

生物材料和生物系统中的力学问题

Mechanics in Biological Materials and Systems: Modeling Strategies

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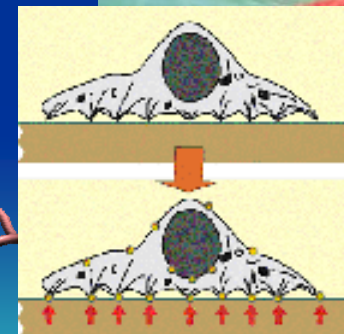
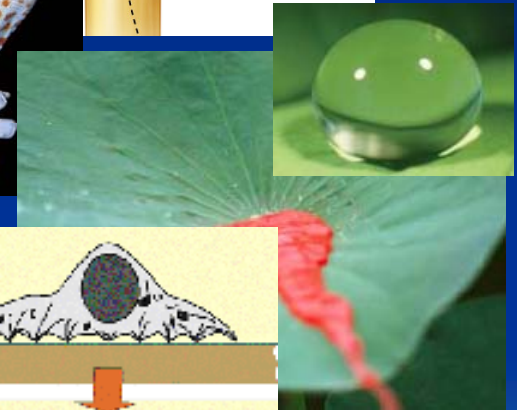
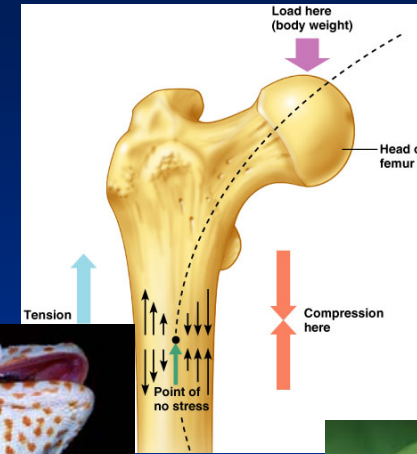
2008-10-31

中国力学学会青年学术沙龙

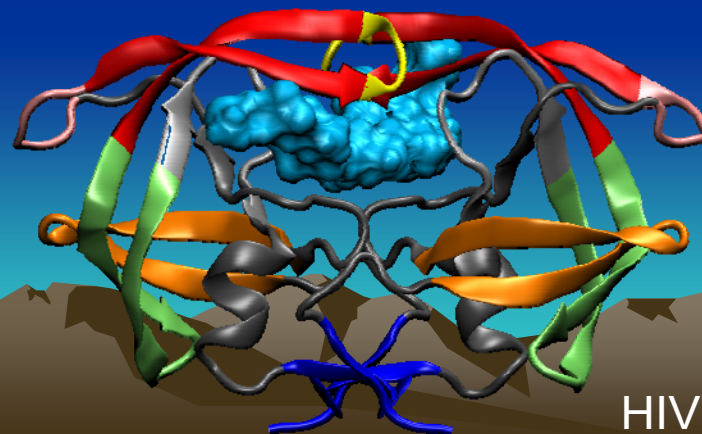


Biological Materials and Systems

- Biological bulk materials
 - Bone, dentin, shells
- Biological surface materials
 - Adhesion systems of Gecko
 - Water-repellent surface of Lotus leaves, water striders
- Cell
- Biomolecules



Focal adhesion

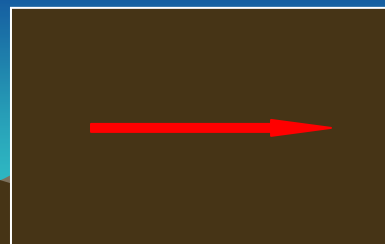


HIV-1 Protease

The Challenges

- Non-equilibrium
- No conservative laws
- No constitutive laws
- Complex systems
- Multiscales
- Emerging properties

Stimulation



Response

Part I

Mechanics of nano to micro hierarchical biological materials – A comparative study among different biological systems including:

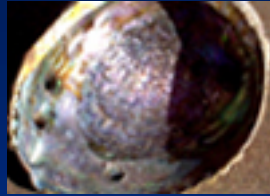
- Bone-like bulk biological materials
- Surface materials of adhesion system of Gecko
- Water-repellent surface of Lotus leaves and water strider's legs



Various bulk biological materials



Conch



Abalone



Nacre



Teeth



Bone



Sanddollar



Coral



Elk's antler



Cowry



Diatom



Oyster

These totally organism-controlled materials are synthesized at ambient temperature and atmospheric conditions.

Table 1. Mechanical properties of shell and its constituents

	Volume concentration	Young's Modulus	Strength	Toughness
Protein	1-5%	50-100 MPa	20MPa	-
Mineral	95-99%	50~100 GPa	30MPa	$\ll 1\text{Nm}^{-3/2}$
Shell	-	50GPa	100-300MPa	3~7Nm^{-3/2}

Table 2. Mechanical properties of bone and its constituents

	Volume concentration	Young's Modulus	Strength	Toughness
Collagen	55-65%	50-100 MPa	20MPa	-
Mineral	40-45%	50~100 GPa	30MPa	$\ll 1\text{Nm}^{-3/2}$
Bone	-	10-20GPa	100MPa	2.8-6.3Nm^{-3/2}

Currey, 1977; Jackson et al, 1988; Norman et al, 1995; Jaeger and Fratzl, 2000; Menig et al, 2001

Questions:

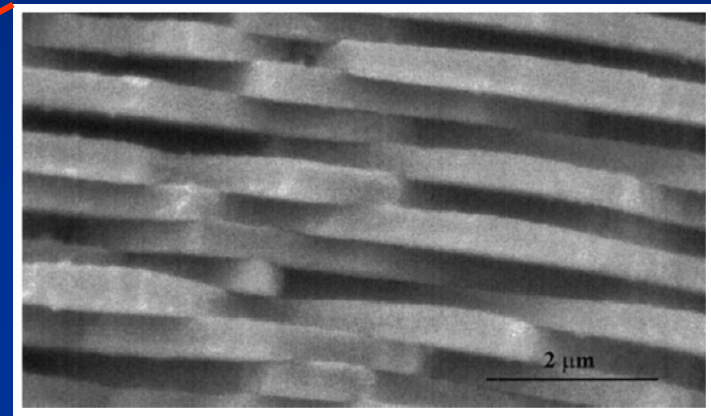
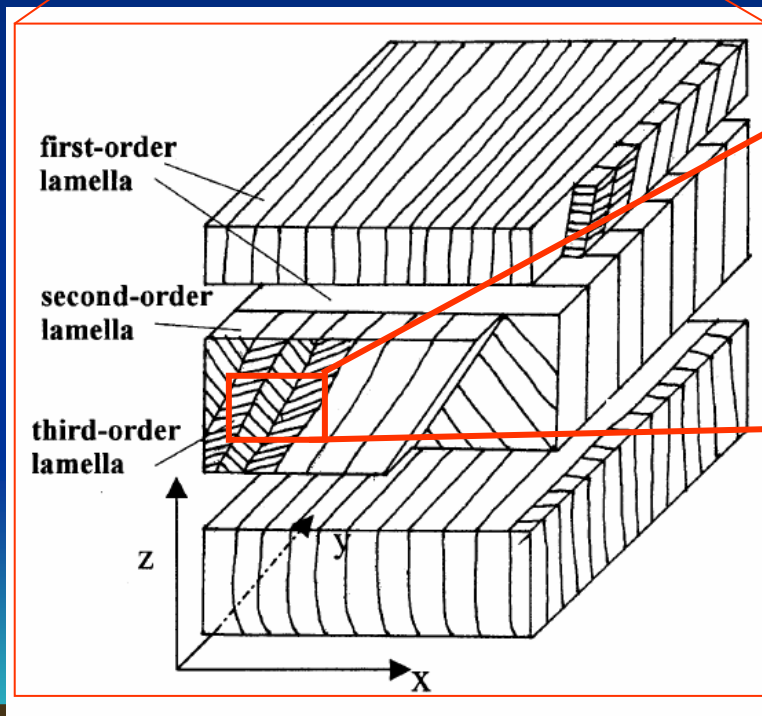
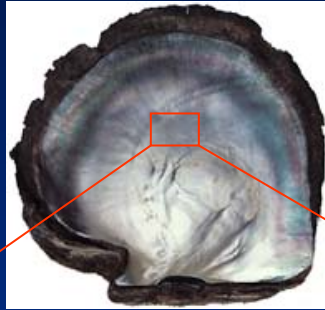
1. How does nature design so hard and tough materials with mineral and protein?
2. Can we synthesize these materials in vitro?

Assumptions:

The microstructures of biological materials have been optimized through billions years of evolution for the survival of animals.



Nanostructures of shells



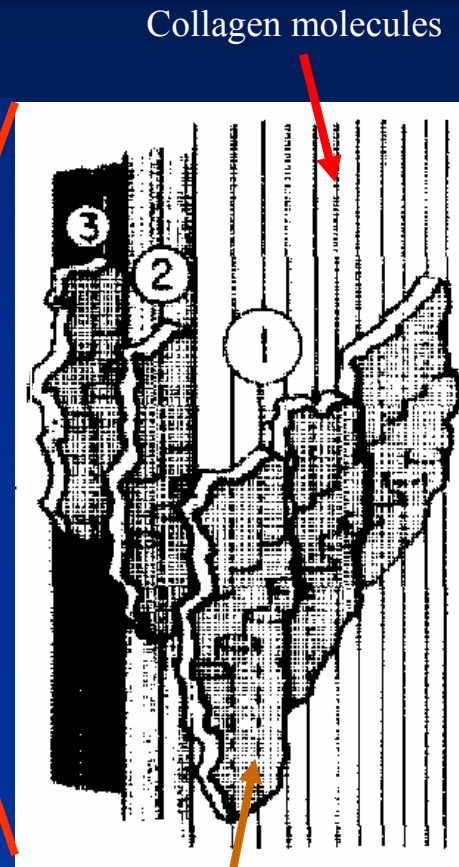
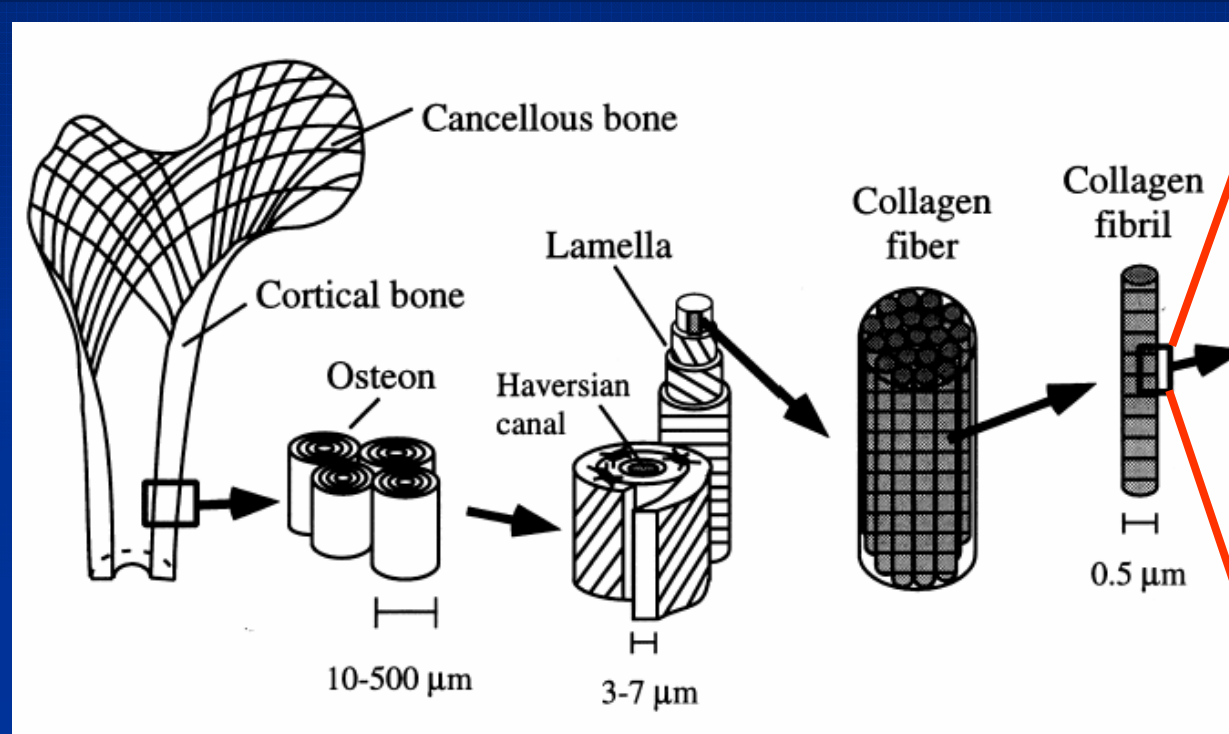
2μm

Menig, et al. Acta mater. 2000

S. Kamat, et al. Nature, 2000

Structures and materials are fully integrated in natural organism. The hierarchical organization of the structure at different spatial scale (nano, micro, macro) is inherent into these system.

Nanostructures of bone



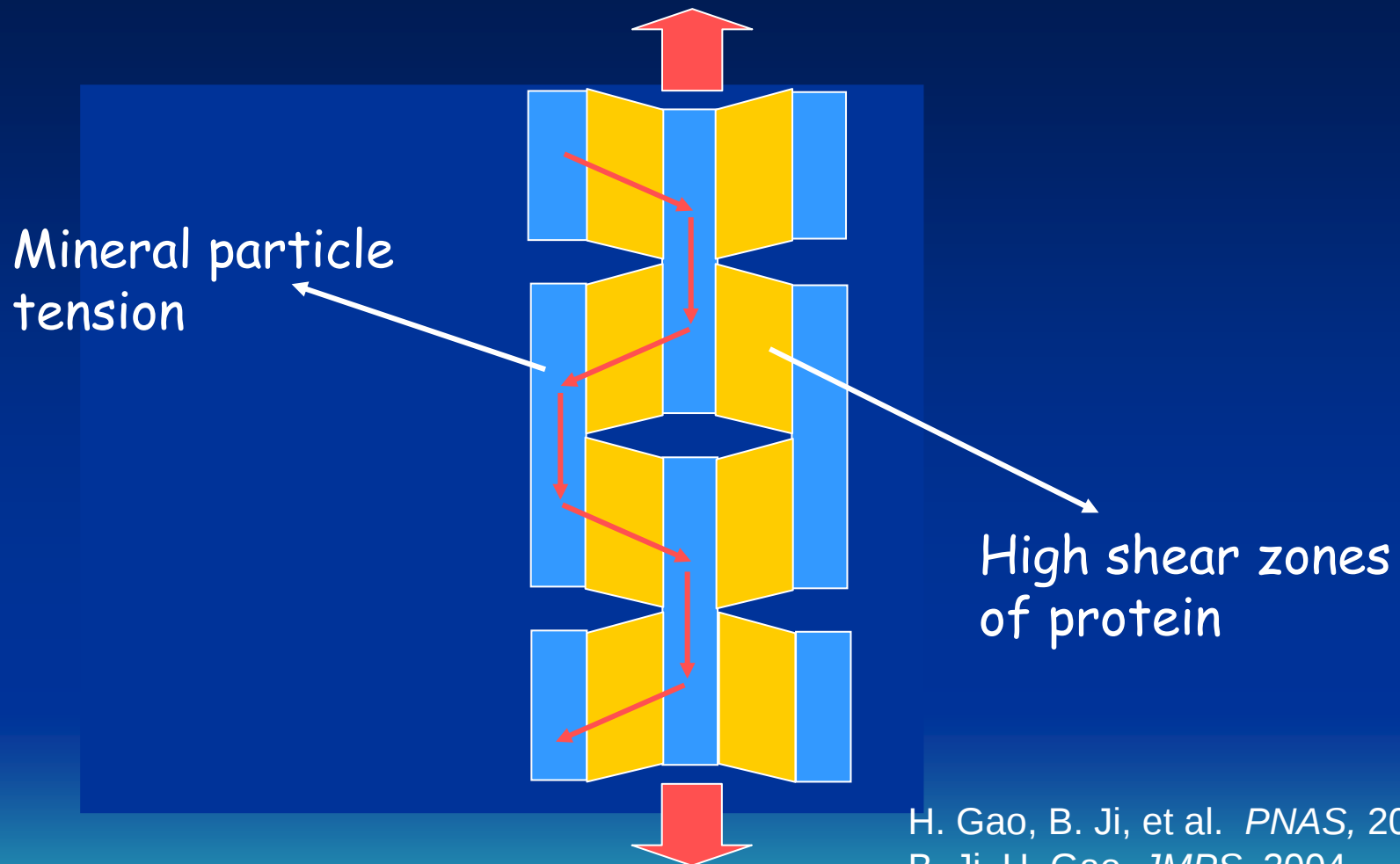
Macrostructure Microstructure Submicrostructure Nanostructure

Bone mineral crystal
100 x 40 x 3

$10^{-1} \sim 10^{-9}$

Rho, et al. Medi.Engng & Phys. 1998

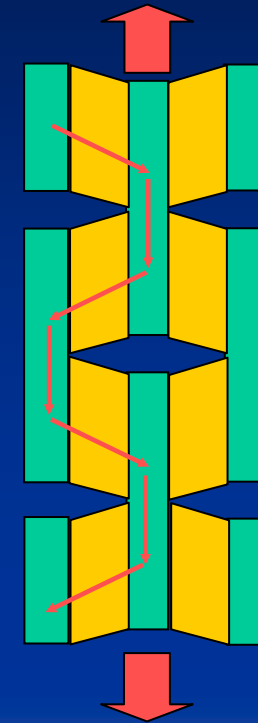
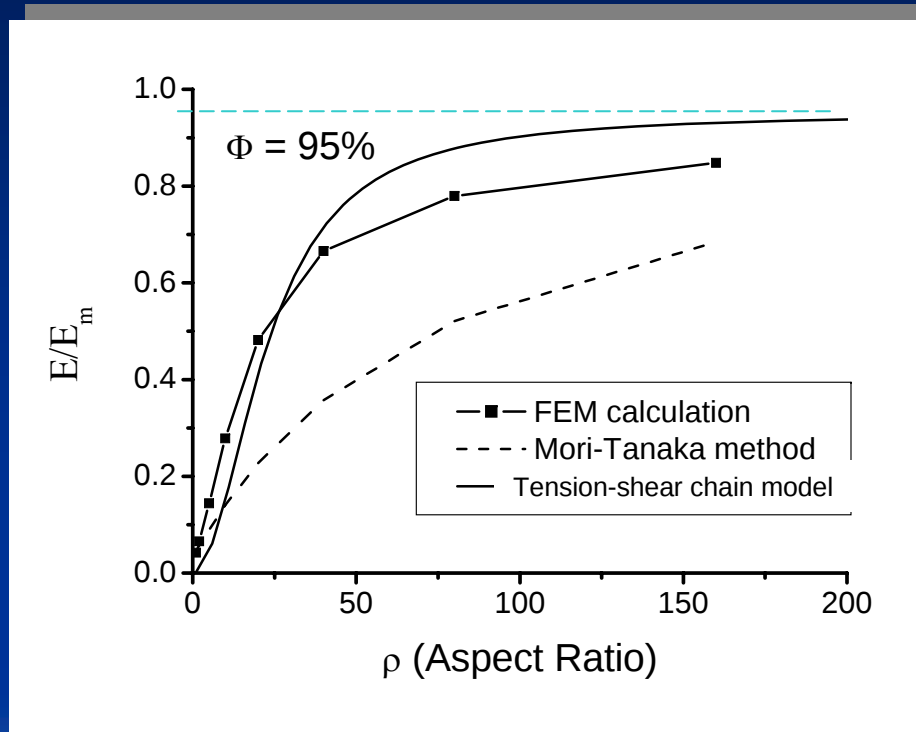
Tension-shear Chain model (TSC)



H. Gao, B. Ji, et al. *PNAS*, 2003
B. Ji, H. Gao, *JMPS*, 2004

The mineral particles carry tensile load while the protein matrix transfer the load between the mineral crystals via shear.

Elastic properties operate on Voigt upper bound



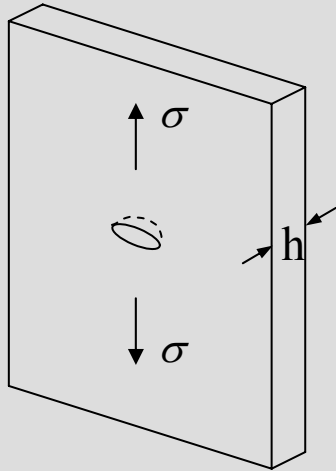
$$\sigma_m = \rho \tau_p$$

$$\frac{1}{E} = \frac{4(1-\Phi)}{\Phi^2 G_p \rho^2} + \frac{1}{\Phi E_m}$$

H. Gao, B. Ji, et al. *PNAS*, 2003
B. Ji, H. Gao, *JMPS*, 2004

The mineral particles should sustain large tensile load without fracture.

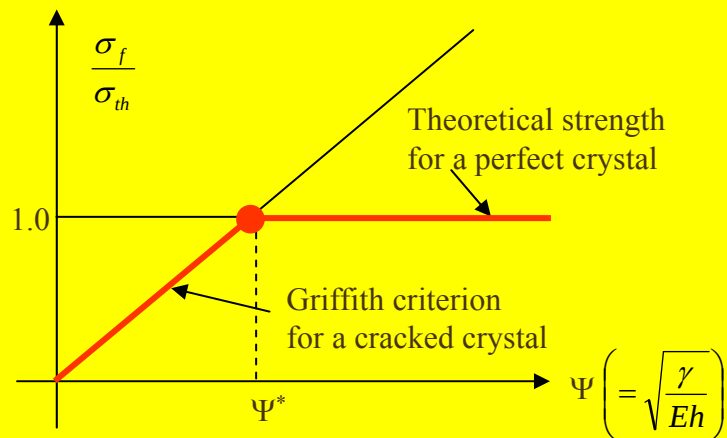
Mineral crystals become insensitive to flaws at nanoscale



Griffith criterion:

$$\partial(W - \Gamma) / \partial c = 0$$

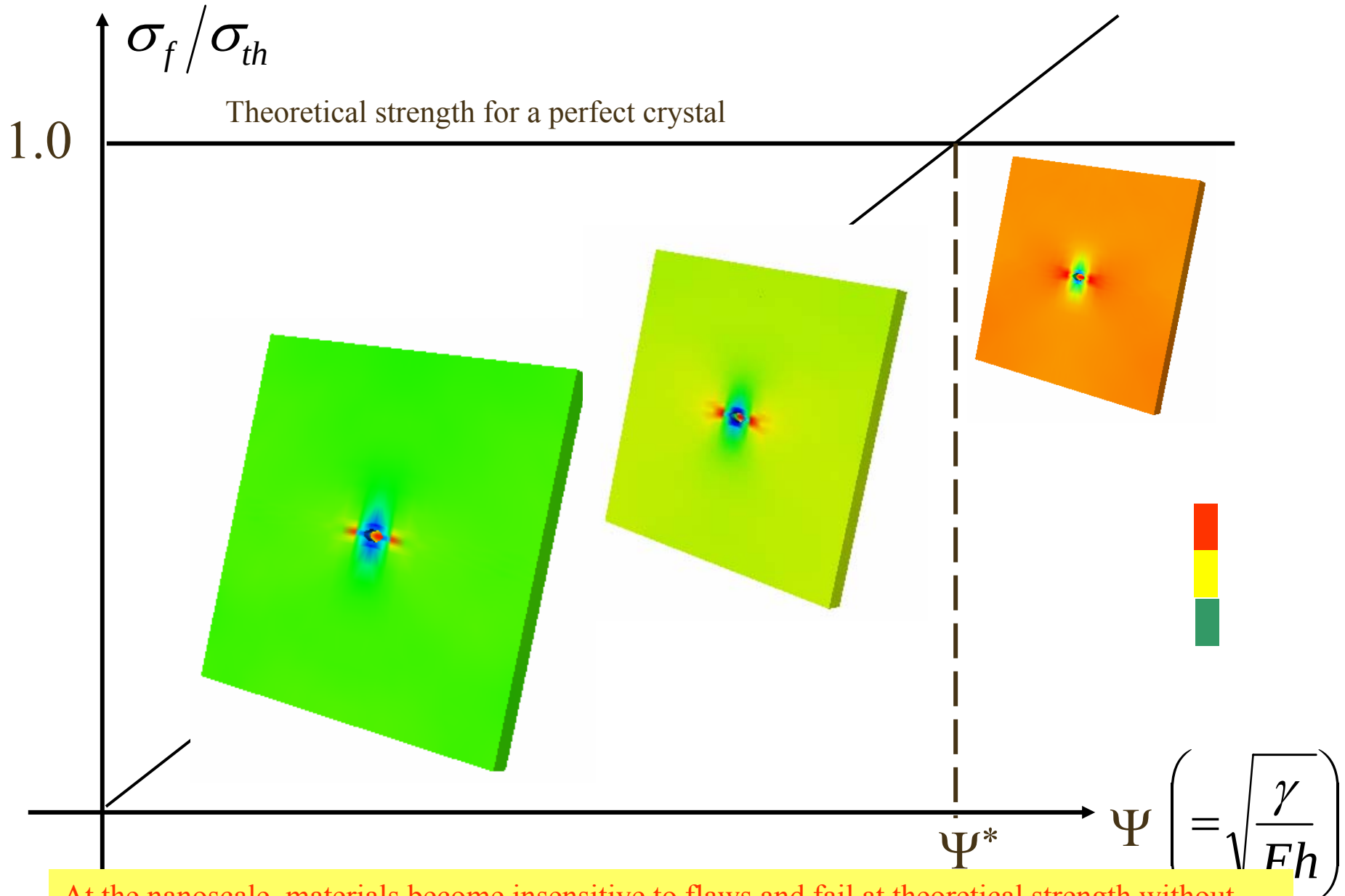
$$\sigma_m^f = \alpha E_m \Psi, \quad \Psi = \sqrt{\frac{\gamma}{E_m h}},$$



$$h^* \approx \alpha^2 \frac{\gamma E_m}{\sigma_{th}^2}$$

$$\text{If } E_m = 100 \text{ GPa, } \gamma = 1 \text{ J/m}^2$$

$$h^* = 30 \text{ nm}$$



A bio-inspired length scale

Young's modulus

Surface energy

$$l = \frac{\gamma E}{\sigma_{th}^2}$$

Theoretical strength

H. Gao, B. Ji, et al. *PNAS*, 2003
B. Ji, H. Gao, *JMPS*, 2004

Nature finds this secrets and hides material defects by designing the elementary structure of biomaterials at the nanoscale to achieve the maximum strength.

Is it universal?

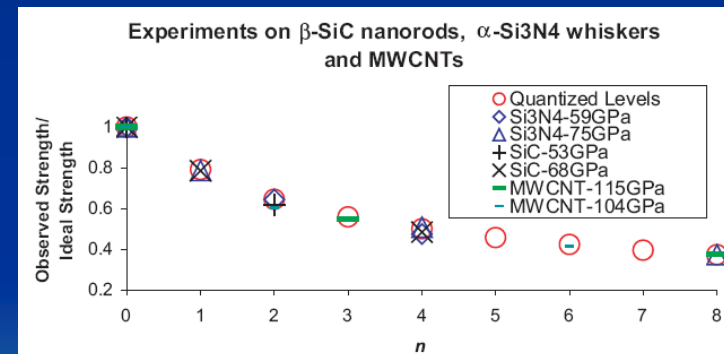
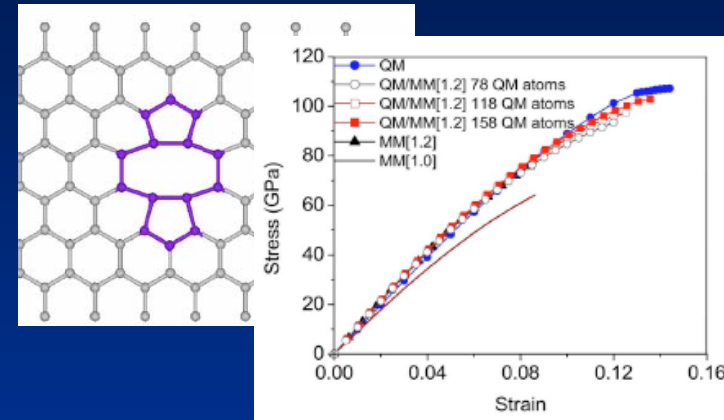
The Young's modulus of various brittle materials can vary, depending on the atomic structure and the purity of the materials.

Typical estimates of the theoretical strength can range between 1% and 10% of the Young's modulus.

If we take $\gamma = 1 \text{ J/m}^2$, $E = 50\text{--}1000 \text{ GPa}$, and $\sigma_{th} = (1\%\text{--}10\%)E$,

the characteristic length l_{cr} for flaw tolerance can be estimated to vary in the range:

$$l_{cr} \approx 2\text{\AA} - 400\text{nm}.$$



Pugno & Ruoff, *Phil. Mag.*, 2004

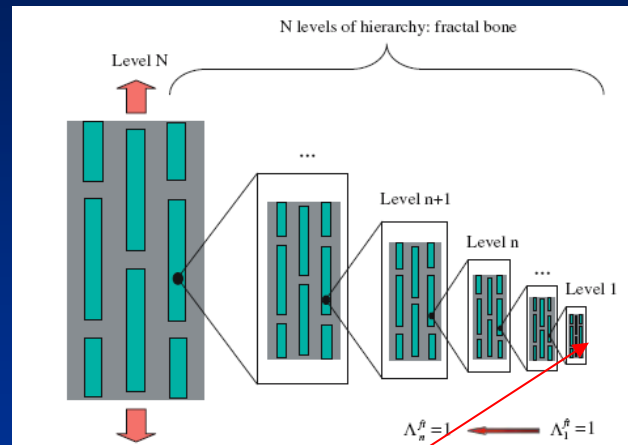
Ballarini et al., *Int. J. Fract.*, 2005

Khare et al., *PRB*, 2007

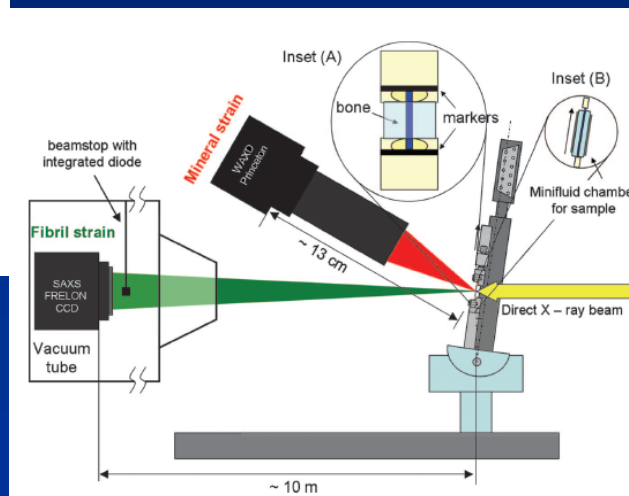
Gao & Chen, *J. Appl. Mech.*, 2005

Ji, *J. Biomech.*, 2008

Theoretical model of bone hierarchical structure

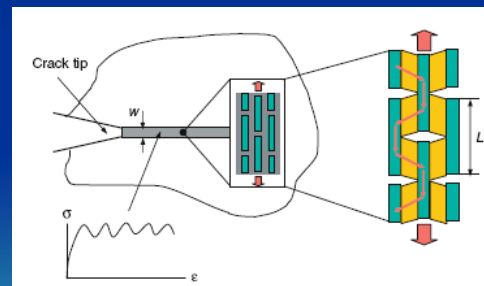


H. Gao, Int. J. Fract. 138, 2006



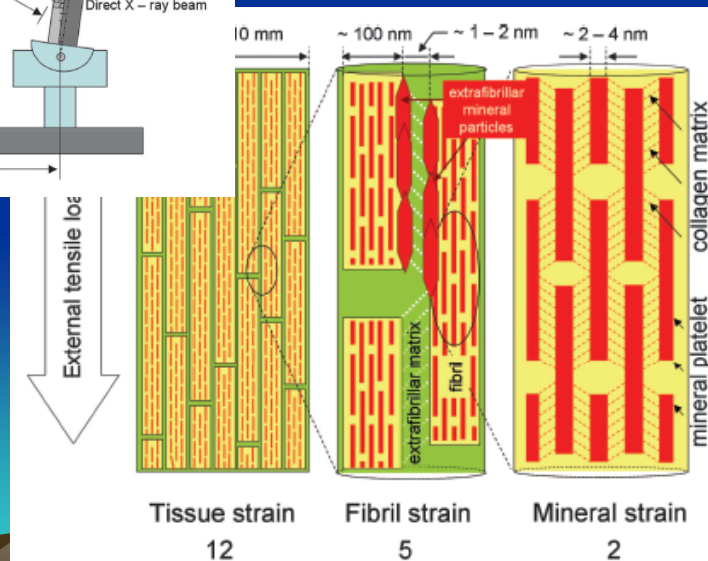
Experimental varification

Gupta et al., PNAS 103, 2006



$$J_c = \frac{1}{2} \xi \Phi \int \sigma_m d\Delta_m + \xi(1 - \Phi)L \int \tau_p d\epsilon_p.$$

B. Ji, J. Biomech. 41, 2008



Perspectives and Applications

MATERIALS SCIENCE

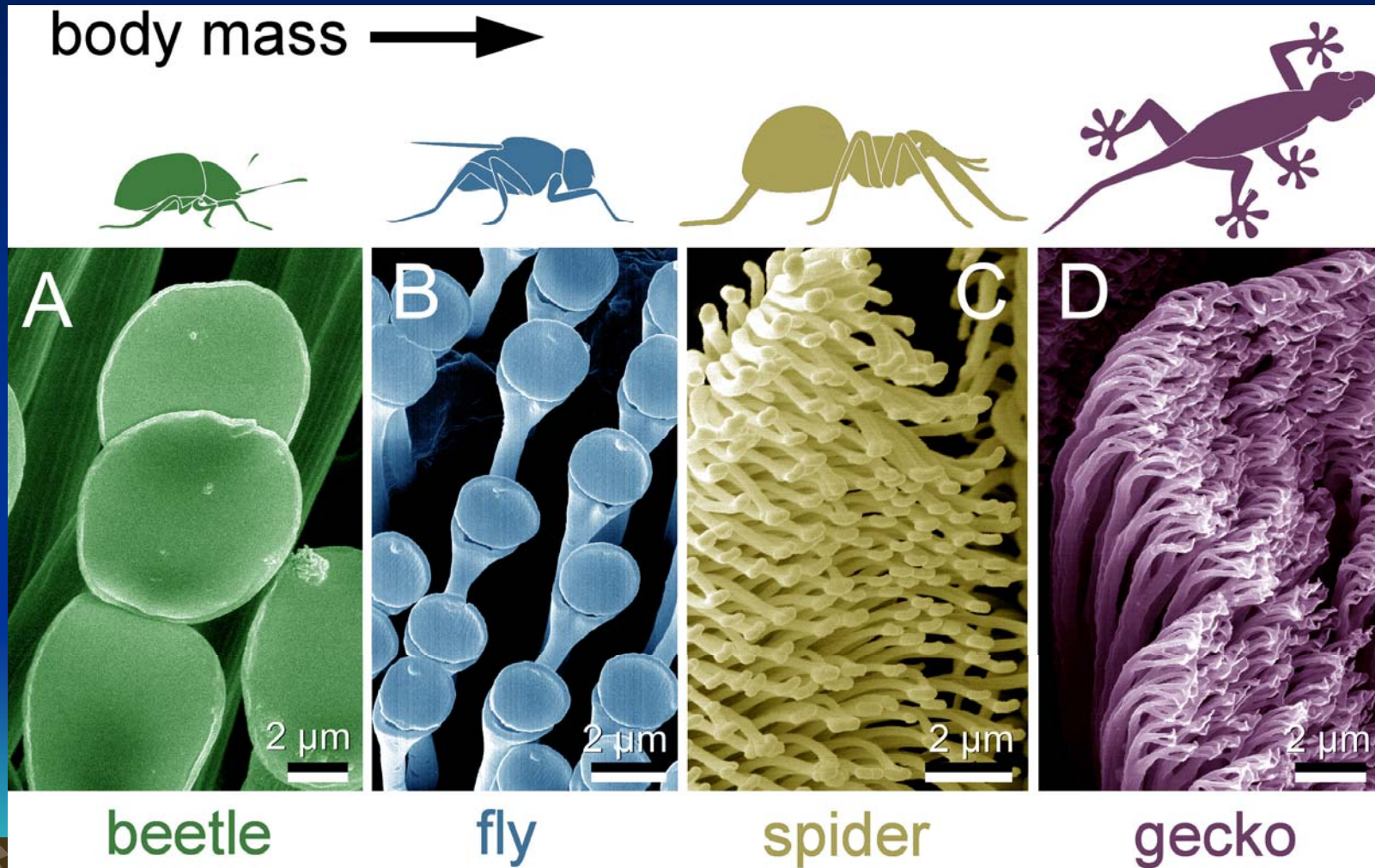
Bioinspired Structural Materials

Christine Ortiz and Mary C. Boyce

“Materials scientists are seeking to create synthetic materials based on the mechanical design principles found in biological materials such as seashell nacre.”

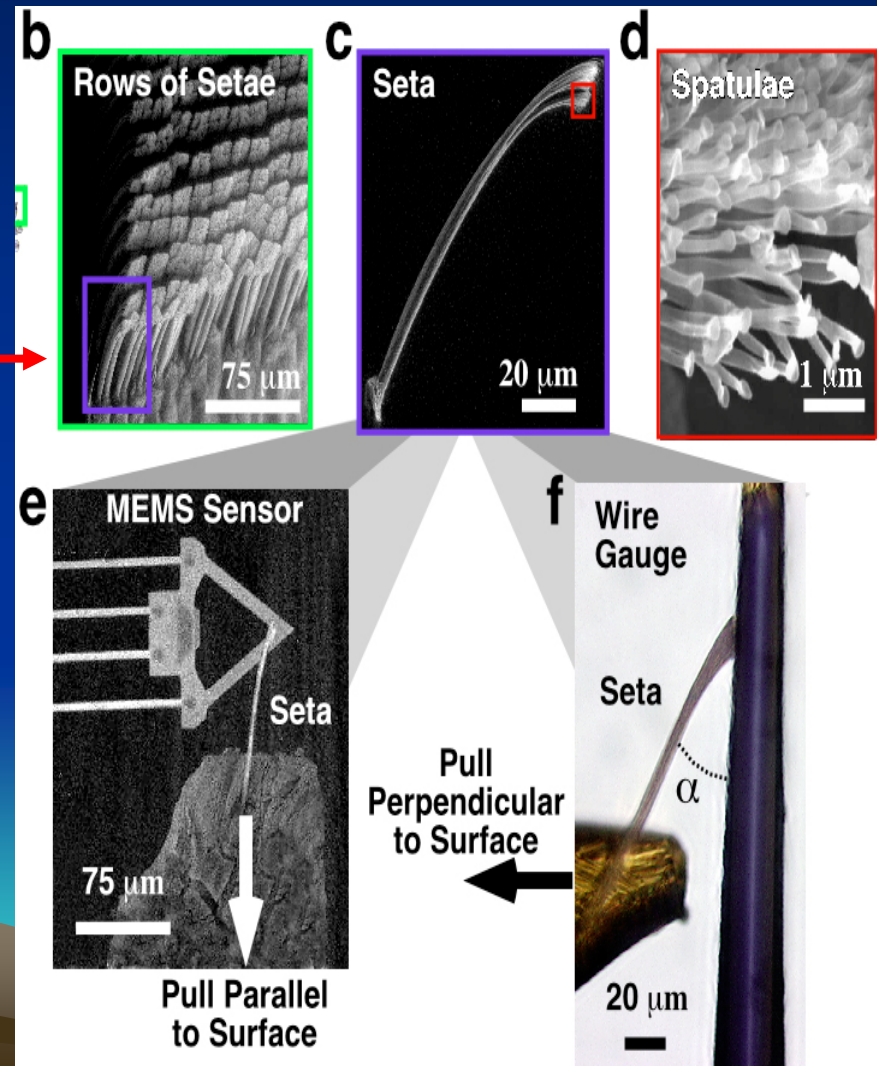
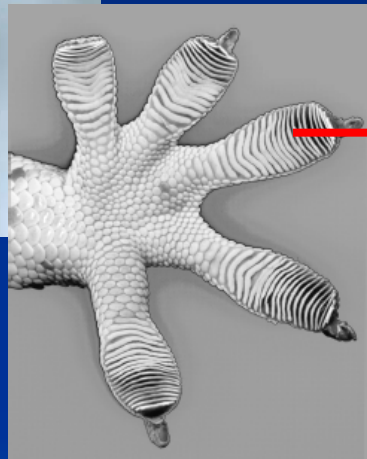
1. Bonderer et al., 2008, "Bioinspired design and assembly of platelet reinforced polymer films", *Science* 319, 1071
2. C. Ortiz and M. C. Boyce, 2008, "Bioinspired structural materials", *Science* 319, 1054
3. Currey, J. D., 2005, "Materials science - Hierarchies in biomineral structures", *Science* 309, 253
4. Mayer, G., 2006, "Rigid biological systems as models for synthetic composites", *Science* 309, 1144

Biological Surface structures



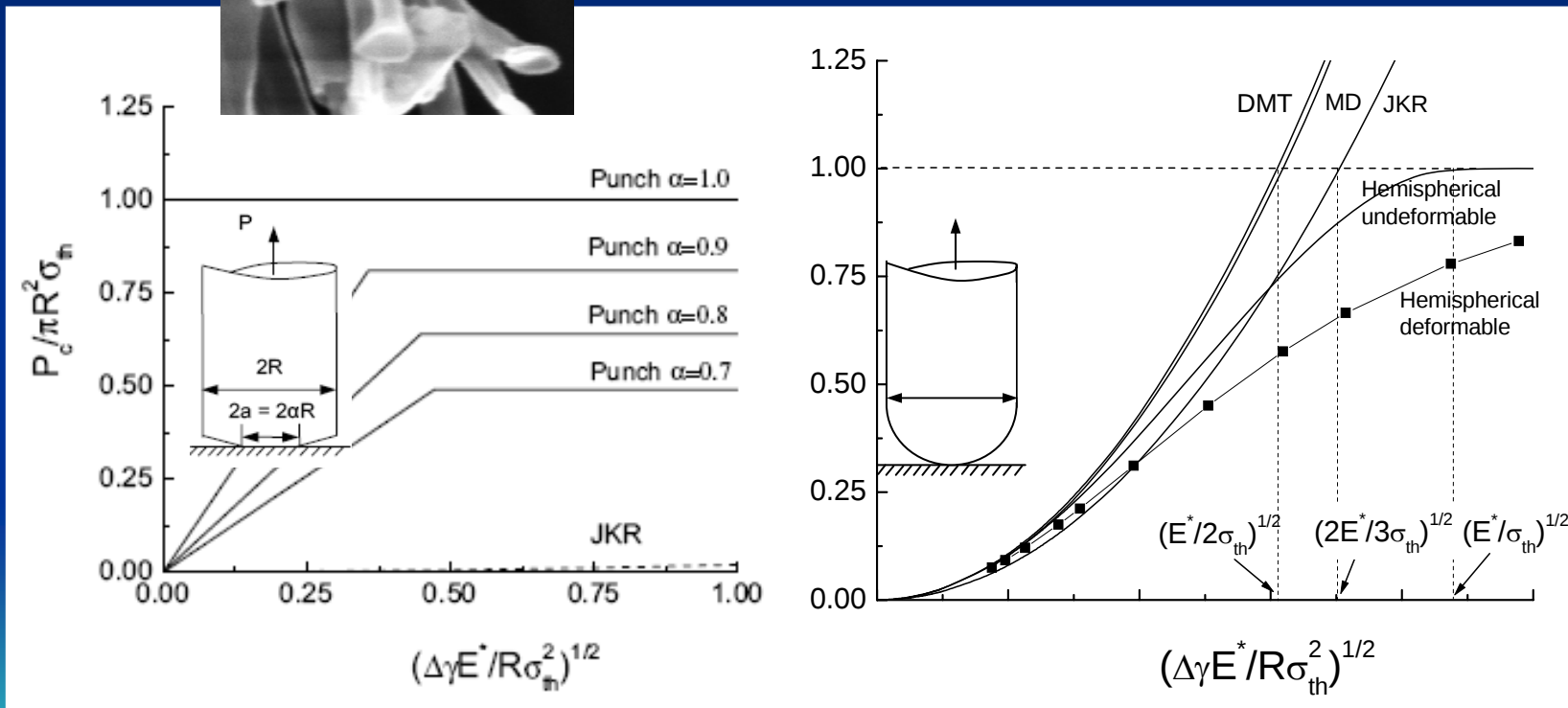
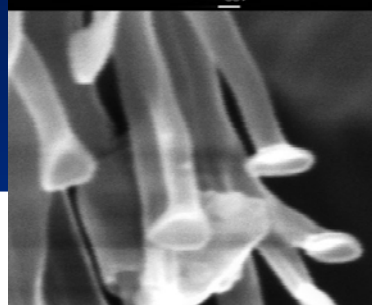
Courtesy of Dr. S. Gorb

Hierarchical adhesion structure of Gecko



Hansen & Autumn, 2005, PNAS 102, 385

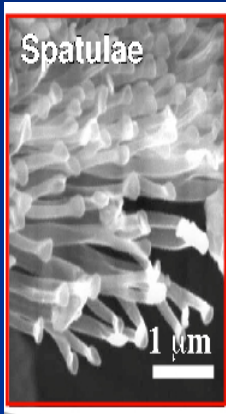
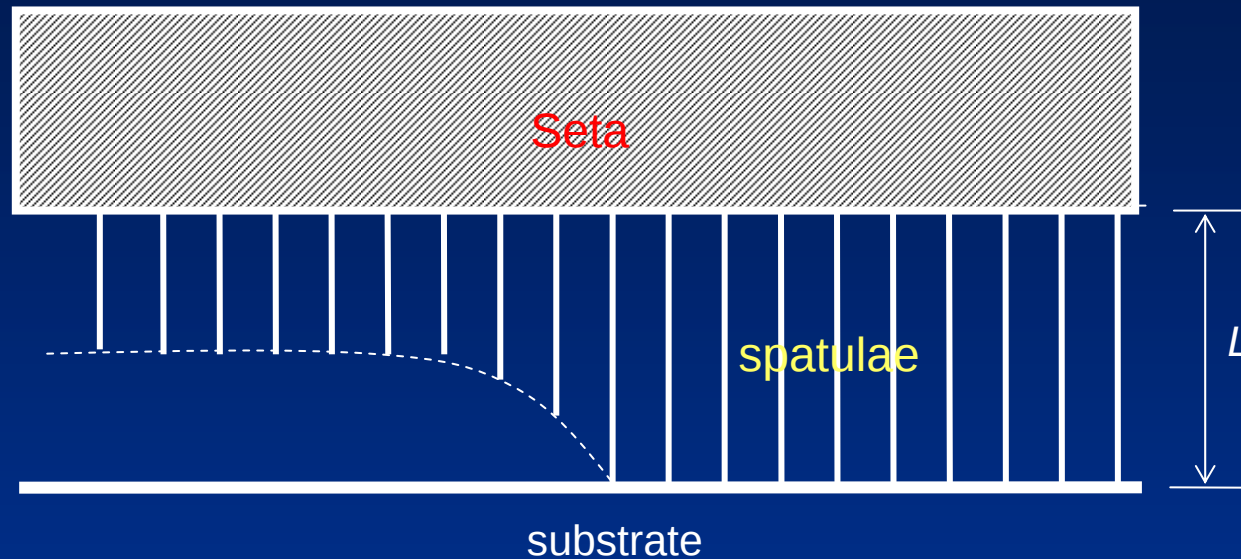
Fracture/JKR models for adhesive contact



H. Gao, B. Ji, et al., 2004, MCB 1, 37

Buehler et al., 2005, Modelling Simul. Mater. Sci. Eng. 14 (2006) 799

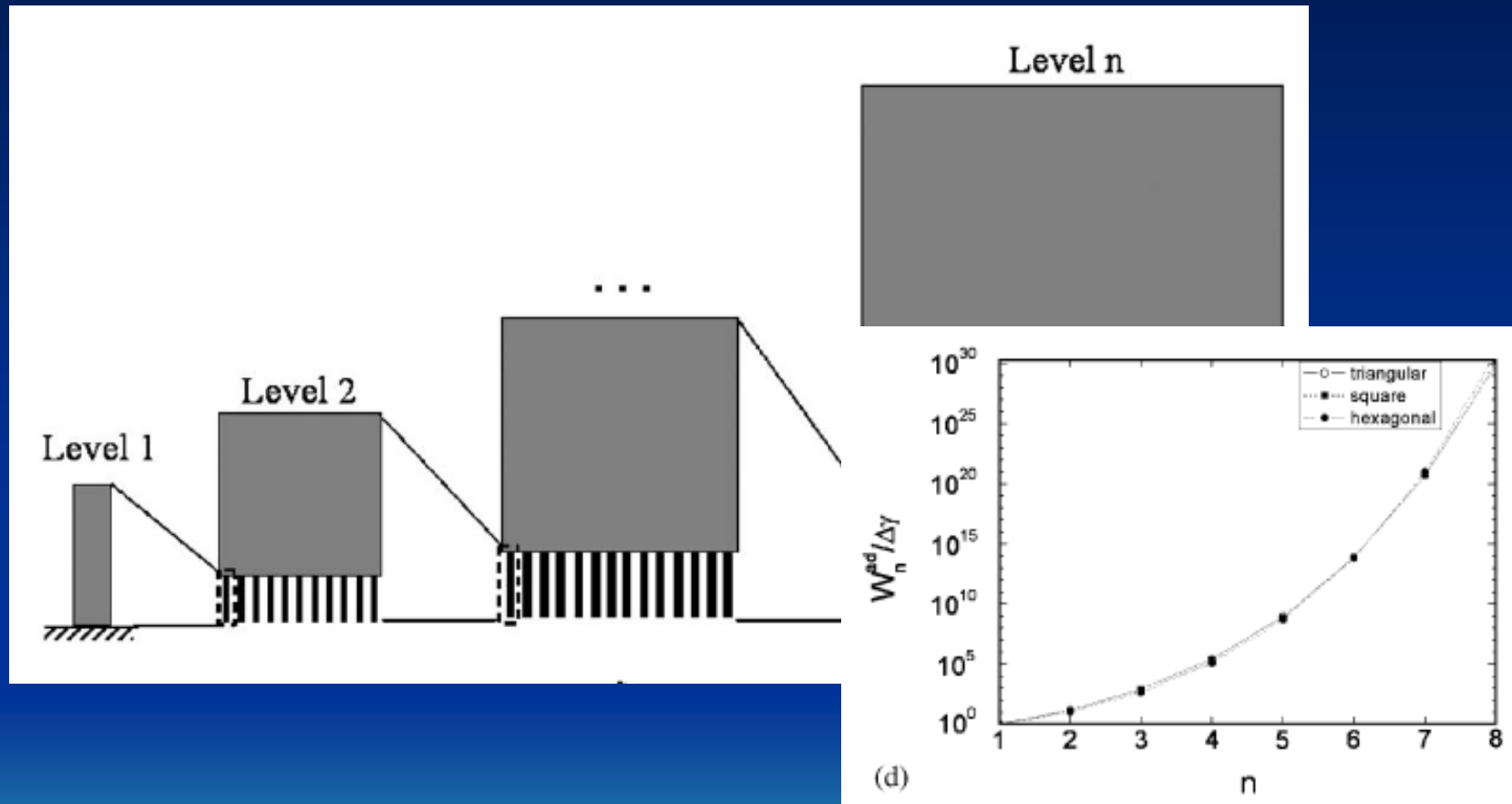
Energy dissipation mechanism



$$J_c = \varphi \Delta \gamma + \underline{L \int \sigma \varphi d\varepsilon} = \varphi \Delta \gamma + \frac{L \sigma_c^2 \varphi}{2E}$$

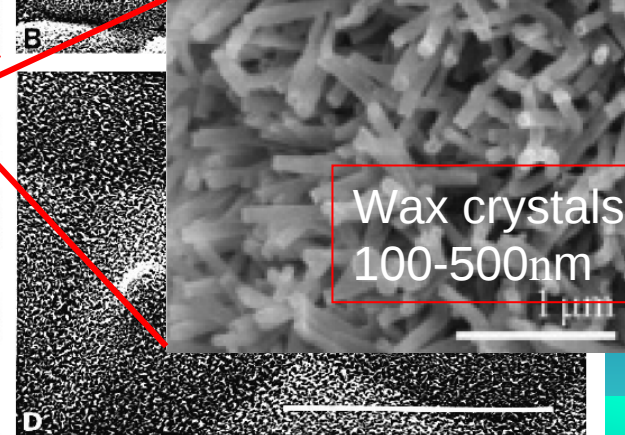
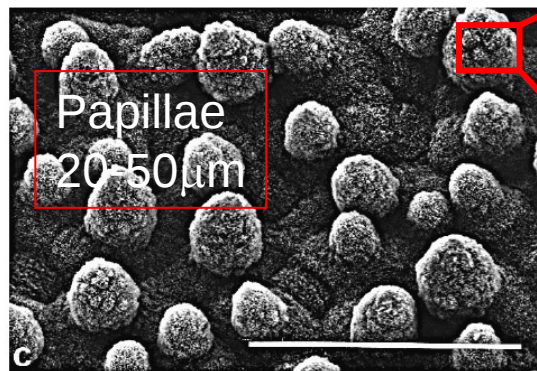
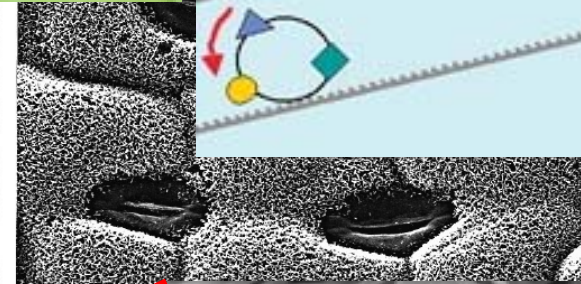
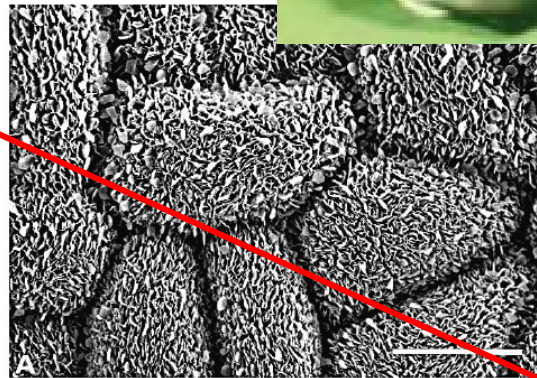
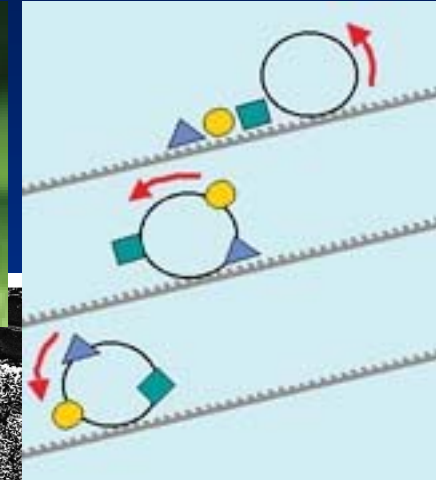
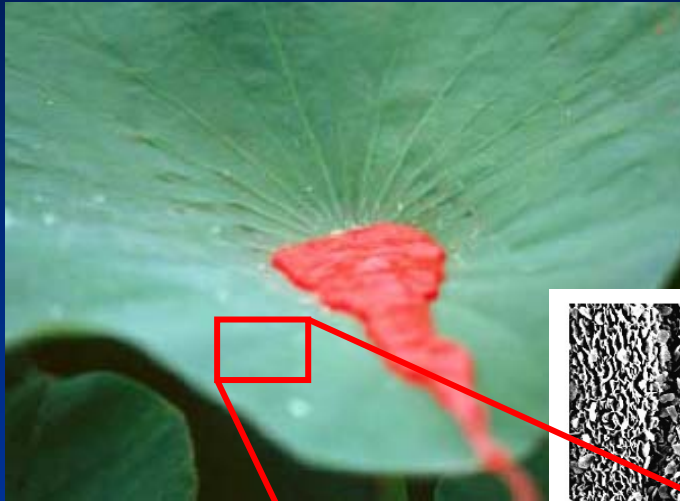
$$\frac{J_c}{\varphi \Delta \gamma} = 1 + \frac{\sigma_{th}}{2E} \left(\frac{L}{\delta} \right)$$

Hierarchical design



$$W_{n+1}^{\text{ad}}(\varphi_n) = \left(W_n^{\text{ad}} + \frac{(S_n)^2 L_n}{2E_f} \right) \varphi_n = \left(W_n^{\text{ad}} + \frac{(\sigma_{\text{th}} \Phi_{n-1})^2 L_n}{2E_f} \right) \varphi_n.$$

Water-Repellent Plant Leaves

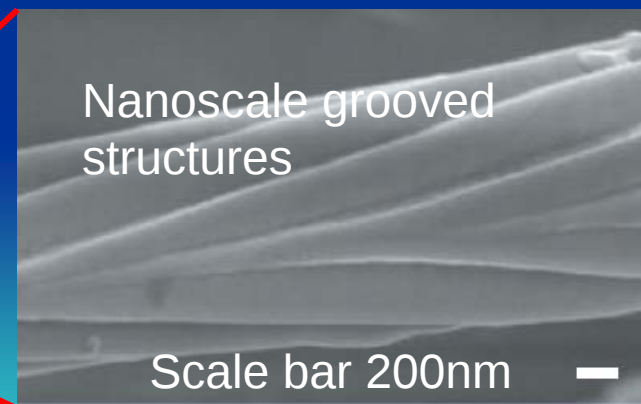
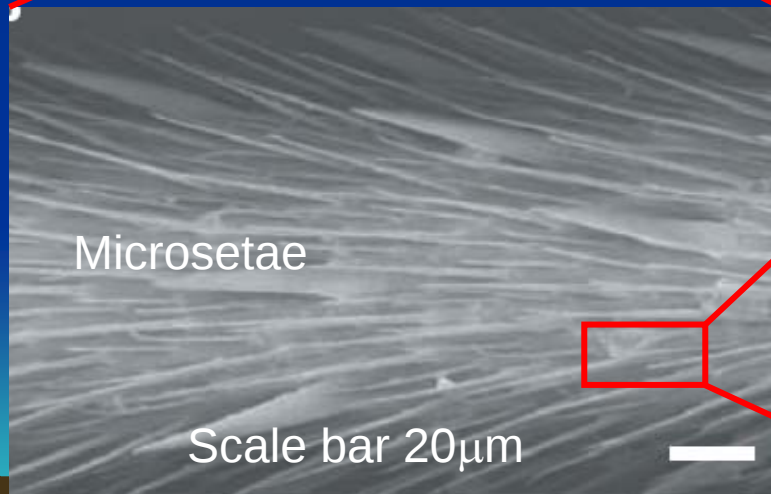


Barthlott and Neinhuis, *Planta*, 1997; Barthlott and Neinhuis, *Annals of Botany*, 1997

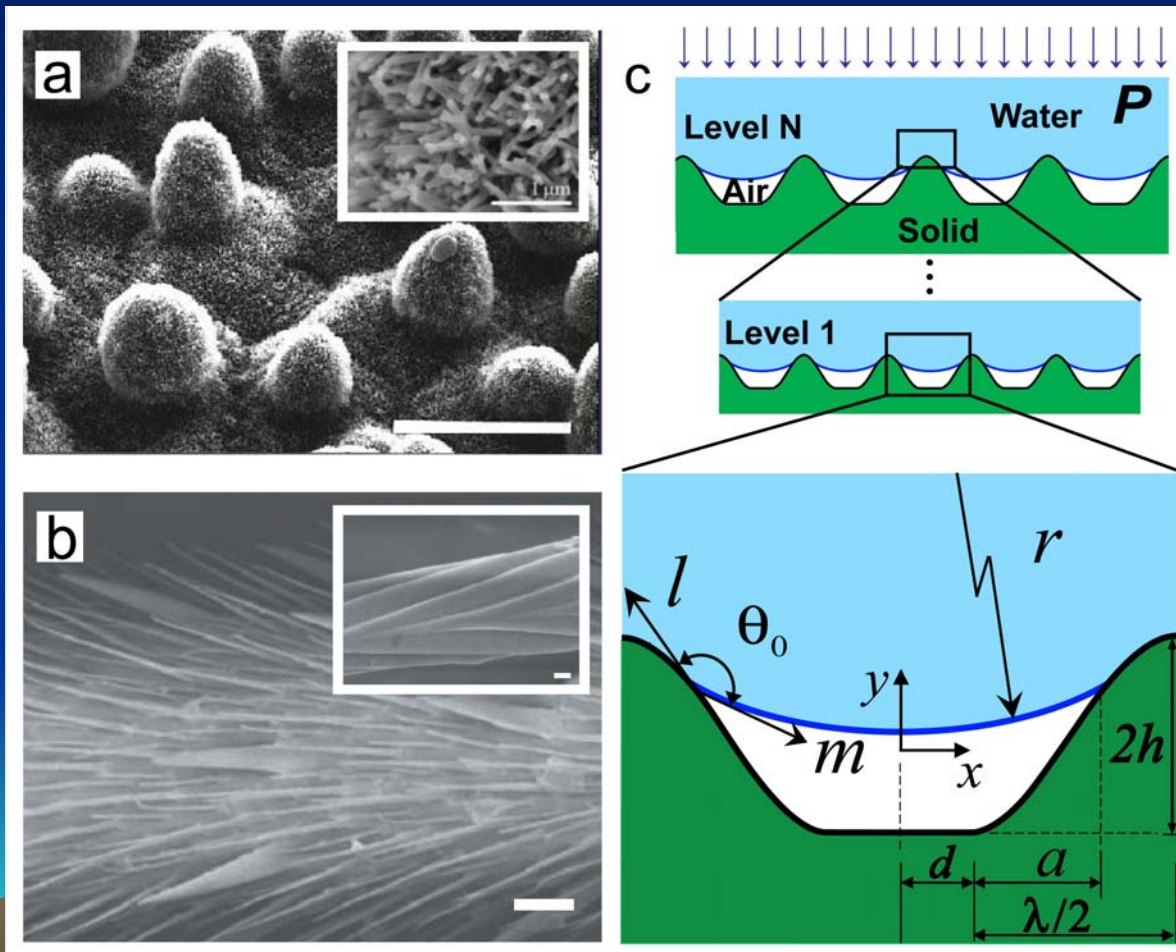
Water-Repellent Insects



Water strider



A theoretical model for hierarchical biological surface structure for **low** adhesion



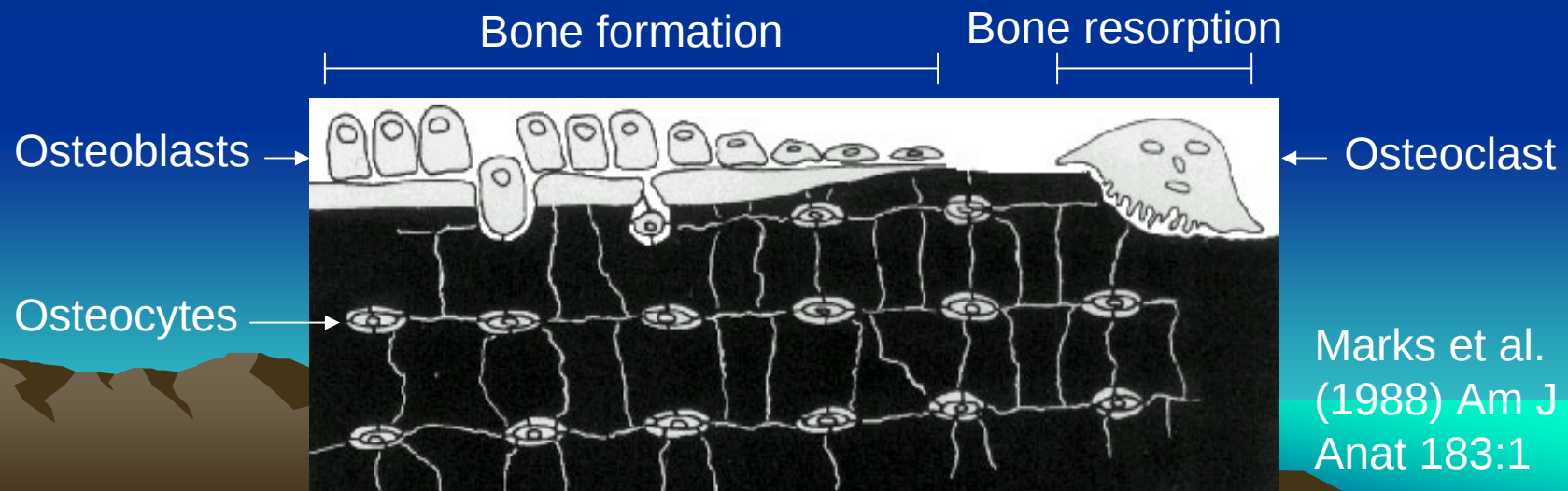
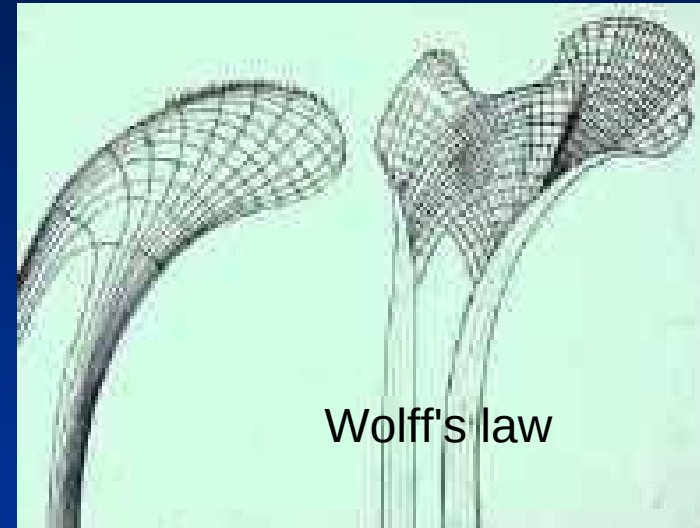
Summary

- It seems that Nature use similar strategies, i.e., with hierarchical design from nanoscale, to optimize or control different material properties.
- At the nanoscale, the structure is not sensitive to flaws, achieving maximum strength of the materials.
- Hierarchical structures are designed for the toughness, energy dissipation and robustness.
- Bio- is the nanotechnology by nature. Biological materials achieve these superior properties through billions years of evolution by adapting their living environment.
- The chemistry and structure are simultaneously used. The geometry of the microstructure is also crucial.
- Biomimicking is a good way for designing man made novel materials.



“Smart” biological materials

1. Bone is capable of adapting in response to mechanical stimulus
2. Osteocyte is the mechanosensor in bone being able to sense and respond to load-induced strains and to translate this information to cells at the bone surface.
3. The loss of these cells from our bones is associated with the human ageing process.



Part II

Modeling of cell adhesion: from molecular level

The growth and instability of adhesion
cluster



Background

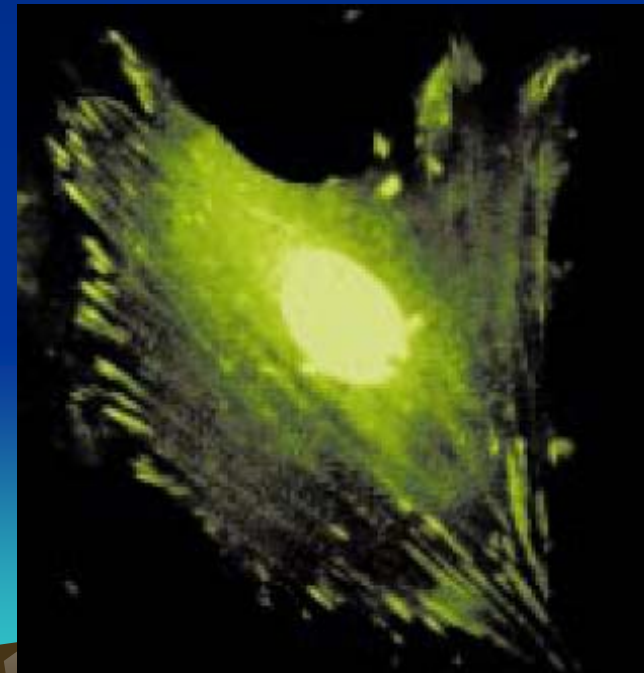


细胞黏附与生物机制

诸如：细胞的分化、运动、凝血机制、病原体侵入、免疫应答...

细胞黏附与疾病

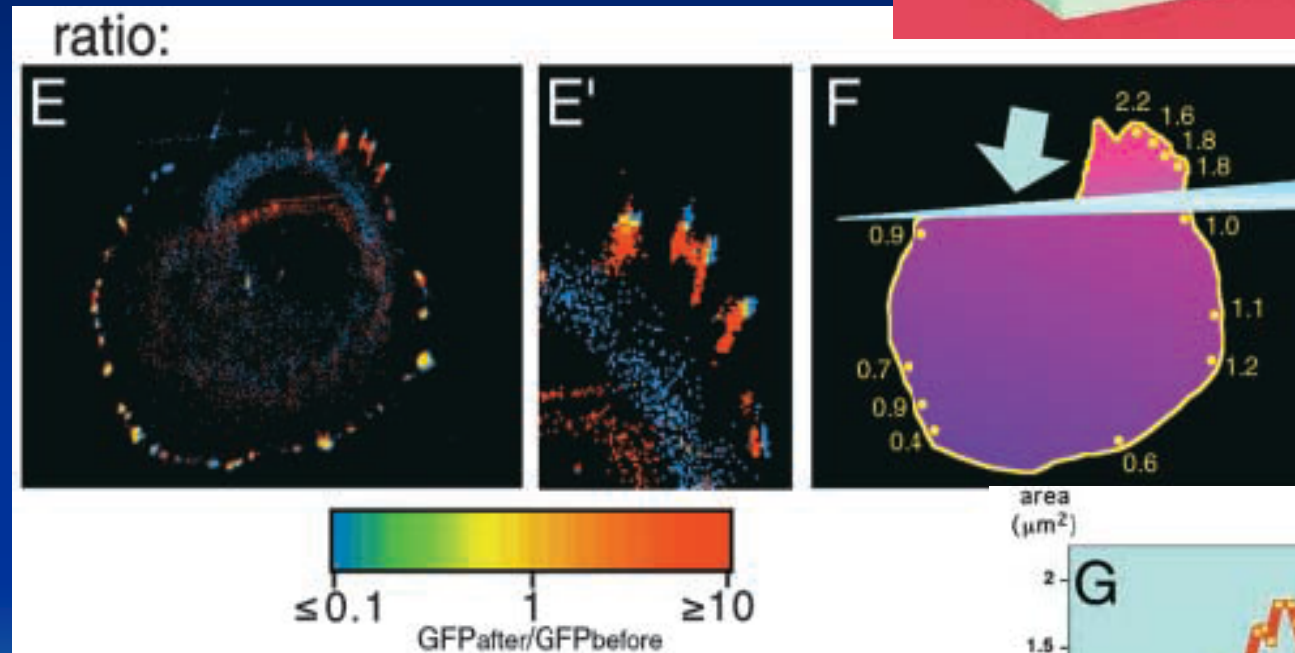
诸如：血栓形成，动脉粥样硬化，肿瘤的浸润和转移...



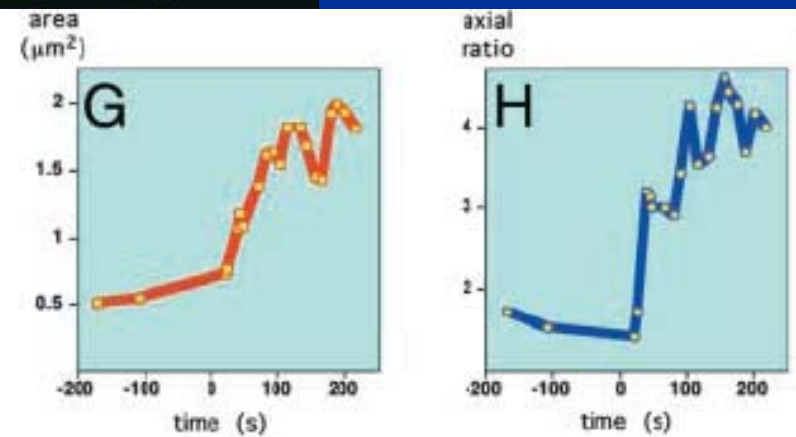
A time to experiment, and a time to theorize (Bershadsky et al., 2006)

- Cell Movement Is Guided by the Rigidity of the Substrate (Engler et al., 2006, Cell 126, 677; Lo et al. 2000. Biophys. J 79, 144; Reinhart-King et al. 2008. Biophys. J, in press)
- Force induced growth of focal adhesion (Riveline et al., 2001. J. Cell Biol. 153, 1175; Kaverina et al., 2002, J. Cell Sci. 115, 2283.)
- Cell reorientation under cyclic stretching (Wang et al., 2001, J. Biomech. 34, 1563; Kaunas et al. 2005. PNAS 102, 15895)
- Cell rheology (Deng et al. 2006. Nature Materials 5, 636; Chowdhury et al. 2008, Biophys. J., in press)

Force induced growth of focal adhesion

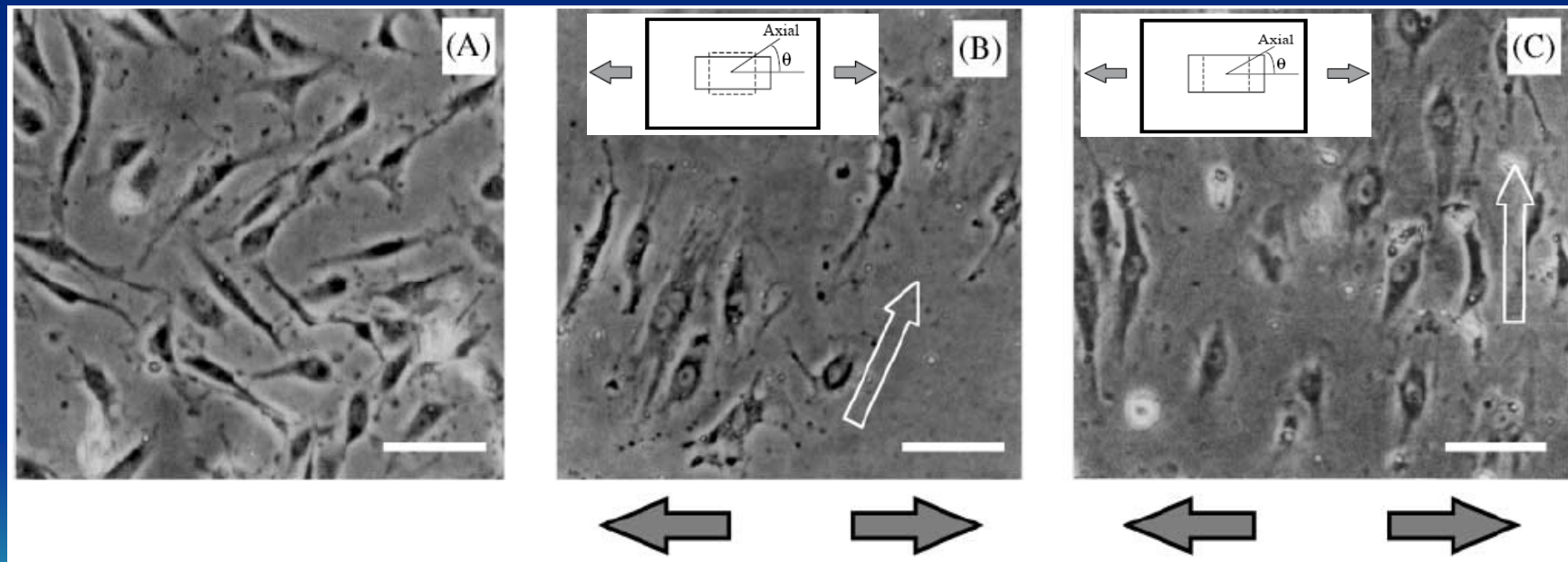
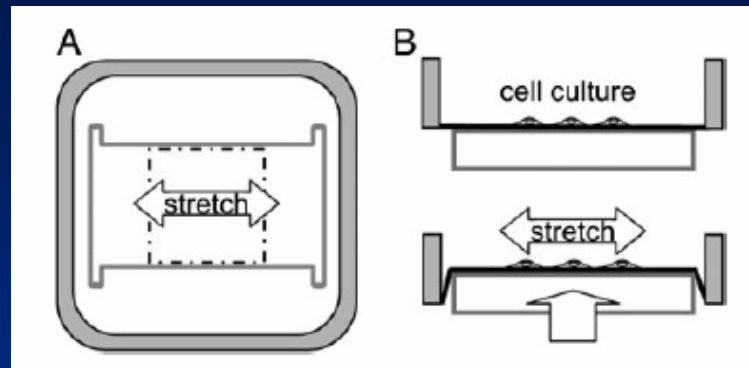


Schemes depicting the method of application of external force.



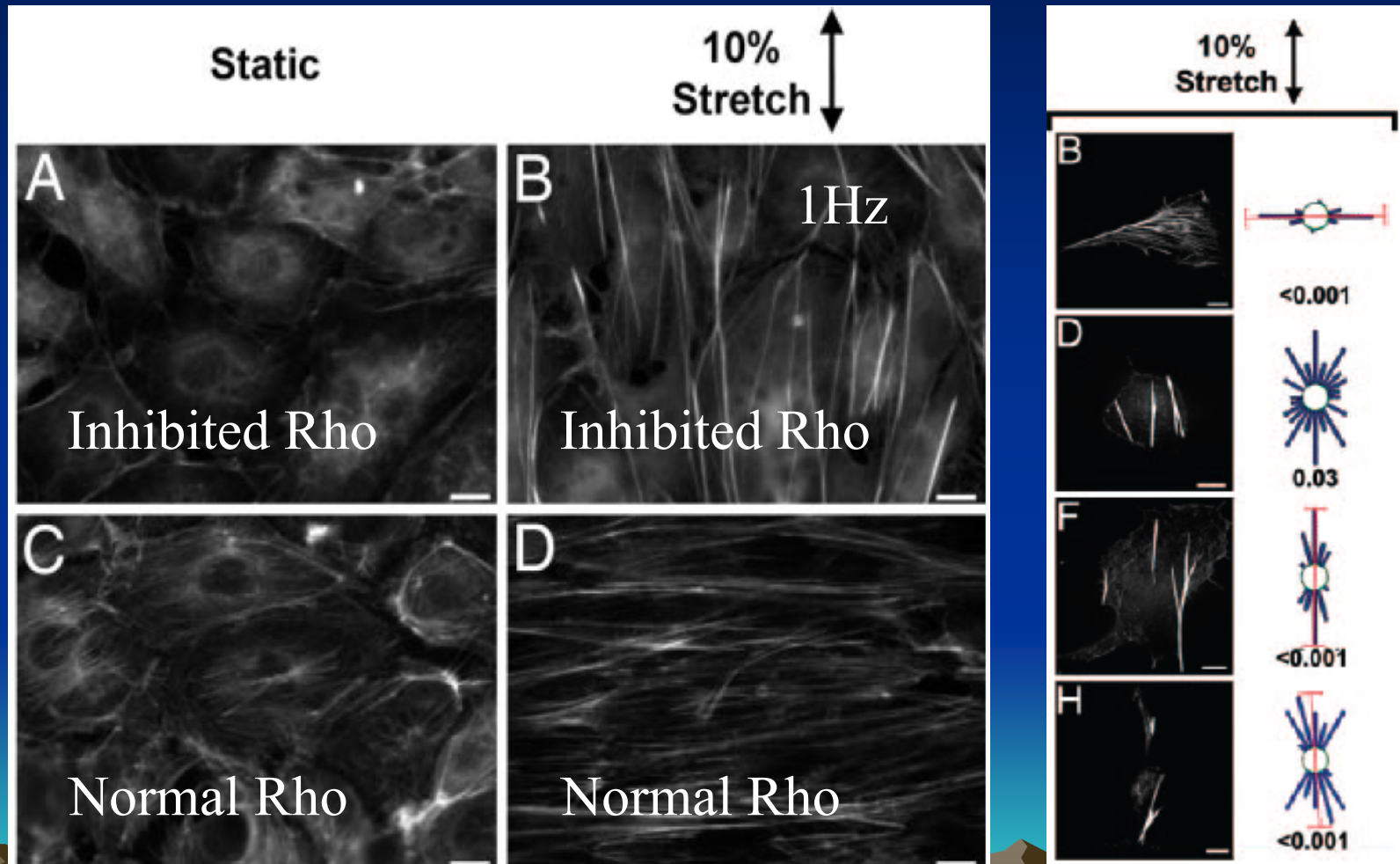
Riveline et al., 2001. J. Cell Biol. 153, 1175

Cell reorientation under cyclic strain

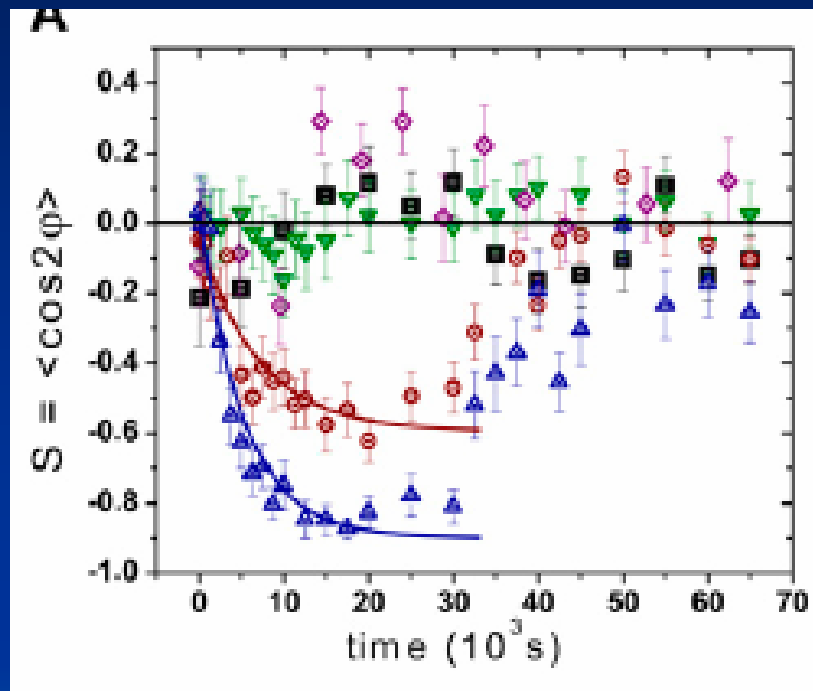


Representative phase contrast microphotographs of endothelial cells: unstretched (A), after 3 h of simple elongation (B), and after 3 h of pure uniaxial stretching (C).

Cell reorientation under cyclic strain

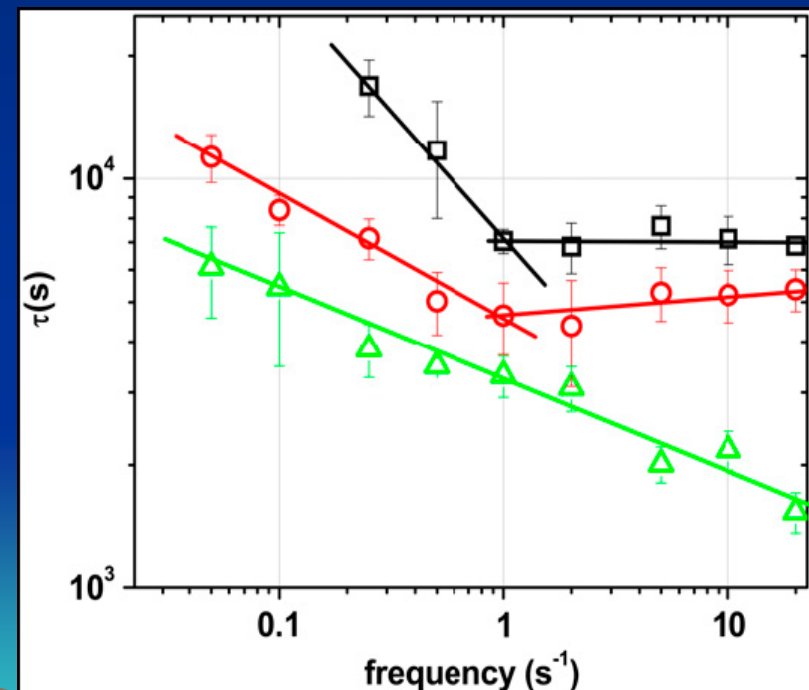


Frequency-dependent Cell reorientation under cyclic strain

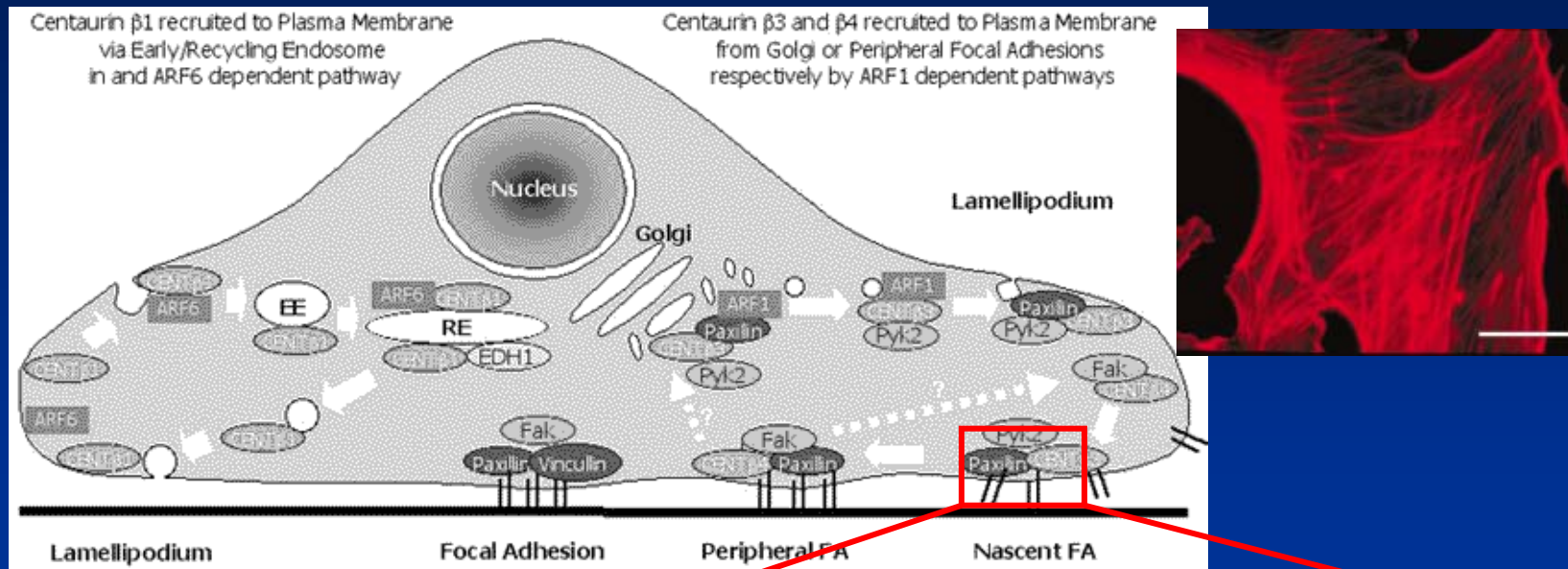


Exponential decrease of the order parameter S from a random orientation to a saturation value at different stretching frequencies

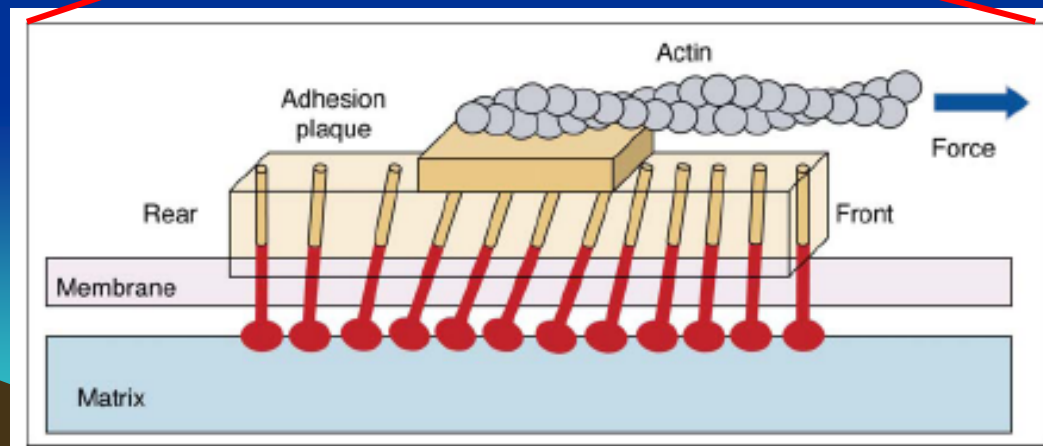
Biphasic characteristics of dynamic cell reorientation



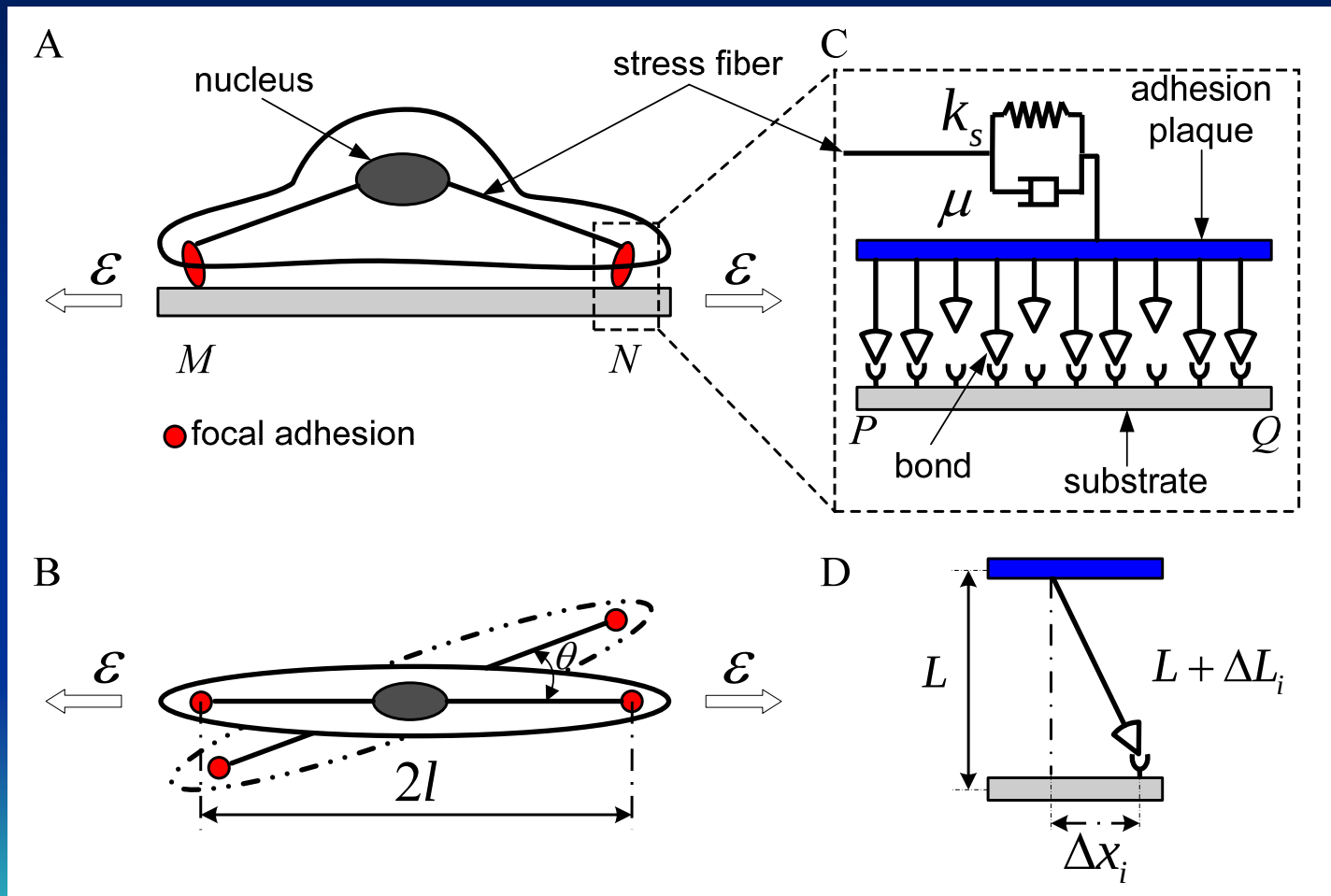
Focal adhesion



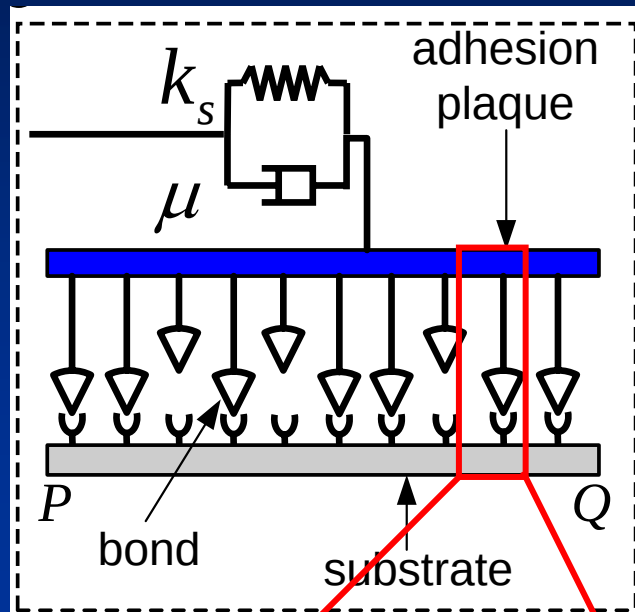
Bershadsky et al., 2006,
Curr. Opin. Cell Biol. 18,
472



A microscopic model



Modeling of adhesion cluster



External cyclic force

$$\varepsilon = \varepsilon_0 |\sin(\pi\omega t)|$$

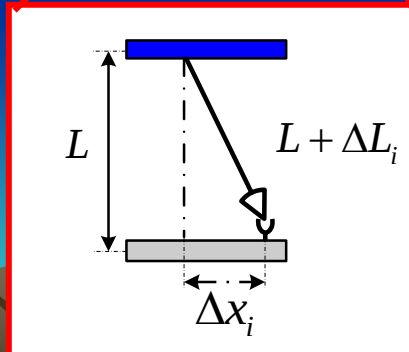
Stress fiber

$$F = k_s \Delta l_s + \mu \frac{\partial \Delta l_s}{\partial t}$$

Displacement of substrate

$$s = l\varepsilon(\cos^2 \theta - \nu \sin^2 \theta)$$

Bond deformation

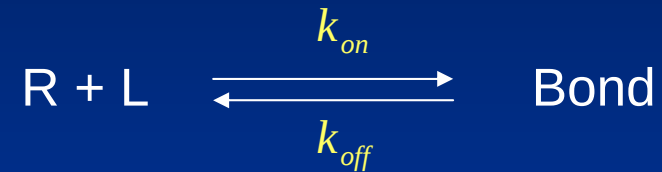
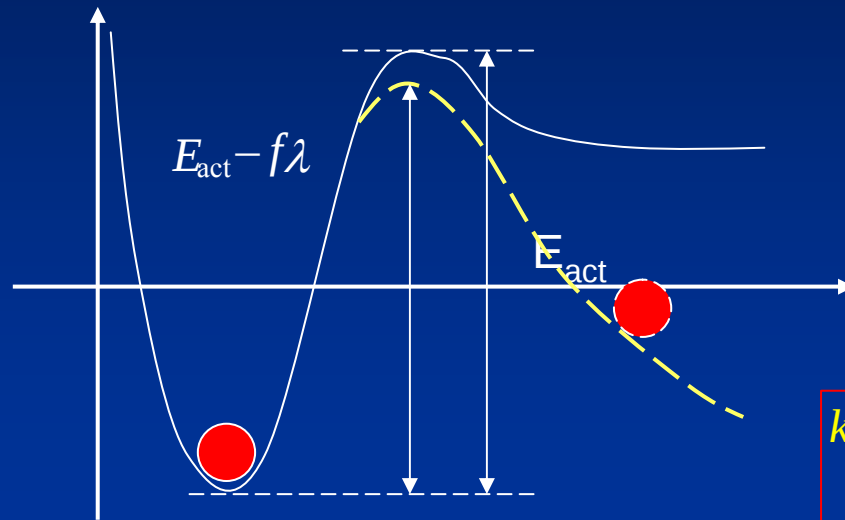


Bond force

$$f = k_b \Delta L$$

Modeling of adhesion cluster (cont.)

Dynamics of adhesion bonds

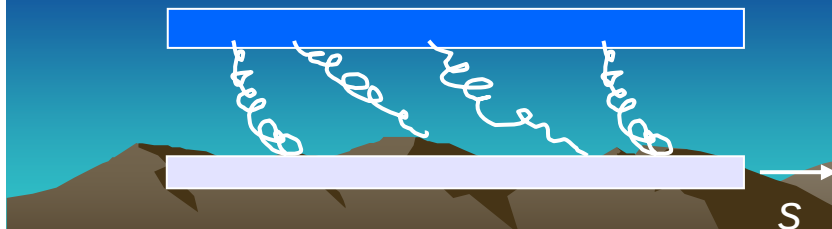


$$k_{off} = k_{off}^0 \exp(f\lambda / k_B T)$$

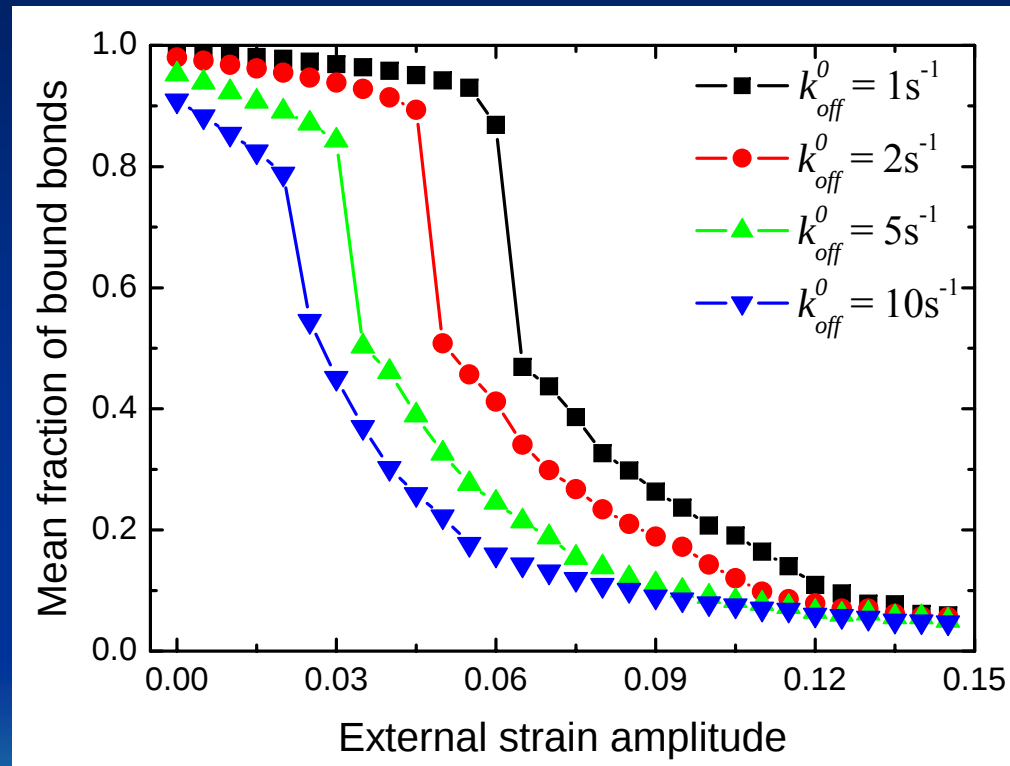
$$k_{on} = k_{on}^0 g(\tau_c, \tau_b) \quad \& \quad g(\tau_c, \tau_b) = \begin{cases} 1, & \tau_c > \tau_b \\ \tau_c / \tau_b, & \tau_c < \tau_b \end{cases}$$

开、合状态的判断

$$q(t + \Delta t) = q(t) - q(t)H(\xi - k_{off}\Delta t) + (1 - q(t))H(\xi - k_{on}\Delta t)$$



Threshold value of external strain



< 2% 开始

5–6% 完成

基底载荷幅值

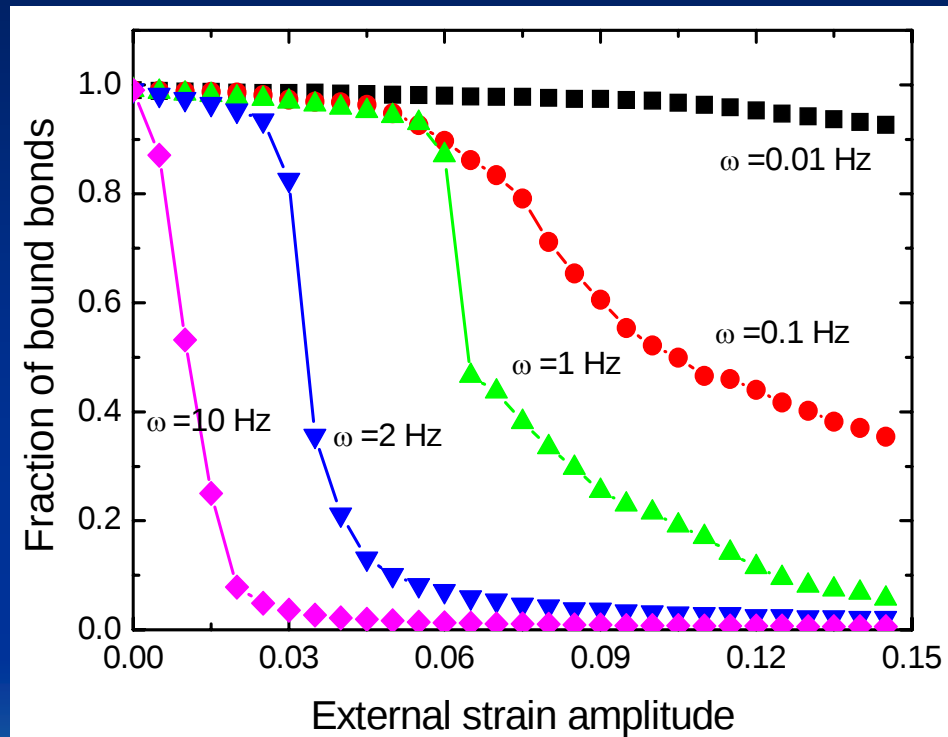
Dartsch and Hammerle, 1986,
Eur. J. Cell Biol. 41: 339–346.

Neidlinger-Wilke et al., 2005, J.
Orthop. Res. 12:70–78.

应变临界值是成键与解离过程竞争的结果

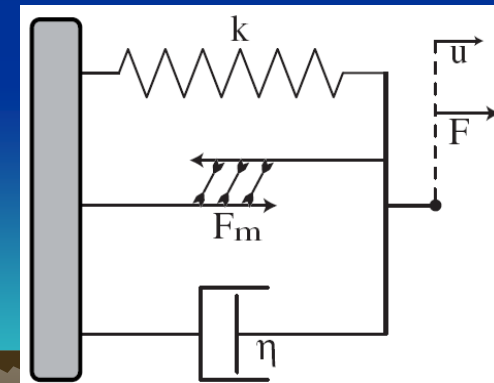
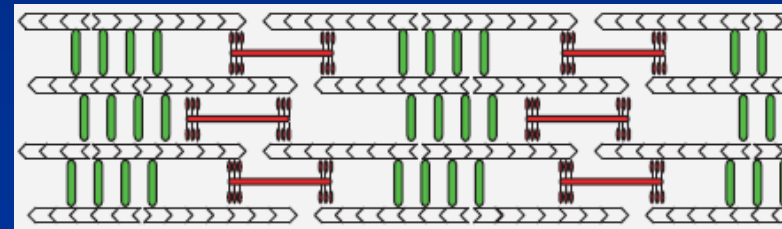
Kong, Ji and Dai, Biophys. J. 2008, 95 4034

Effect of loading frequency



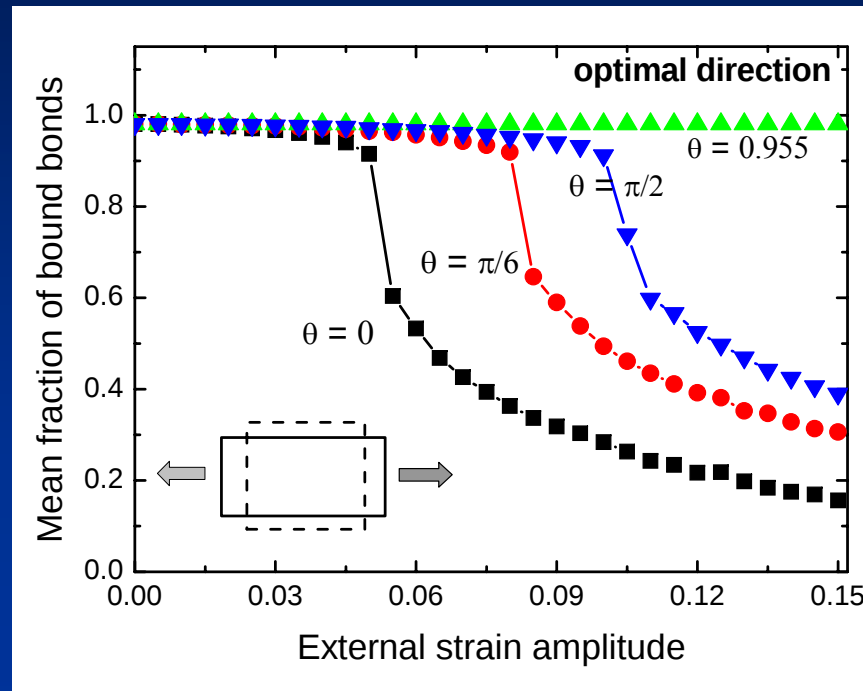
1. 对黏附分子反应的影响

2. 对应力纤维的影响

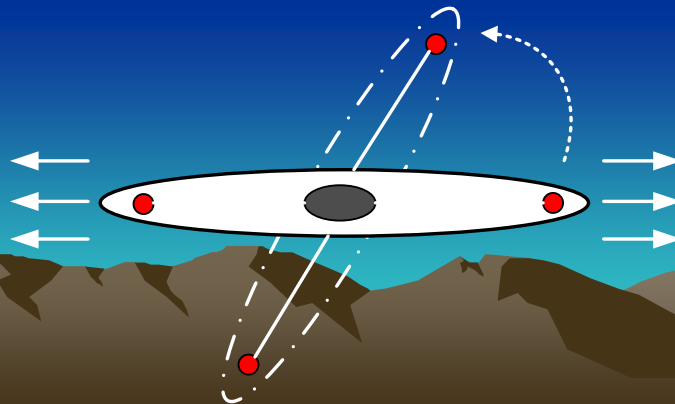
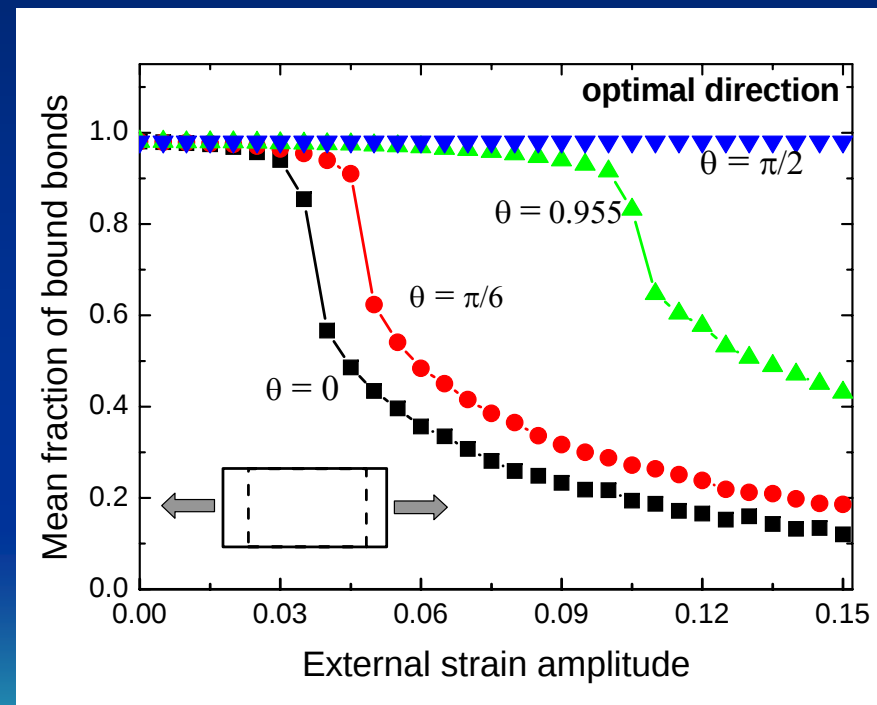


成键时间VS接触时间

Optimum orientation

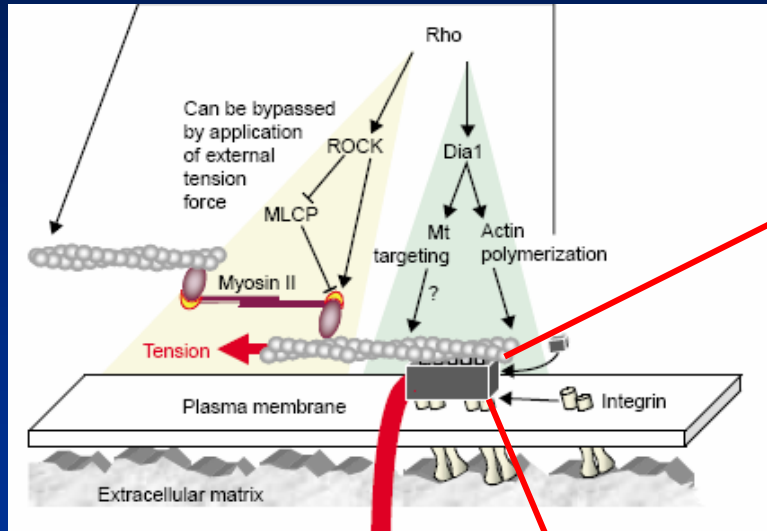


细胞趋向外力最小的方向。



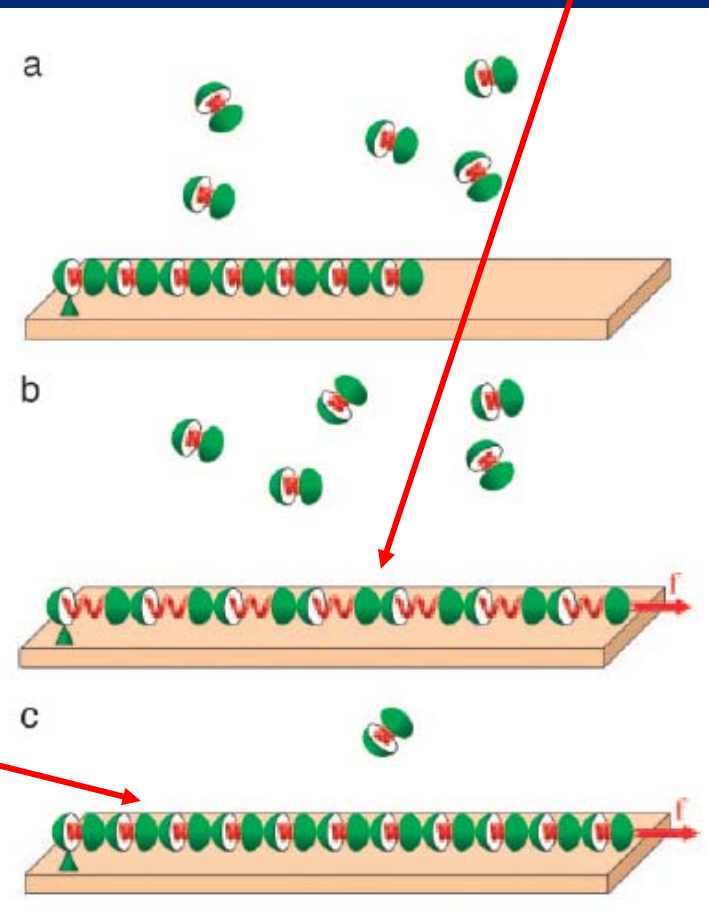
Kong, Ji and Dai, Biophys. J. 2008, 95 4034;
Wang et al., 2001, J. Biomech. 34, 1563

Growth mechanism



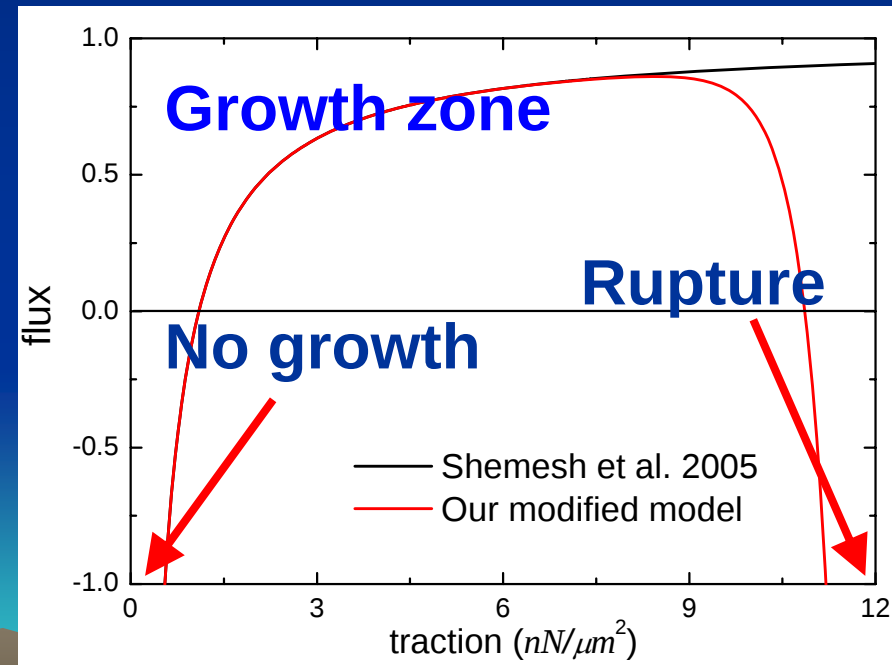
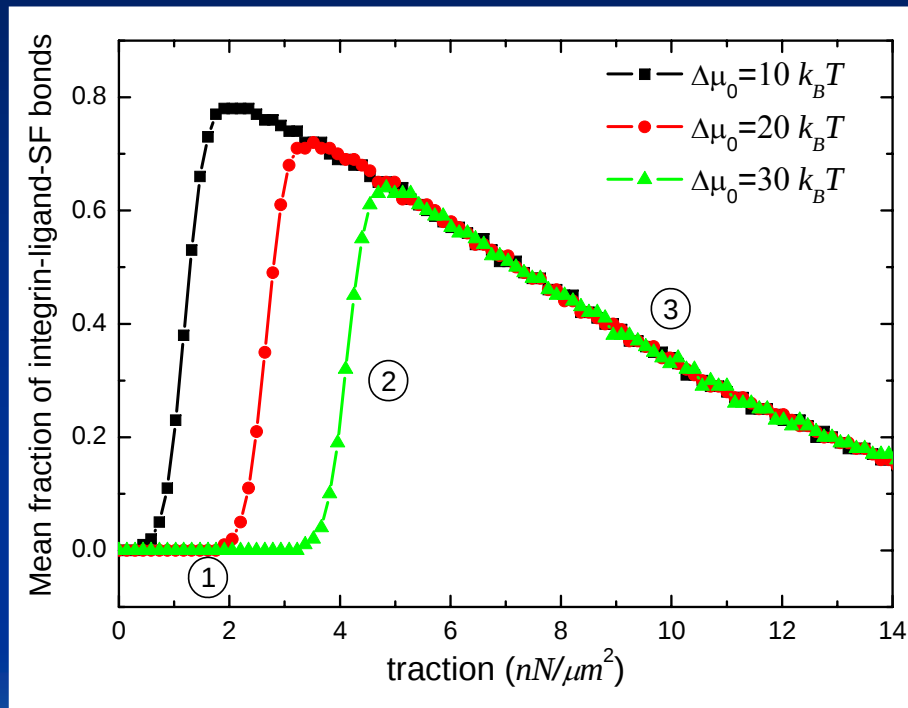
$$\Delta\mu = \Delta\mu_0 - \gamma \cdot l_0$$

$$g_{on} = g_{on}^0 \cdot e^{-\Delta\mu / k_B T}$$



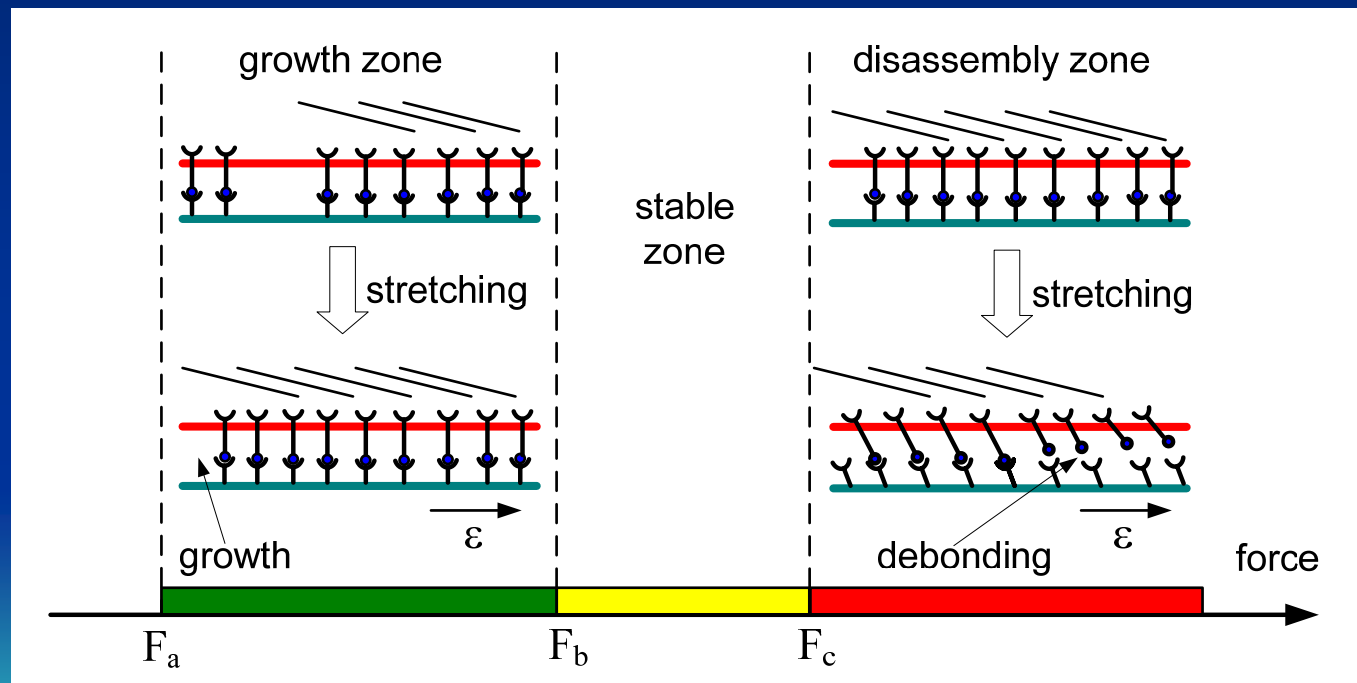
A unified model

黏附斑生长 $\rightarrow$ 黏附斑破坏 $\rightarrow$ 细胞尺度取向变化



A unified model (cont.)

黏附斑生长 $\rightarrow$ 黏附斑破坏 $\rightarrow$ 细胞尺度取向变化



$5.5 \text{ nN}/\mu\text{m}^2$

$<$

$48 \text{ nN}/\mu\text{m}^2$

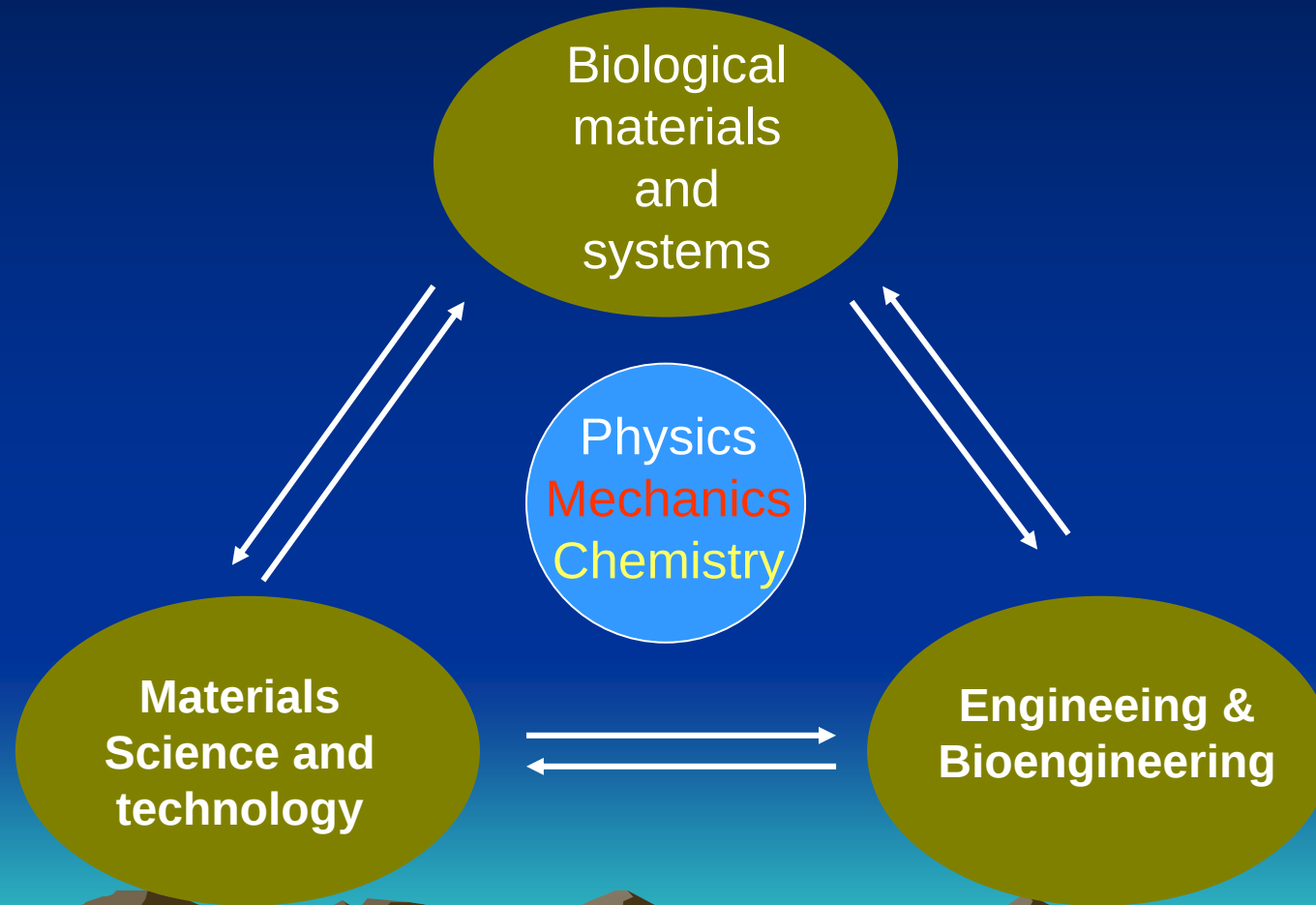
Kong, Ji and Dai, Biophys. J. 2008, 95, 4034

Summary

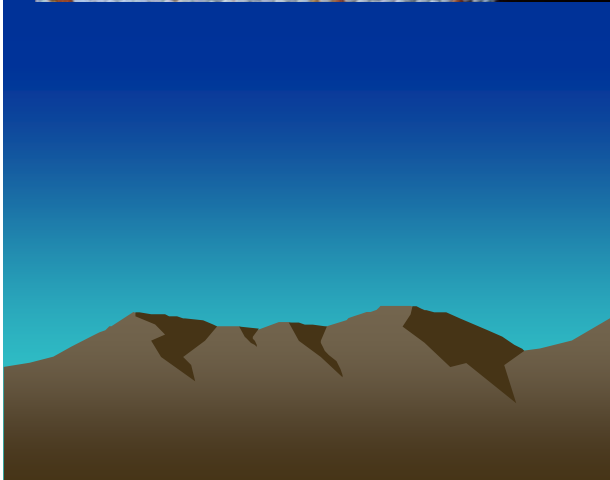
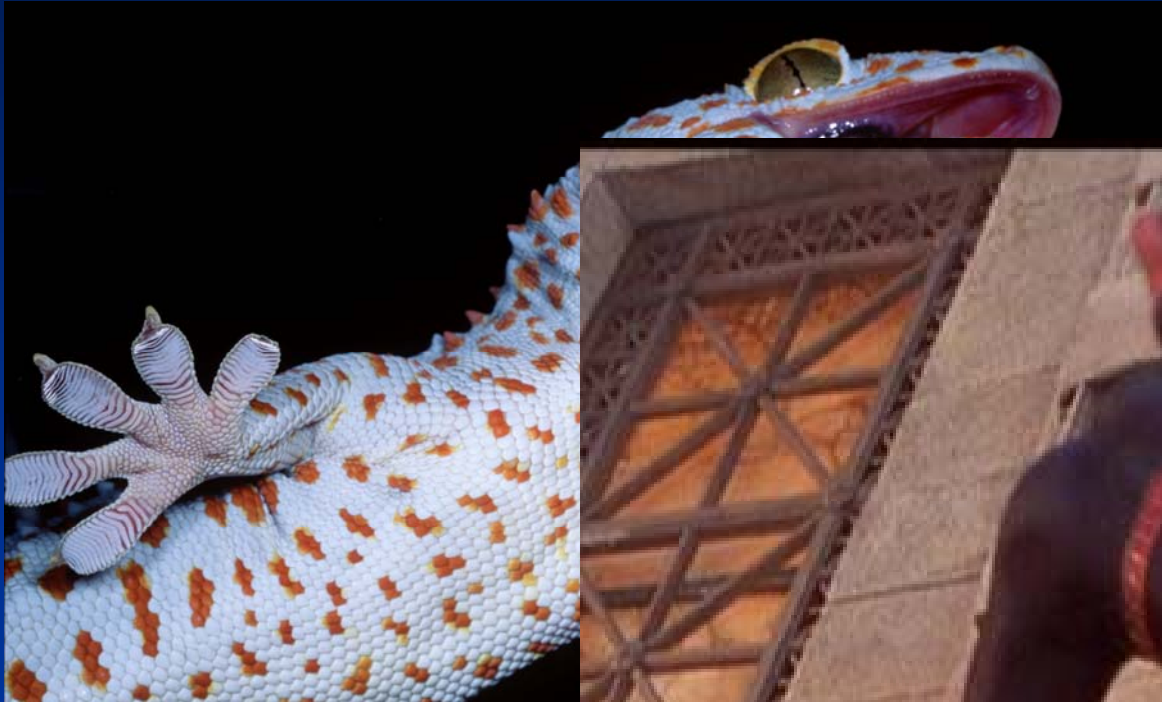
- With the microscopic model, we identified three force zone for different cell behaviors.
- Focal Adhesion grows due to the decrease of local chemical potential under external force.
- In addition to the biochemical aspects, active reorientation of the cell/stress fiber may represent a mechanism by which cells reduce the increase in intracellular tension generated by cyclic stretching.



Perspectives & Strategies

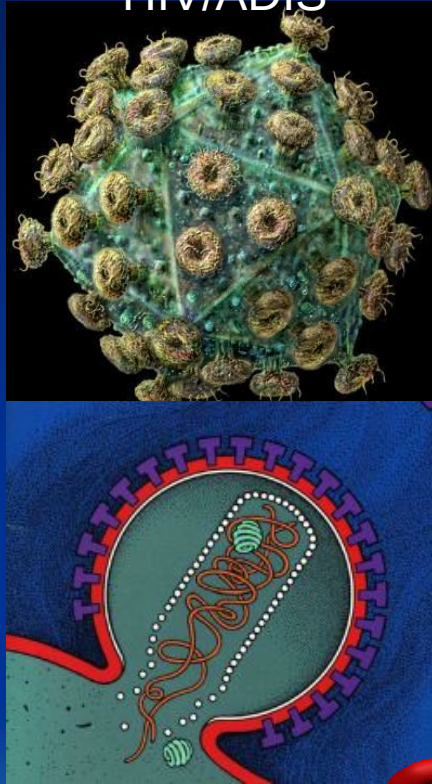


Man-made advanced materials

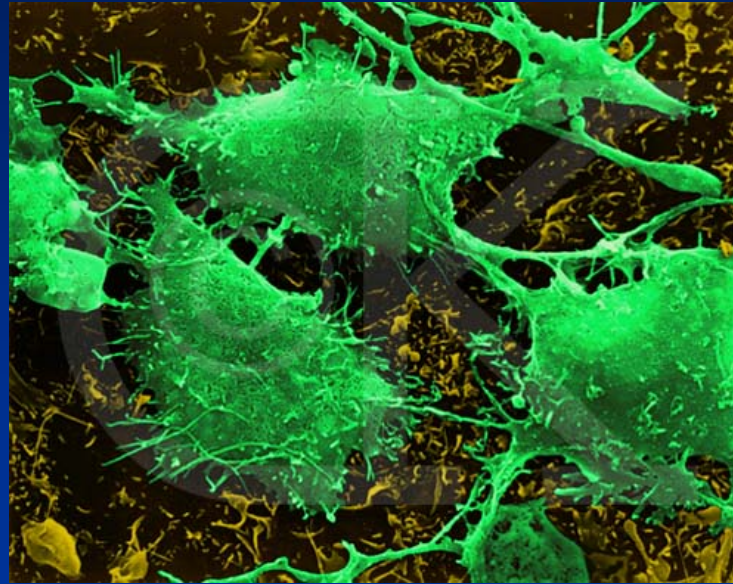


Understanding the mechanisms of the vital diseases and malfunctions

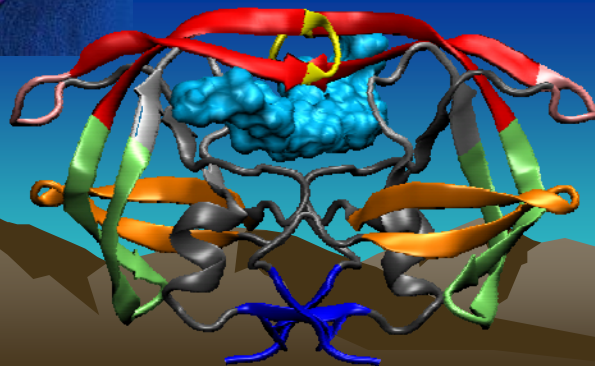
HIV/AIDS



Cancer



Osteoporosis/bone loss



Supports :

This work is supported by the National Natural Science Foundation of China through Grant No. 10442002, 10502031, 10628205, 10732050, and 973 Grant No. 2004CB619304.

