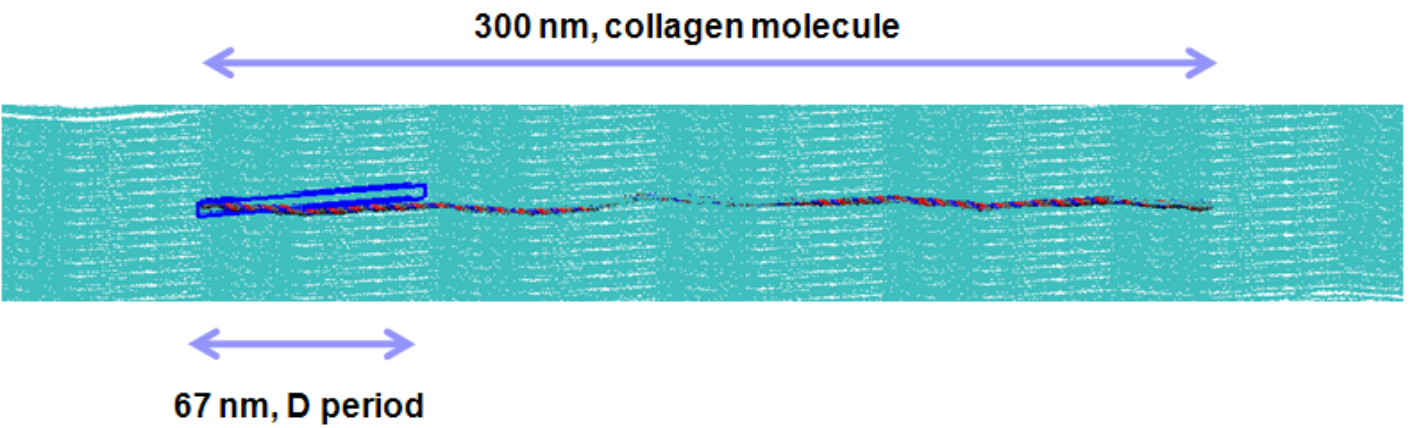


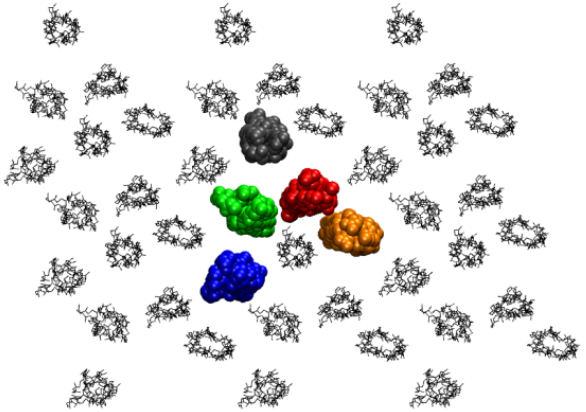


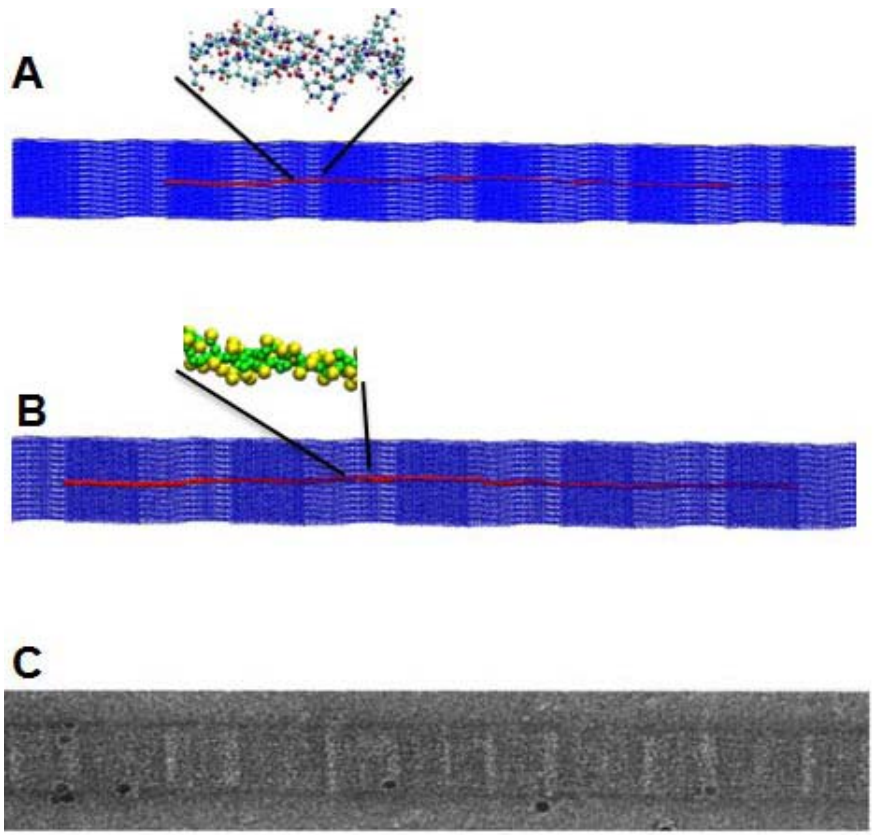


Full-atomistic model

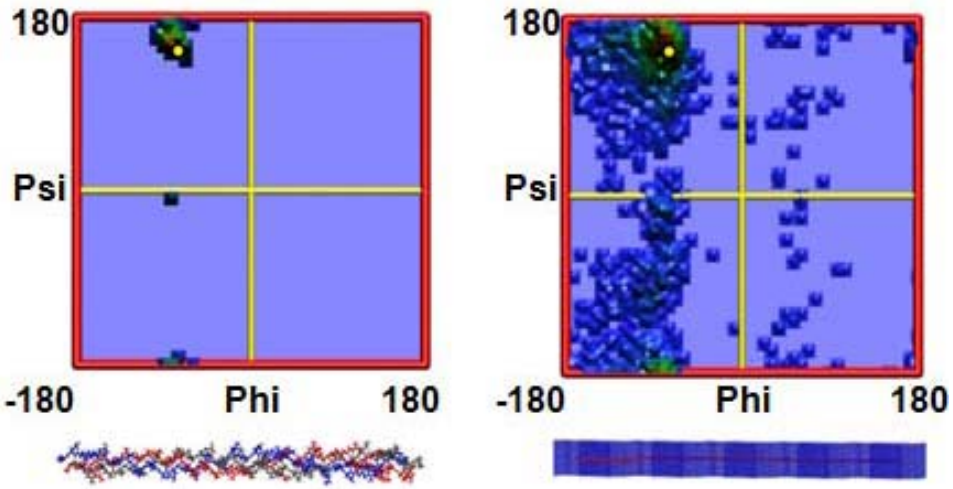
Collagen fibril mechanics—structure



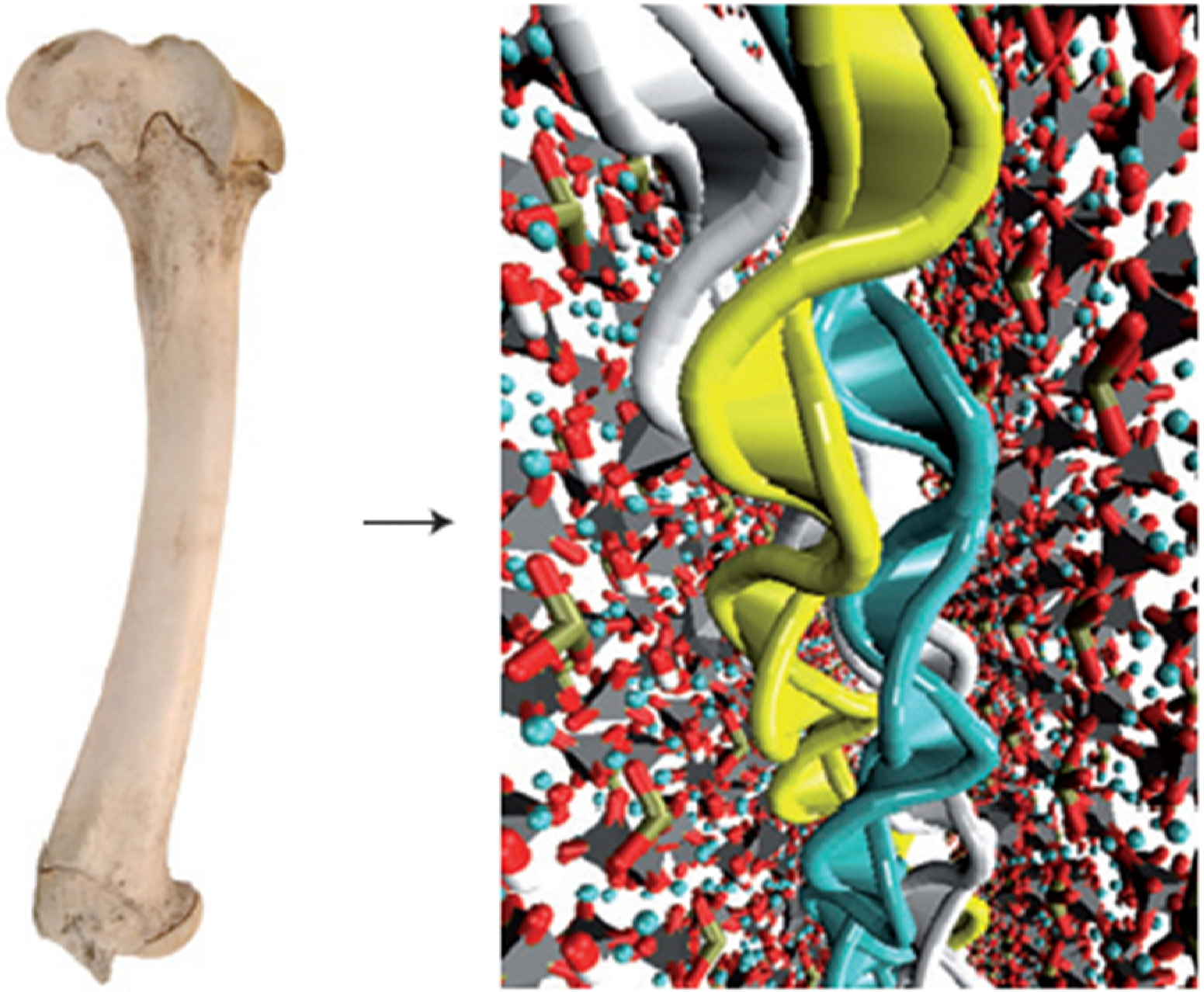




Model features key structural features of collagen fibrils, <u>in particular D-banding</u>; Consider atomistic and coarse-grained representation

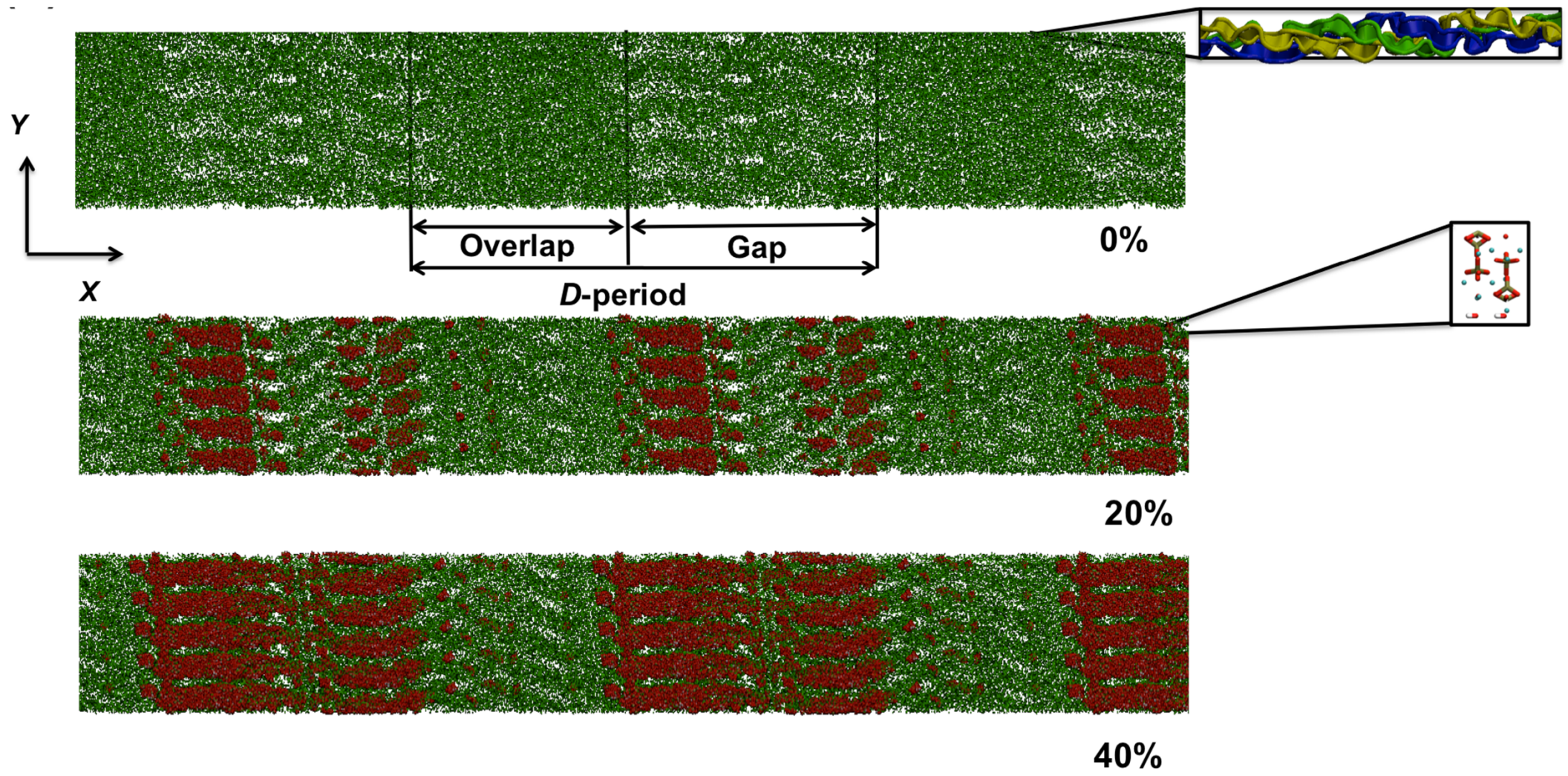


Gautieri, Redaelli, Buehler *et al., Nano Letters,* 2011



M. Solar, M.J. Buehler, *Nature Nanotechnology*, 2012

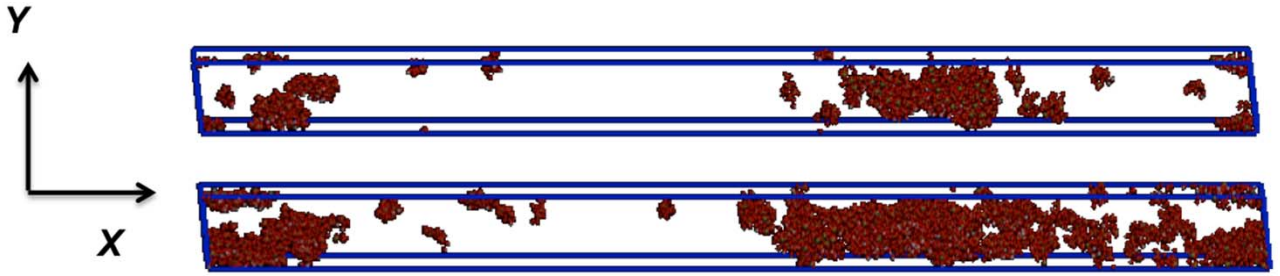
Mineralization approach



Successive addition of mineral crystals into collagen fibril; different cutoff yields different mineral density (0%....40%)

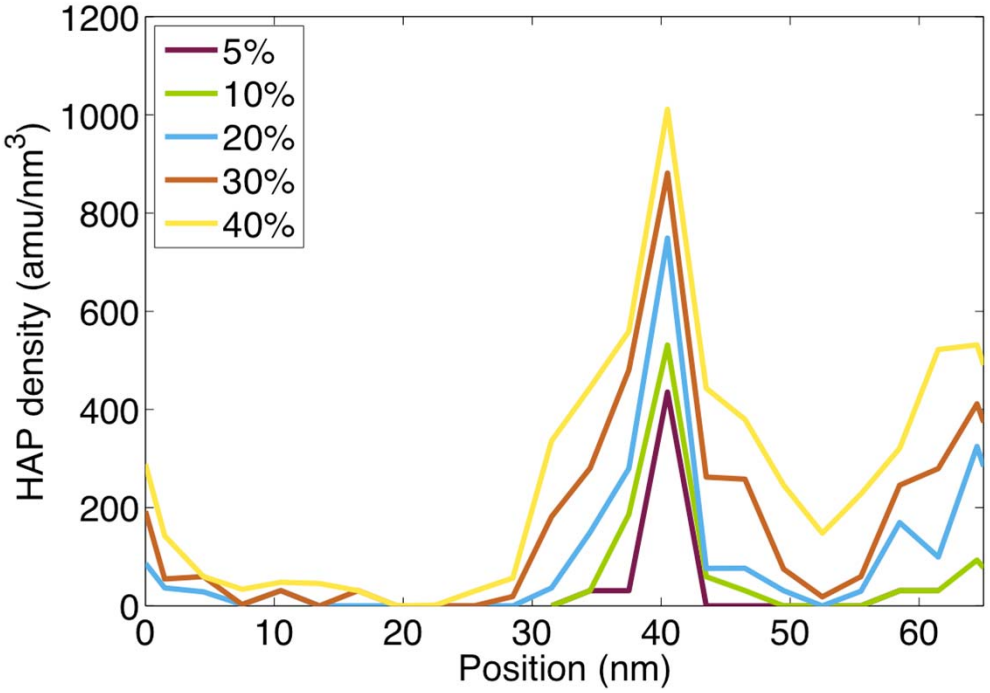
A. Nair, S. Chang, M.J. Buehler, *et al*., *Nature Comm*., 2013

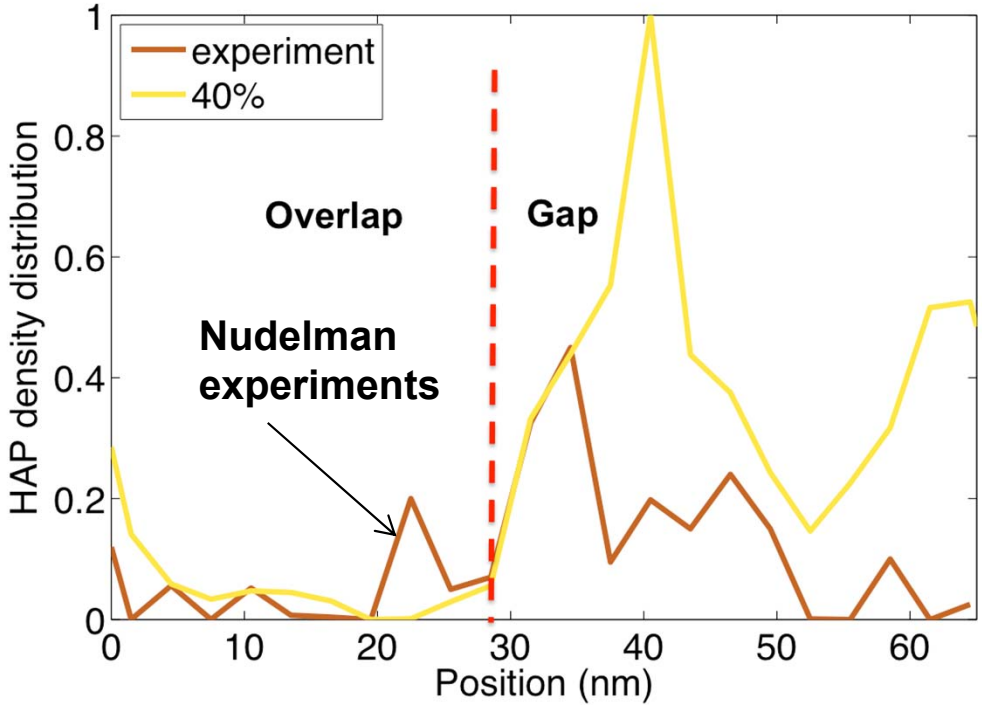
Hydroxyapatite distribution



Crystal sizes

$\approx 15 \times 3 \times 1.6\ \mathrm{nm}^3$

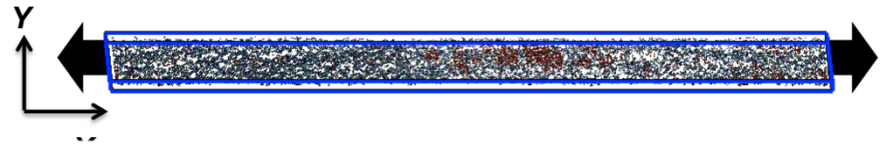


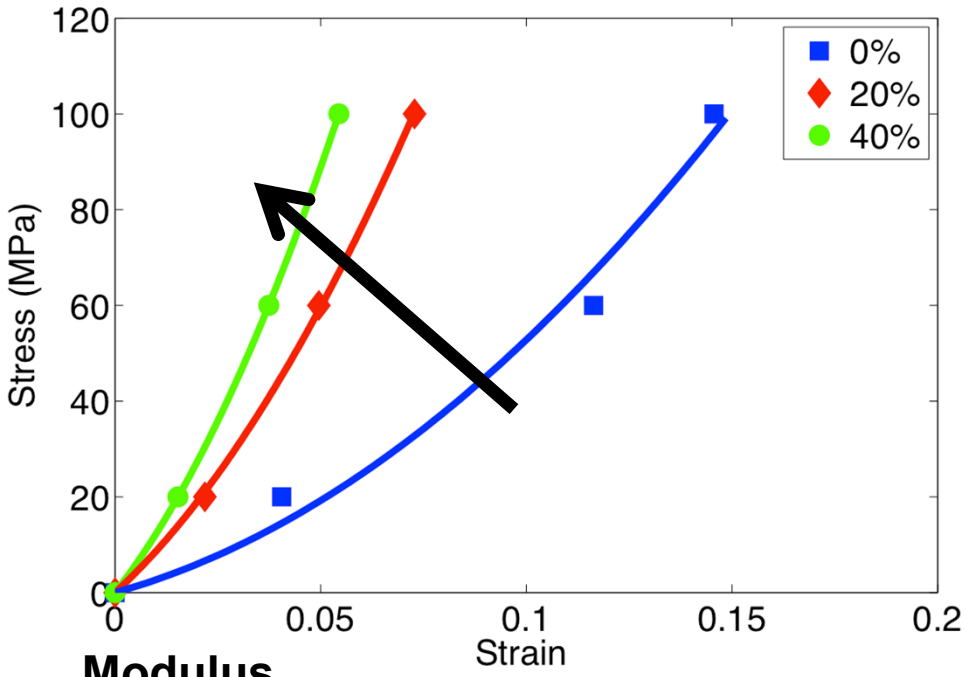


Hydroxyapatite is predominantly present in gap region (30-40 nm of the D-period) consistent with experiments.

Experimental results: Nudelman, *Nature Mat.,* 2010

Mechanical testing





Modulus

0% case 1.1 GPa at 100 MPa

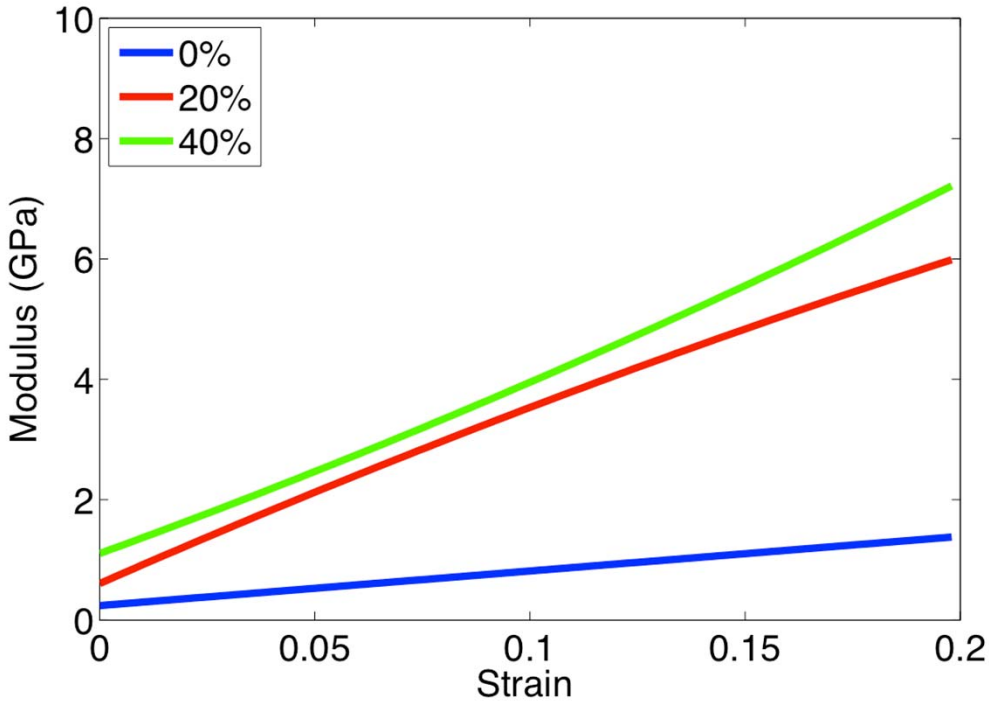
40% case 2.8 GPa at 100 MPa

150% increase

Experiment: 2-3 GPa

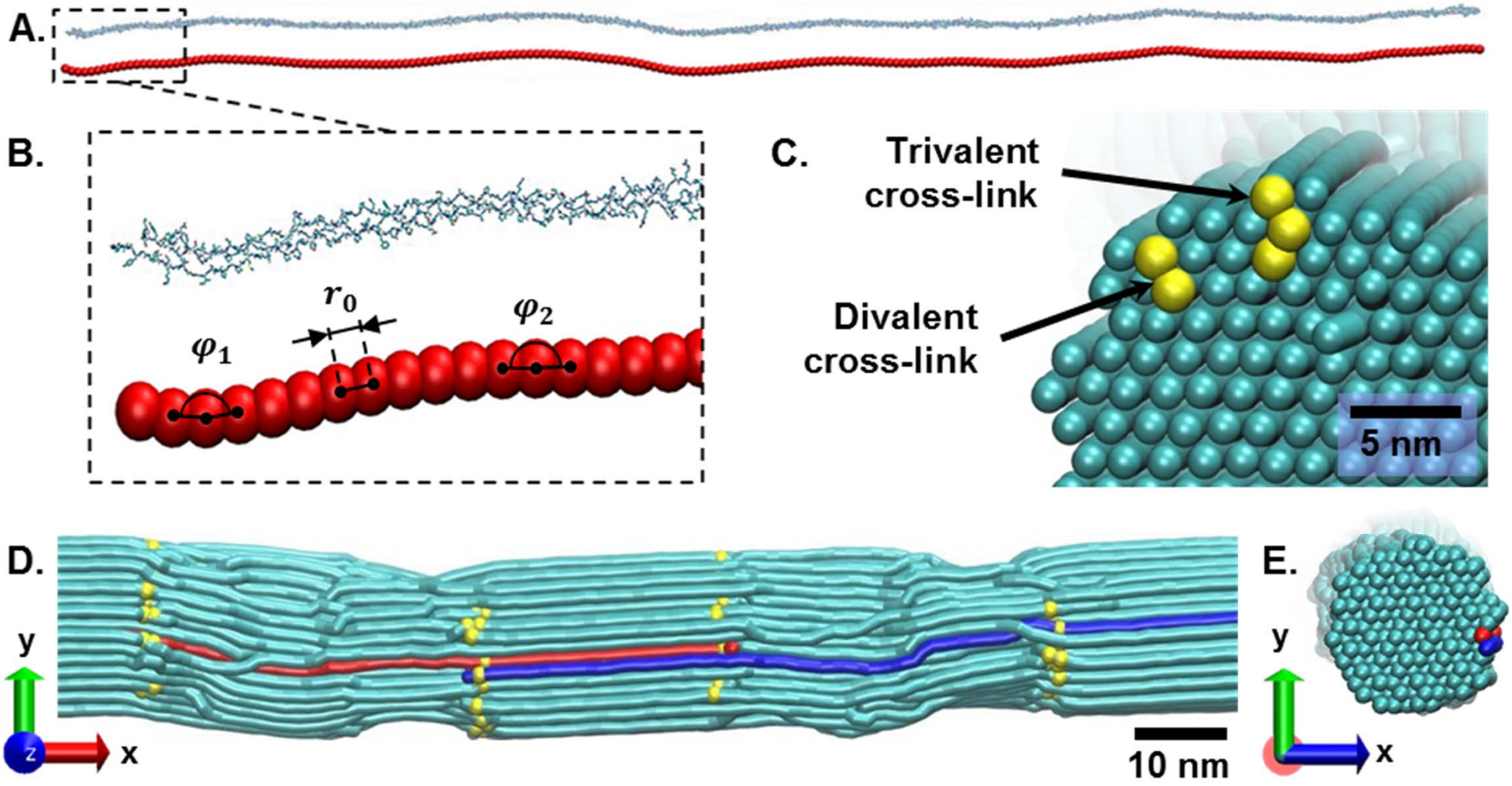
Hang and Barber *et al*., *J. R. Soc. Interface,* 2011

- Load applied to unit cell using *NPT* ensemble.
- **Computational time: 0.2 ns/week for 40% case (each data point = several months**

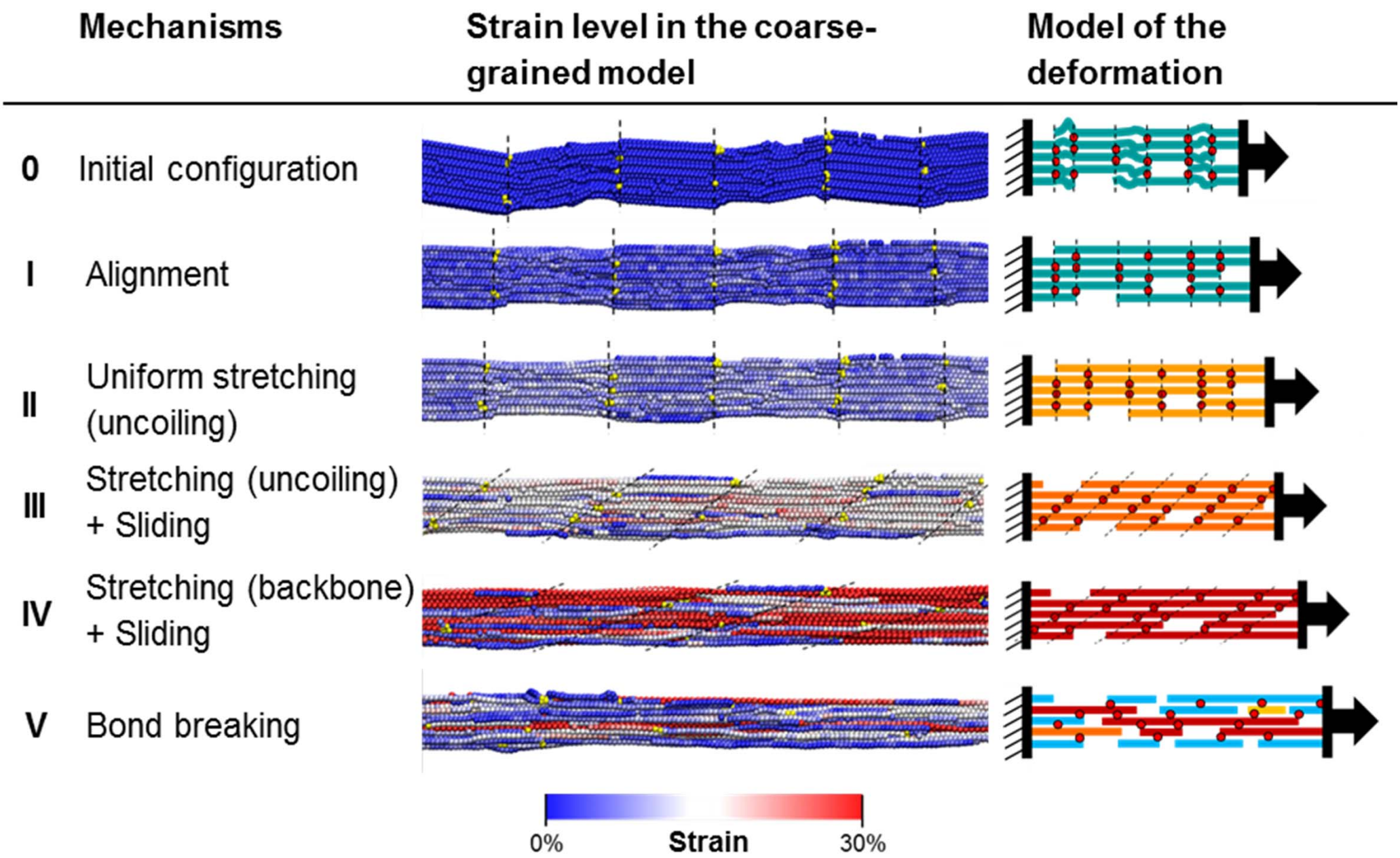


A. Nair, S. Chang, M.J. Buehler, *et al*., *Nature Comm*., 2013

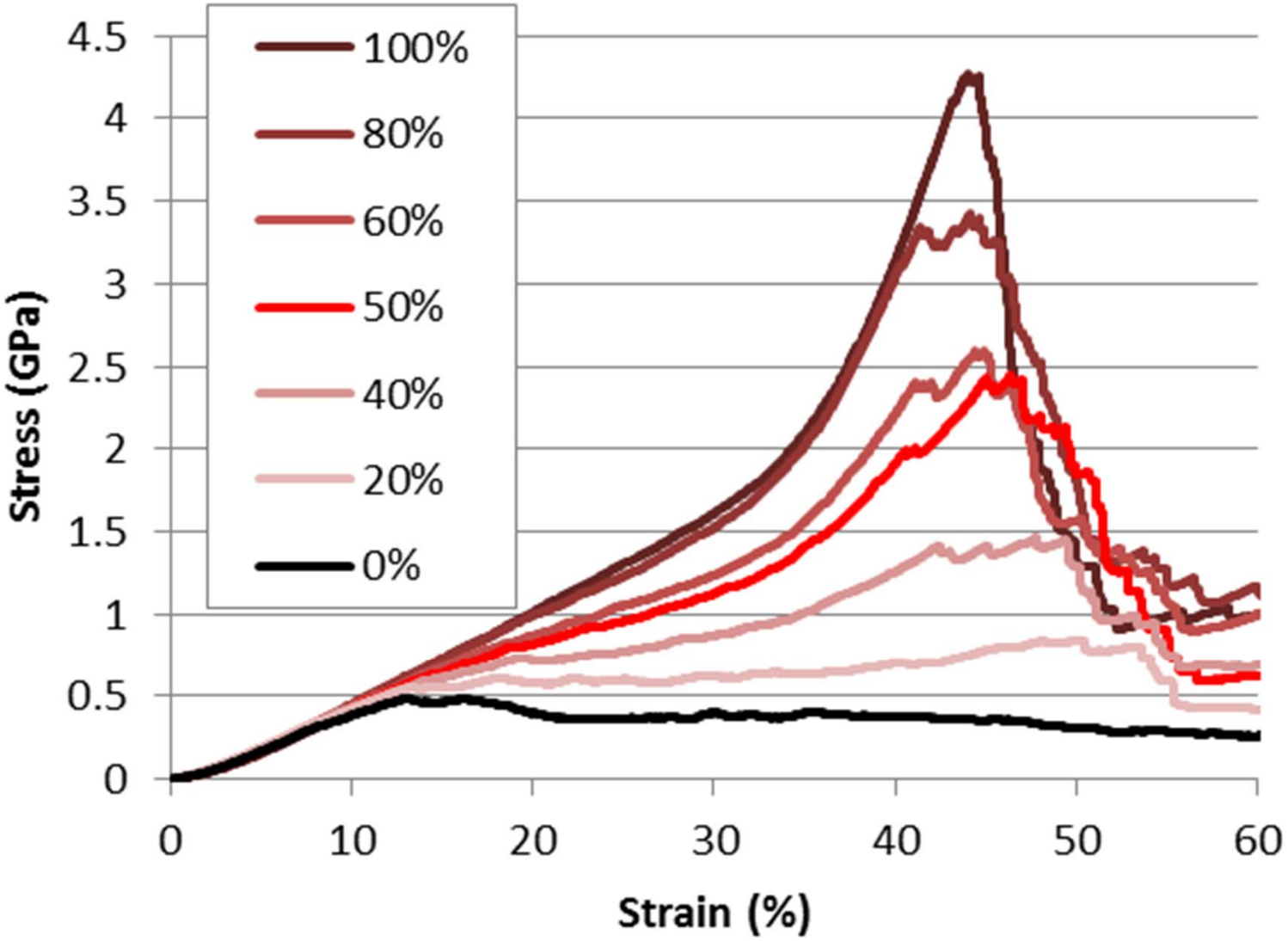
Coarse-grained collagen fibril model



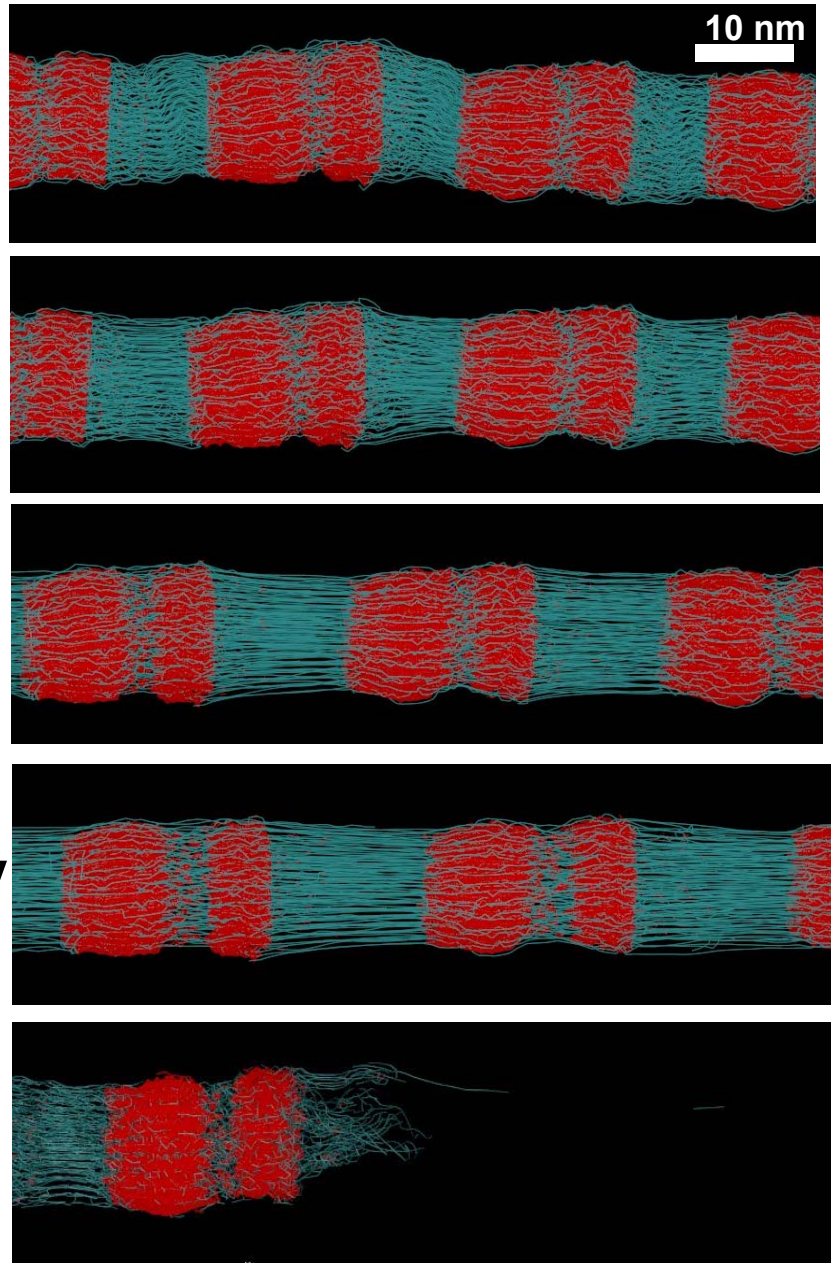
Coarse-grained collagen fibril model

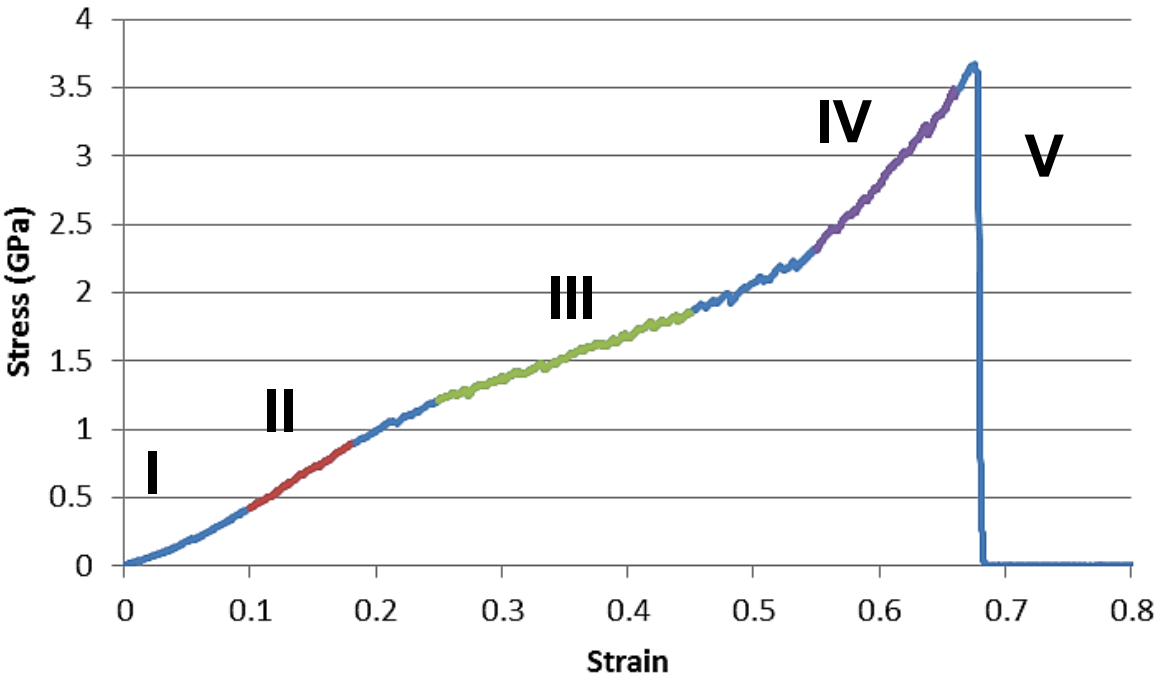


Coarse-grained collagen fibril model



Failure of mineralized collagen under mechanical loading

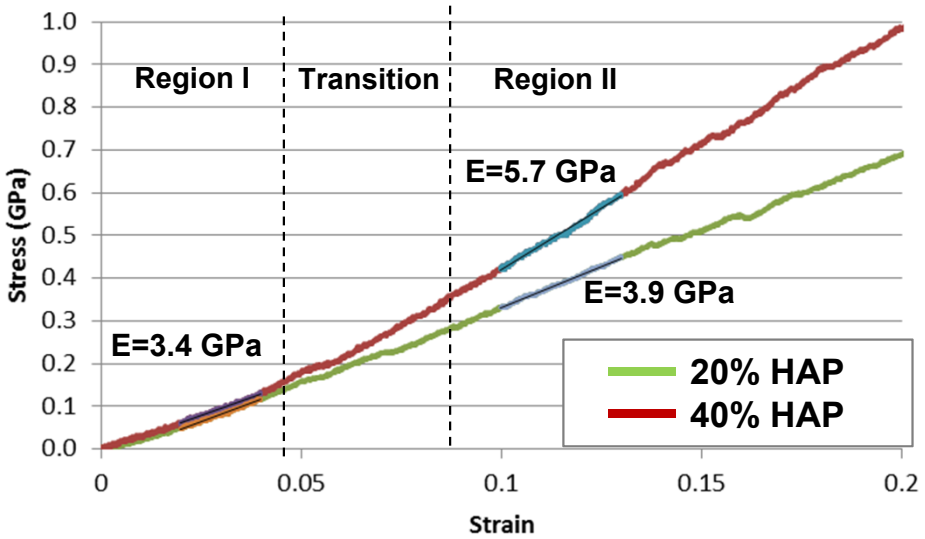




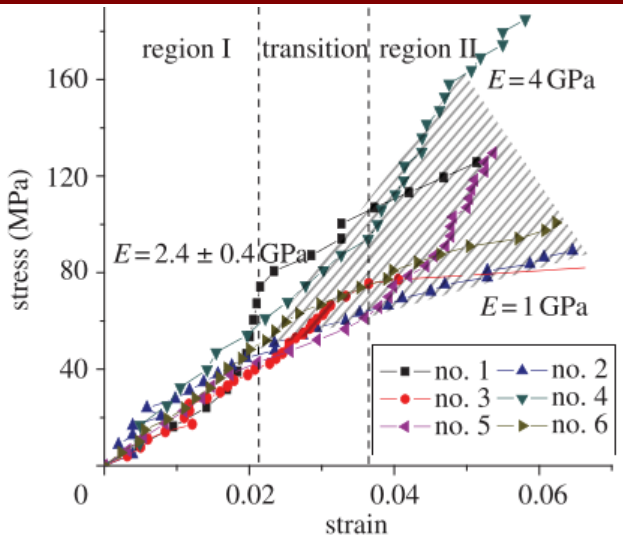
Necking at failure

B. Depalle, M.J. Buehler, *et al*., in prep.

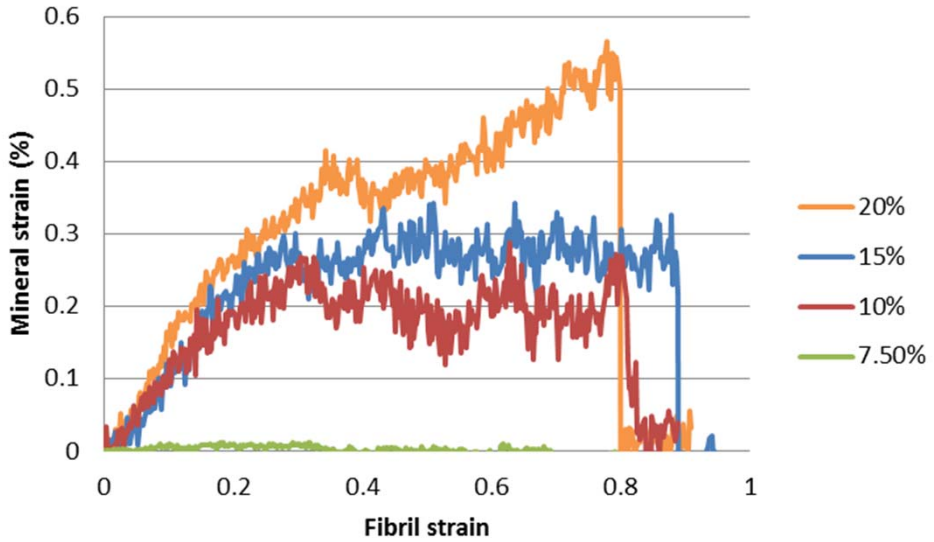
Mineralized collagen fibril: comparison with experiments



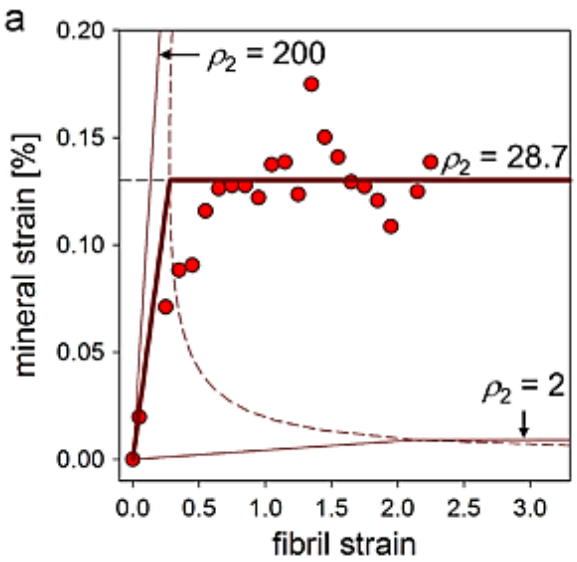
CG model stress-strain response for different mineral density



Tensile test on mineralized collagen fibrils (Hang, 2011 J. R. Soc. Interface)



CG model mineral strain



SAXS results for antler (no extrafibrillar mineralization) (Gupta, 2013 JMBBM)

B. Depalle, M.J. Buehler, *et al*., in prep.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