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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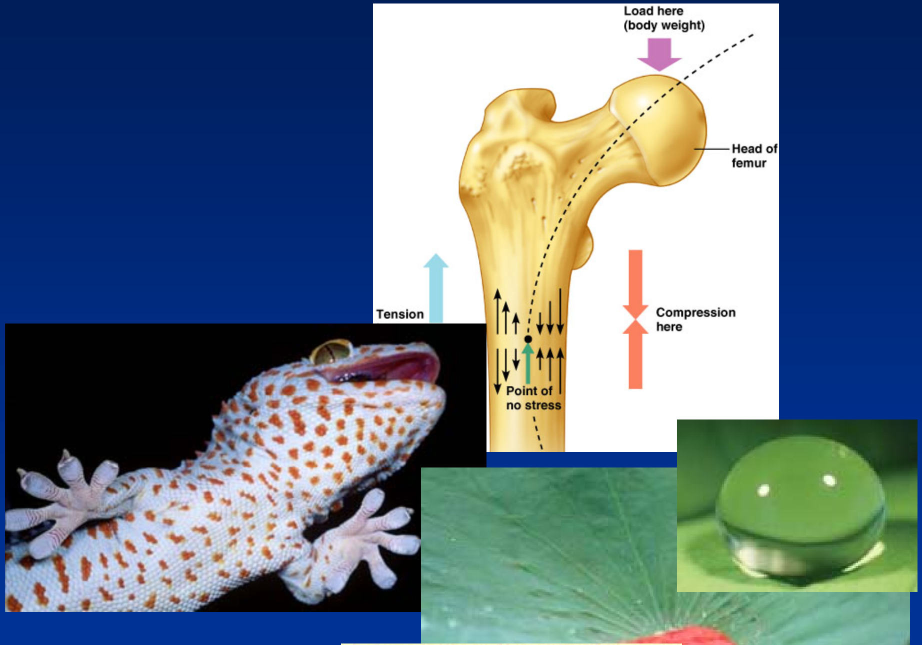
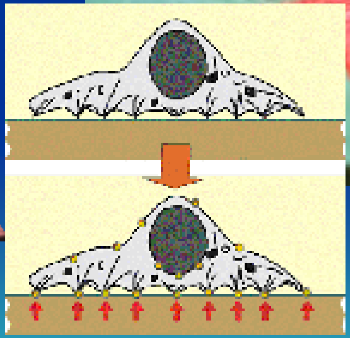
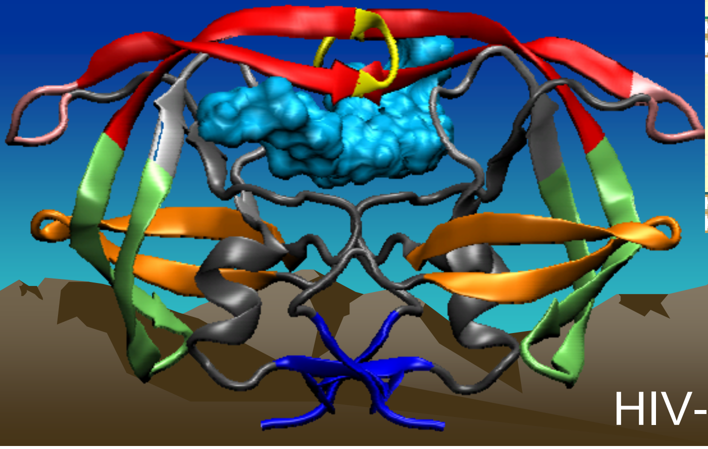
Biological Materials and Systems

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





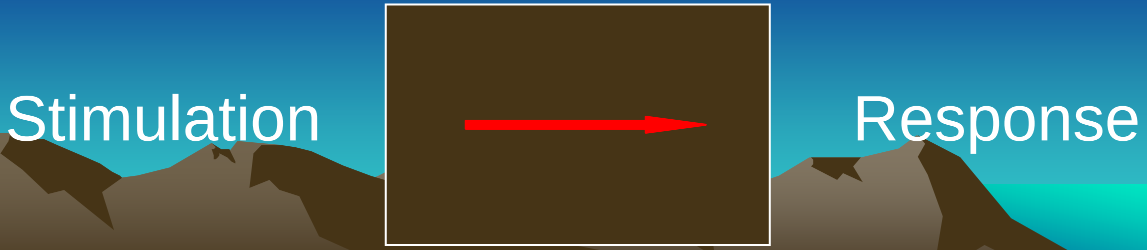
Focal adhesion



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 mateirals – 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

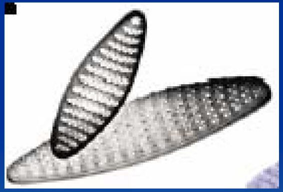

Bone


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	<<1Nm$^{-3/2}$
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	<<1Nm$^{-3/2}$
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

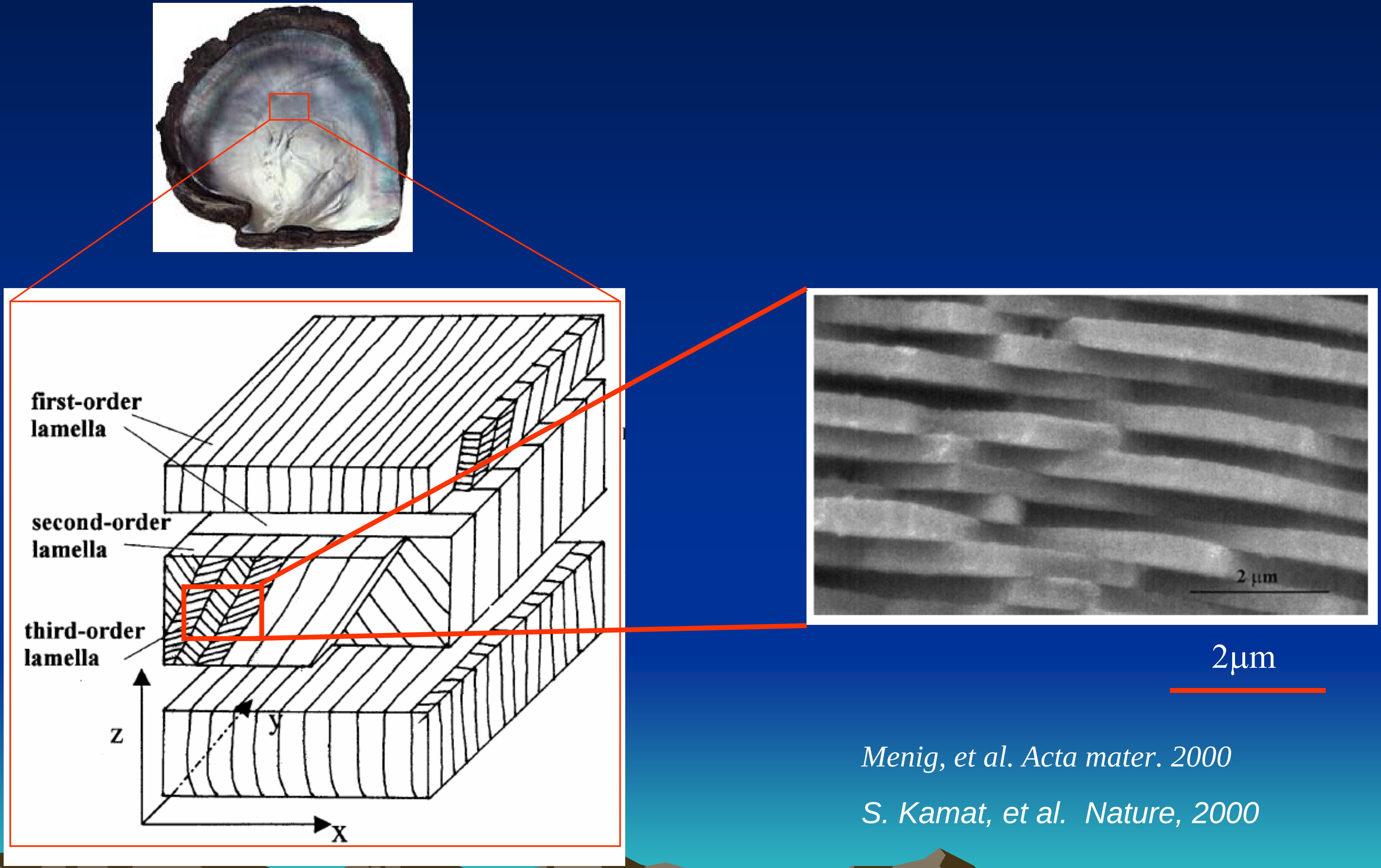
Questions:

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



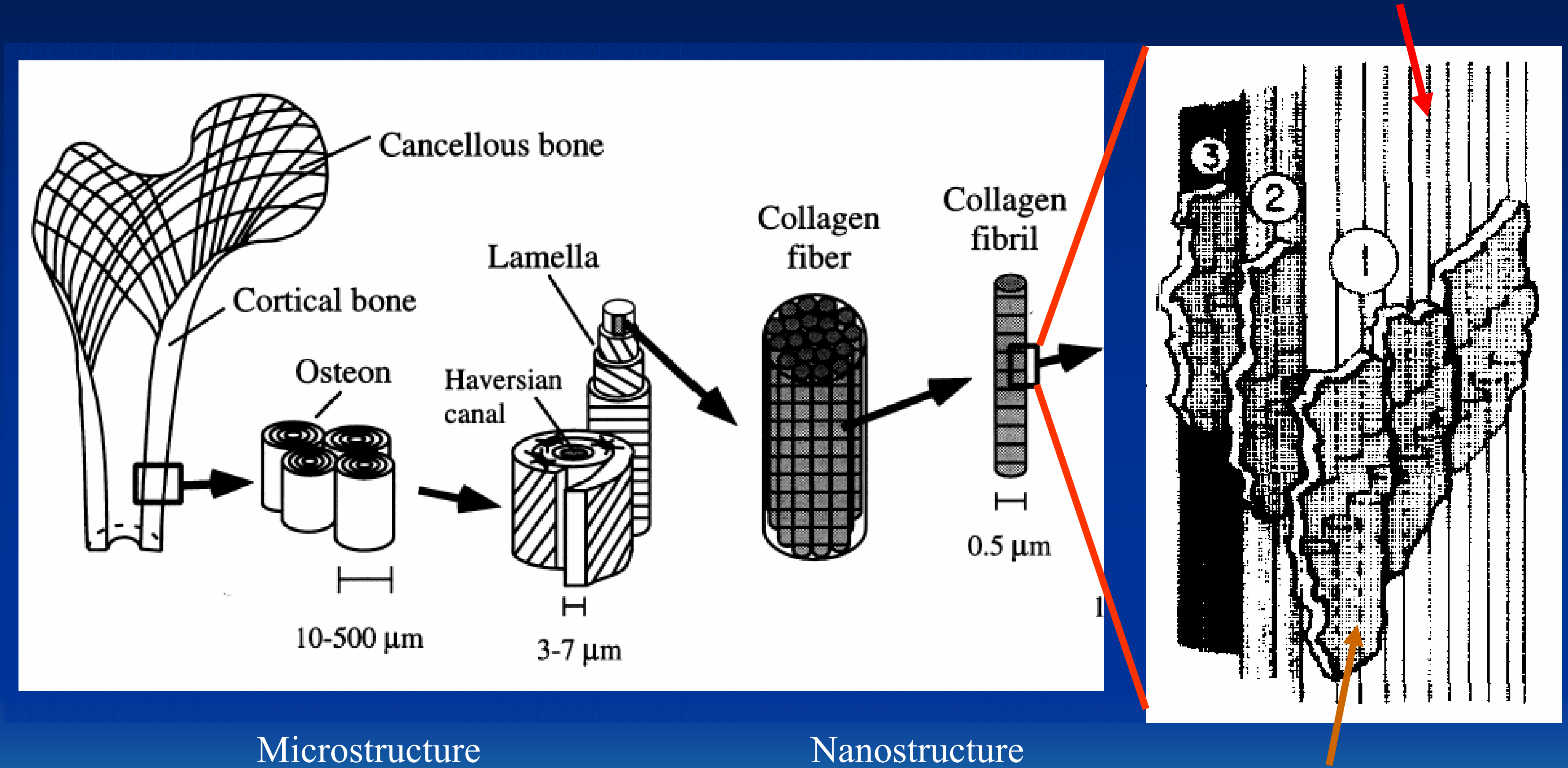
Menig, et al. Acta mater. 2000

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

Collagen molecules



Bone mineral crystal
100 x 40 x 3

Microstructure

Nanostructure

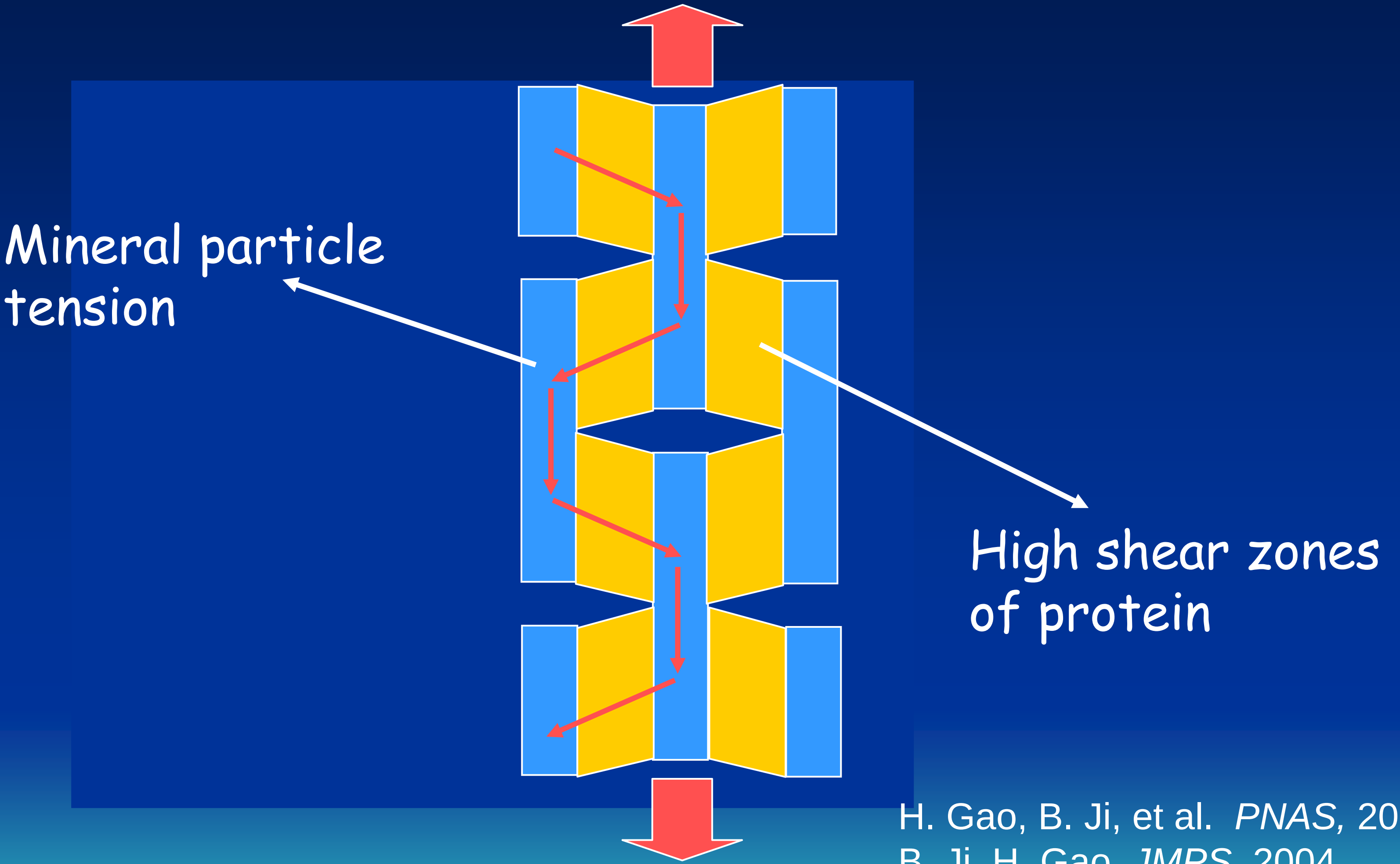
Macrostructure

Submicrostructure

$10^{-1}\sim10^{-9}$

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

Tension-shear Chain model (TSC)



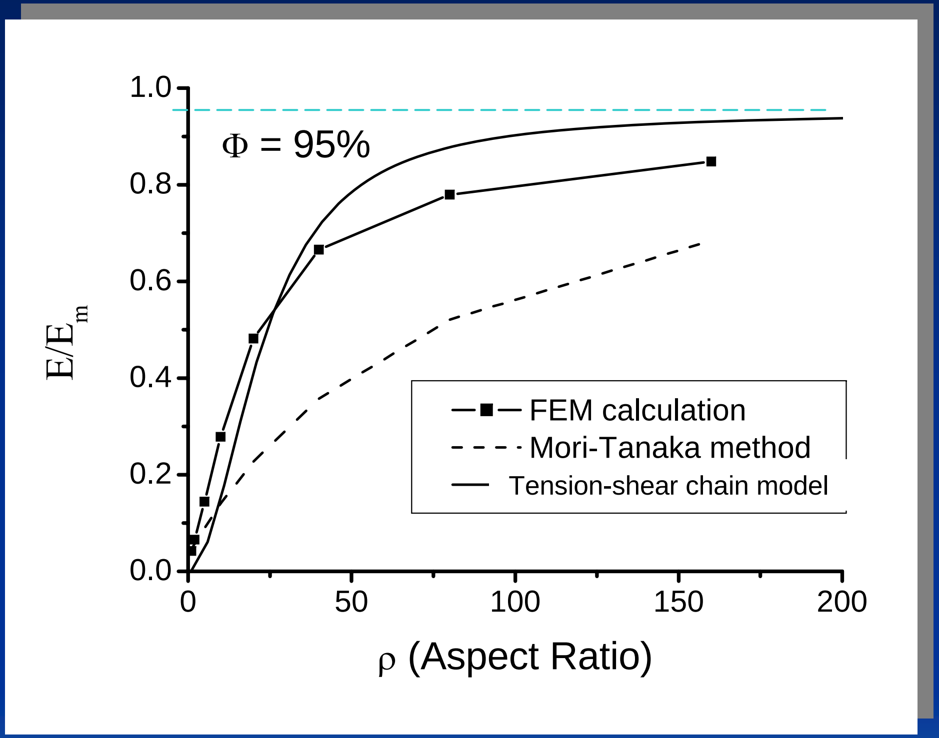
Mineral particle tension

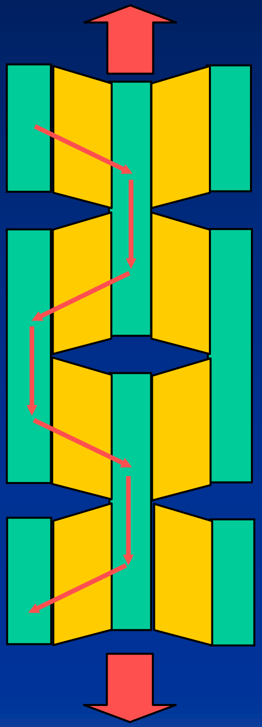
High shear zones of protein

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





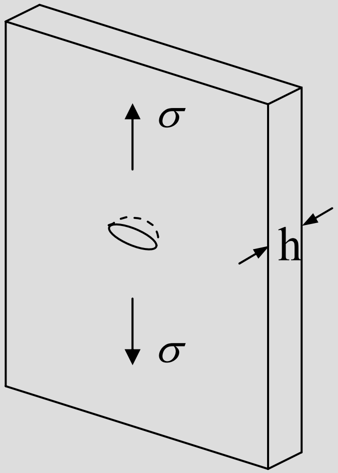
$$\sigma_m = \rho\tau_p$$

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

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

The mineral particles should sustain large tensile load without fracture.

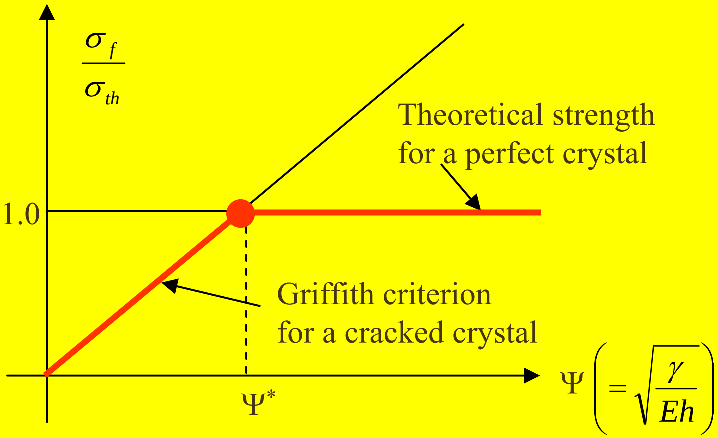
Mineral crystals become insensitive to flaws at nanoscale



Griffith criterion:

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

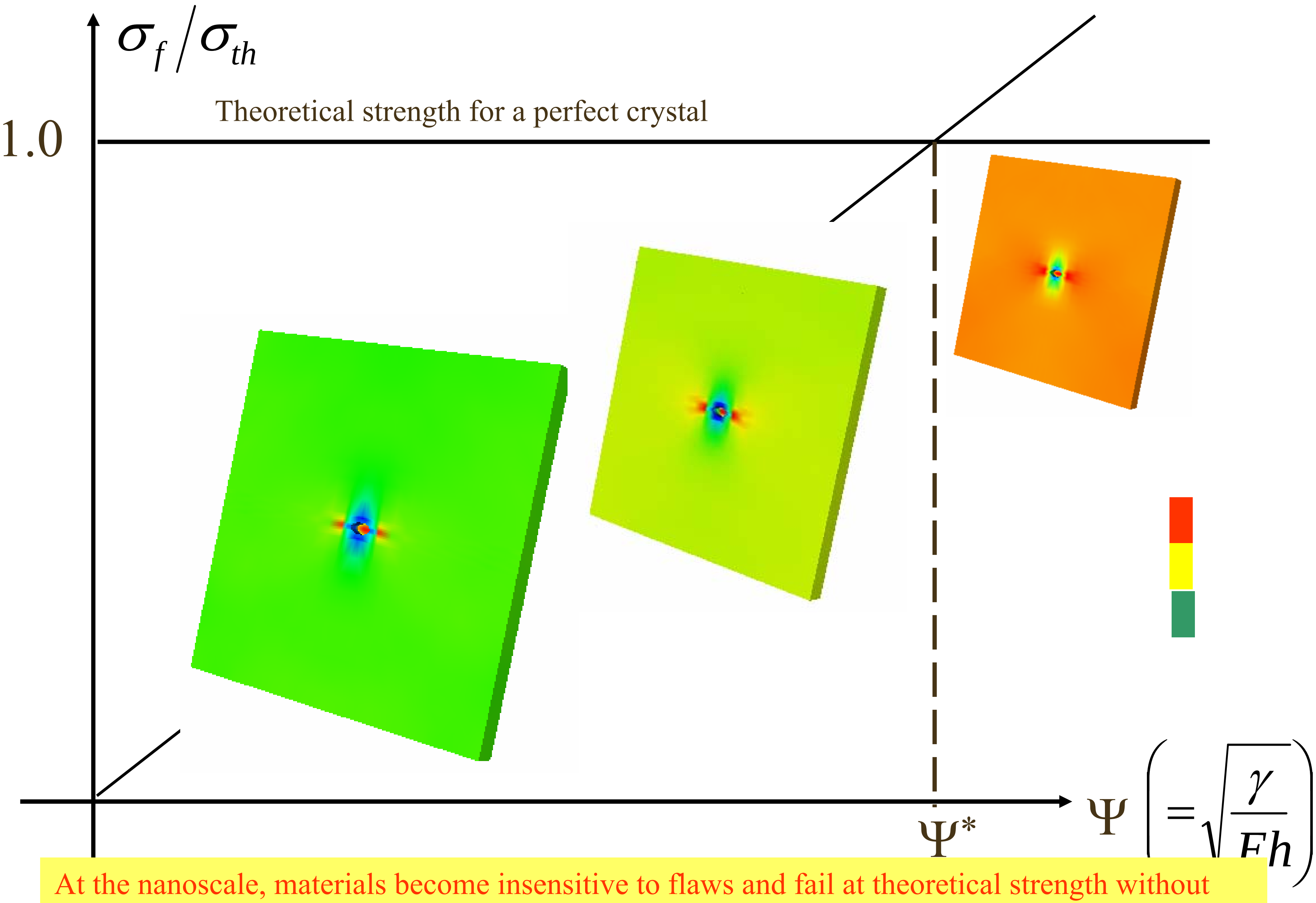
$$\sigma_m^f = \alpha E_m \Psi, \qquad \Psi = \sqrt{\frac{\gamma}{E_m h}},$$



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

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

h* = 30nm



At the nanoscale, materials become insensitive to flaws and fail at theoretical strength without stress concentration

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?

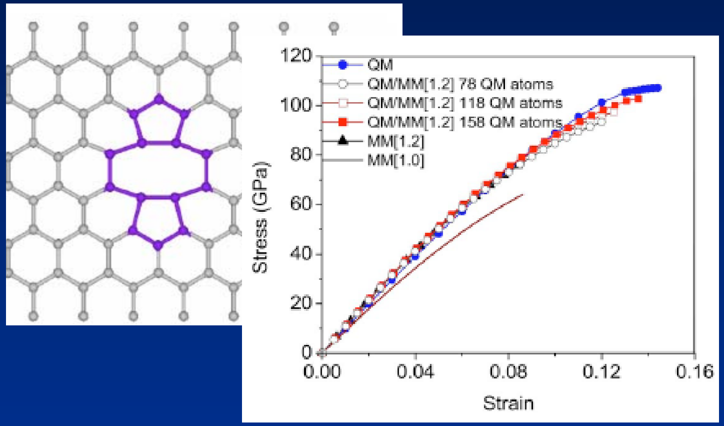
The Young’s modulus of various brittle materials can vary, depending on the atomic structure and the purity of the materials.

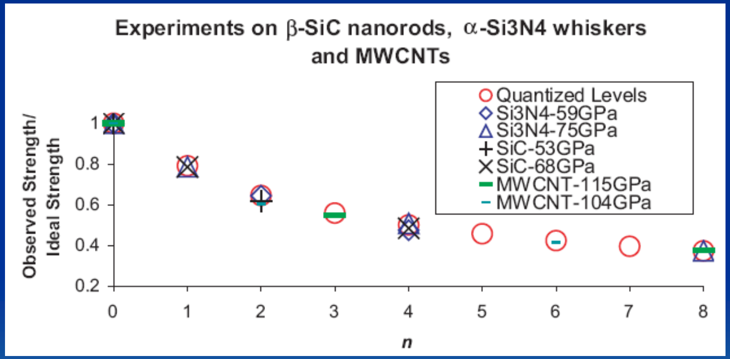
Typical estimates of the theoretical strength can range between 1% and 10% of the Young’s modulus.

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

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

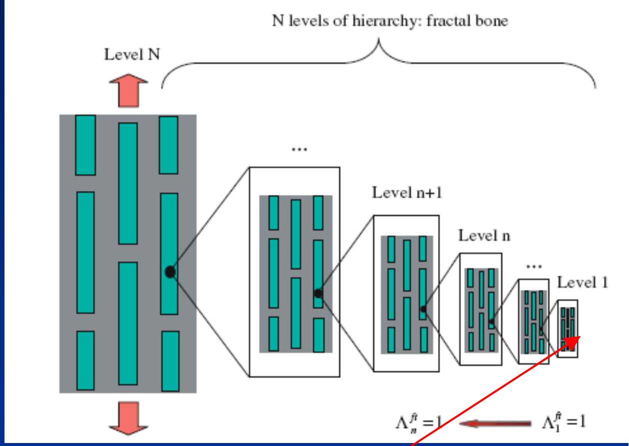
$l_{cr} \approx 2\text{Å–}400\,\mathrm{nm}$.



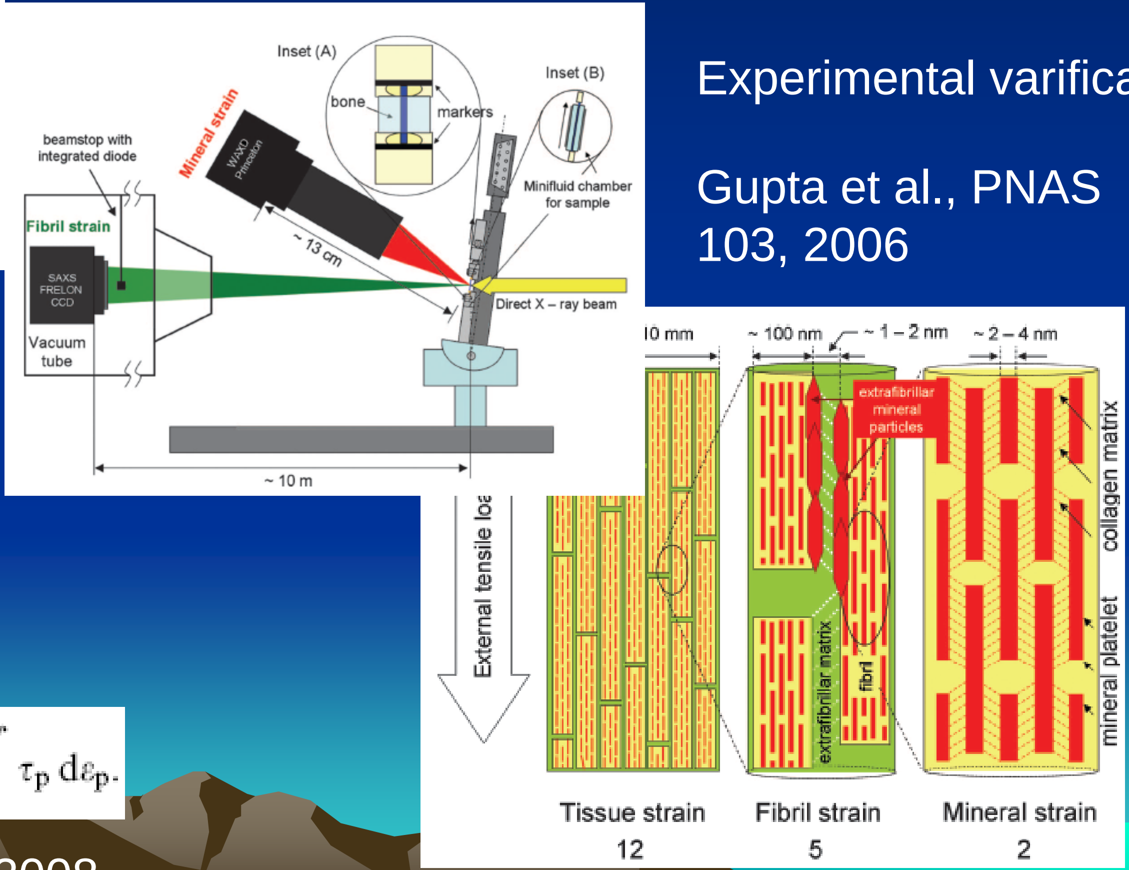


Pugno & Ruoff, *Phil. Mag.*, 2004
Ballarini et al., *Int. J. Fract.*, 2005
Khare et al., PRB, 2007
Gao & Chen, *J. Appl. Mech.*, 2005
Ji, *J. Biomech.*, 2008

Theoretical model of bone hierarchical structure

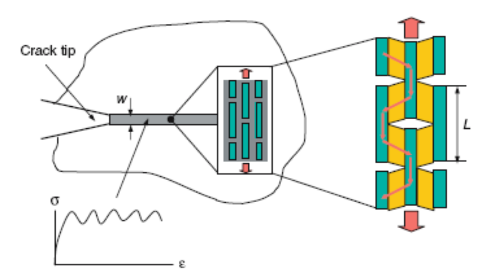


H. Gao, Int. J. Fract. 138, 2006



Experimental varification

Gupta et al., PNAS 103, 2006



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

B. Ji, *J. Biomech*. 41, 2008

Perspectives and Applications

MATERIALS SCIENCE

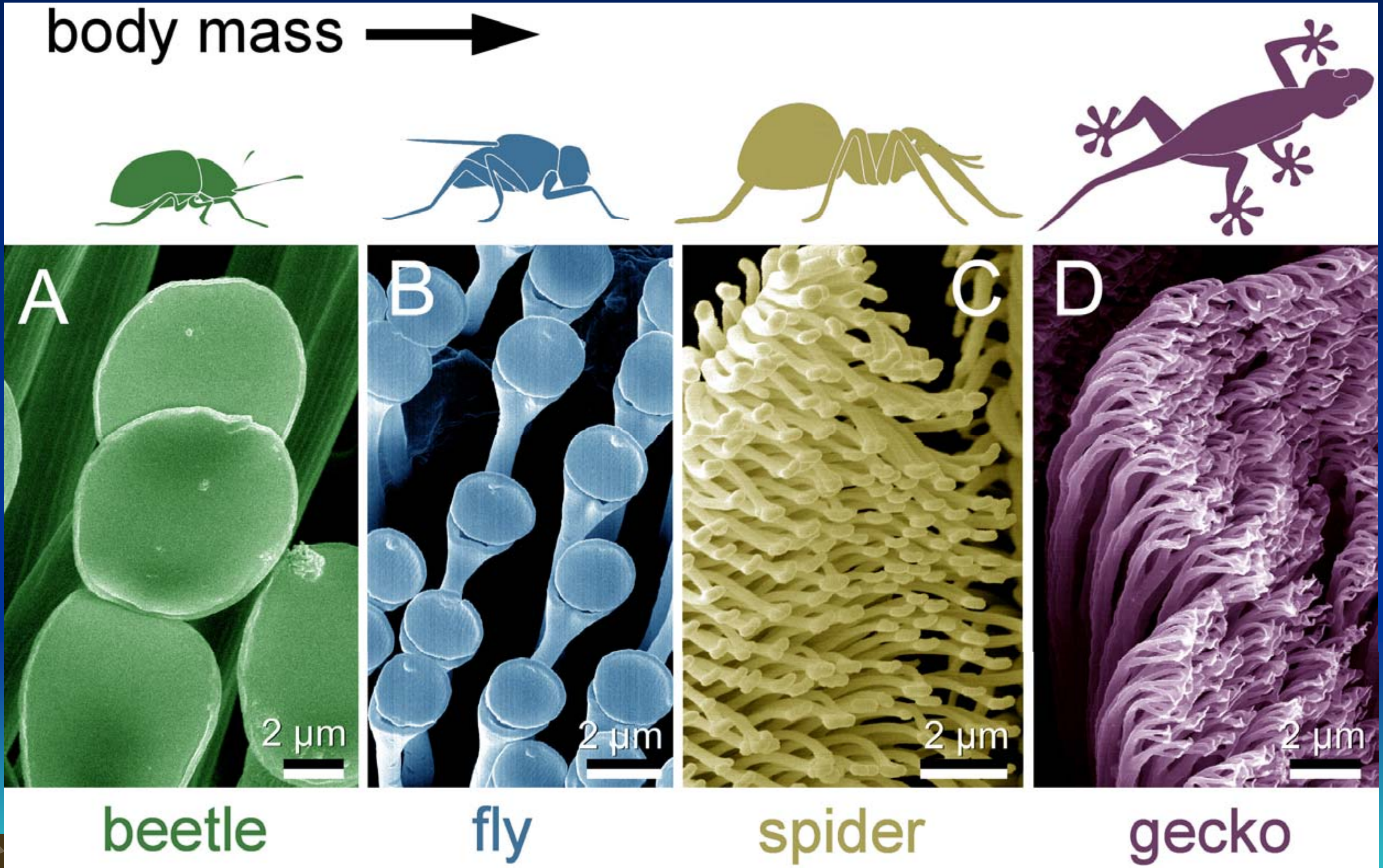
Bioinspired Structural Materials

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.”

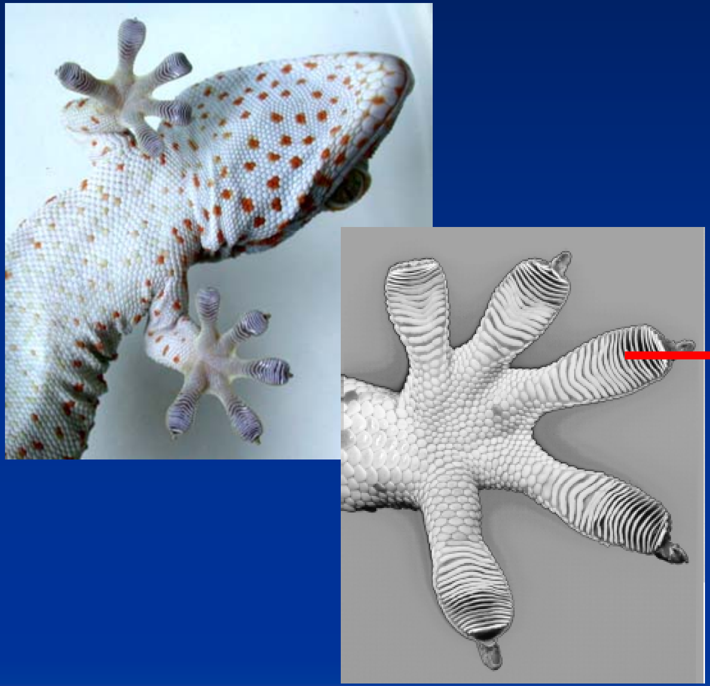
1. Bonderer et al., 2008, "Bioinspired design and assembly of platelet reinforced polymer films", Science 319, 1071
2. *C. Ortiz and M. C. Boyce, 2008, “Bioinspired structural materials”, Science 319, 1054*
3. *Currey, J. D., 2005, "Materials science - Hierarchies in biomineral structures", Science 309,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

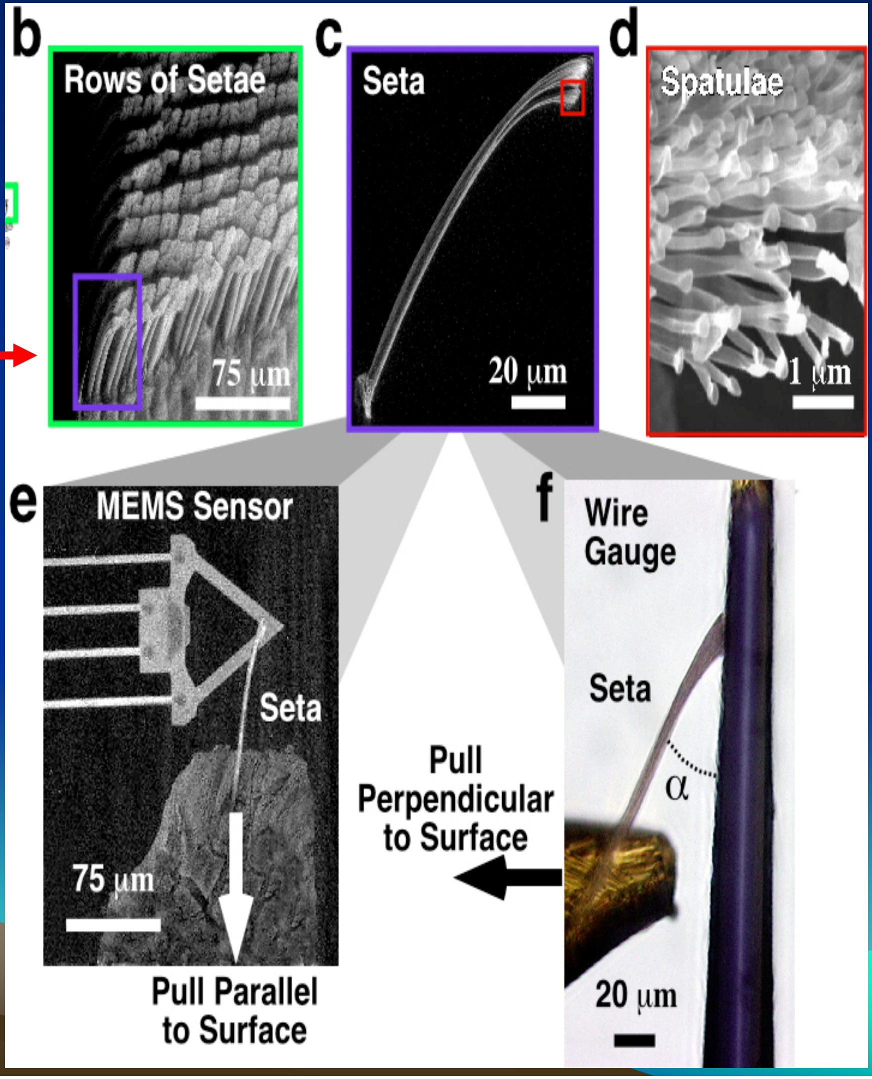
Biological Surface structures



Courtesy of Dr. S. Gorb

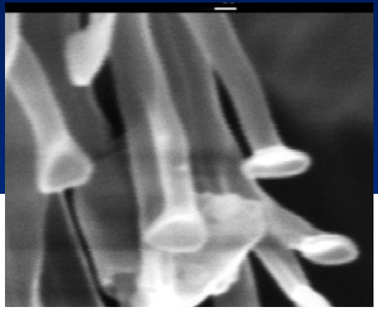
Hierarchical adhesion structure of Gecko

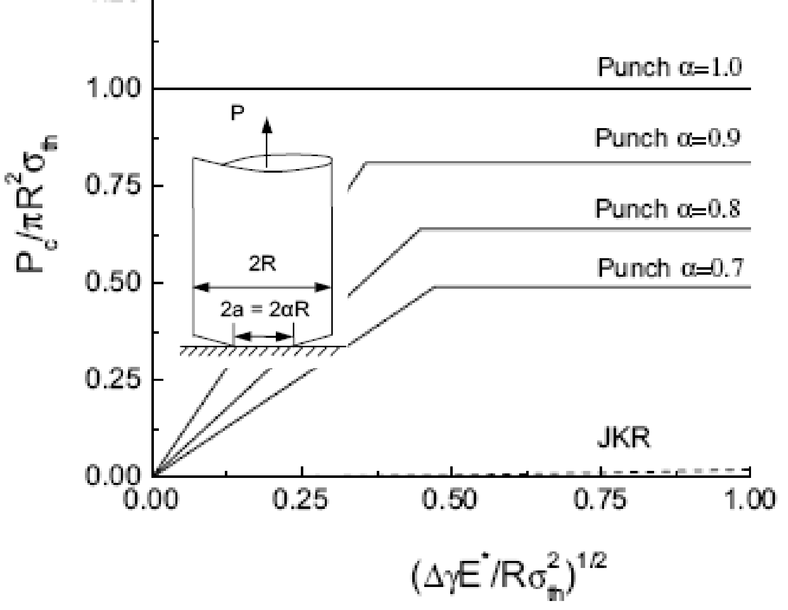


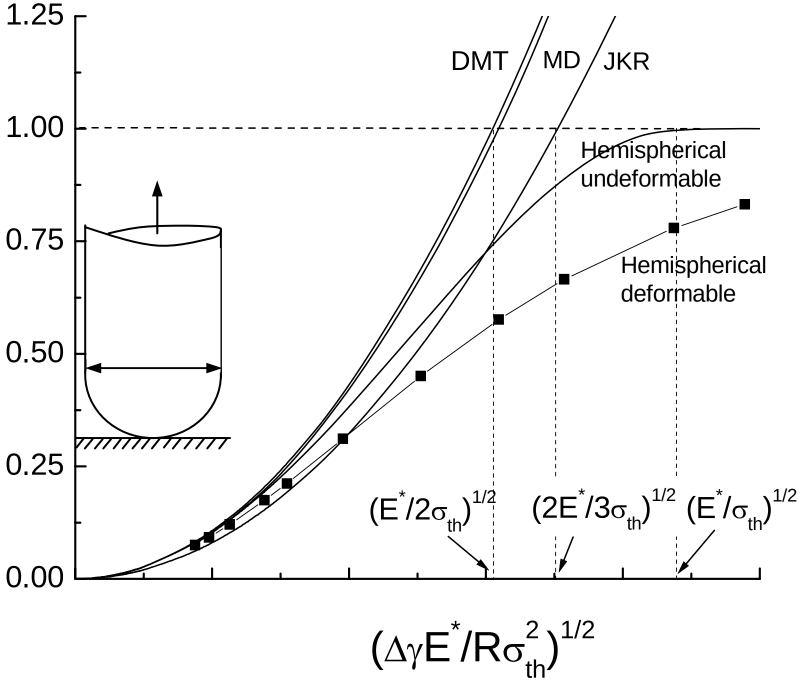


Hansen & Autumn, 2005, PNAS 102, 385

Fracture/JKR models for adhesive contact



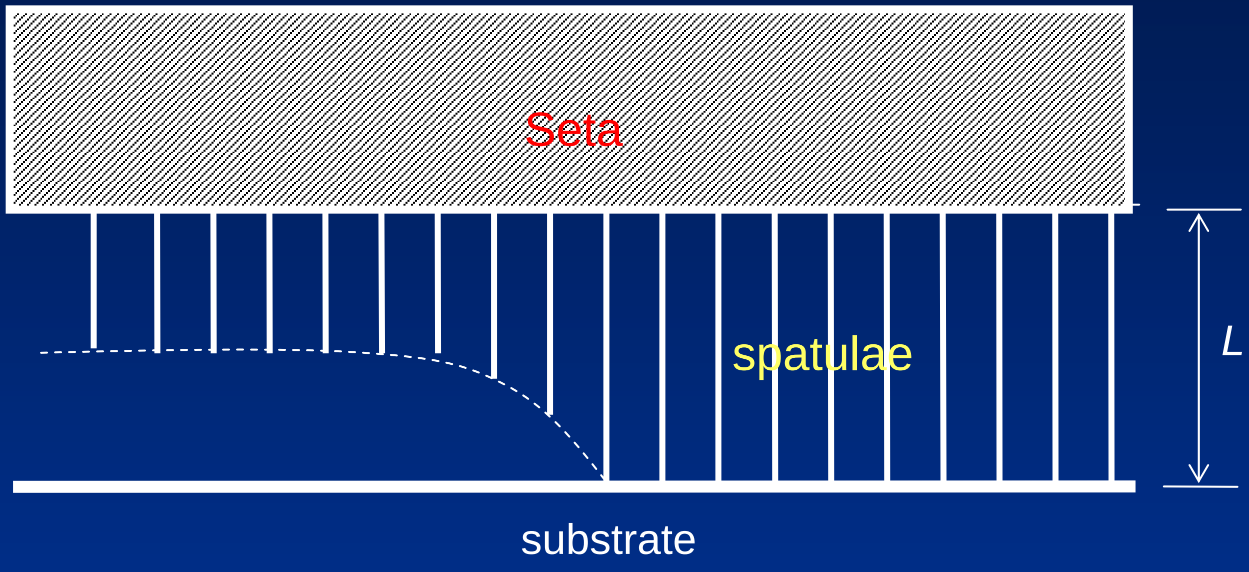


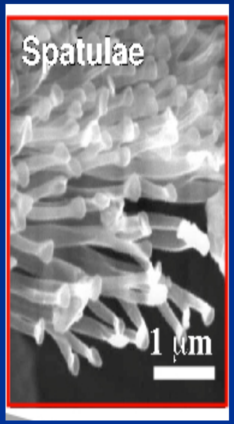


H. Gao, B. Ji, et al., 2004, MCB 1, 37

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

Energy dissipation mechanism



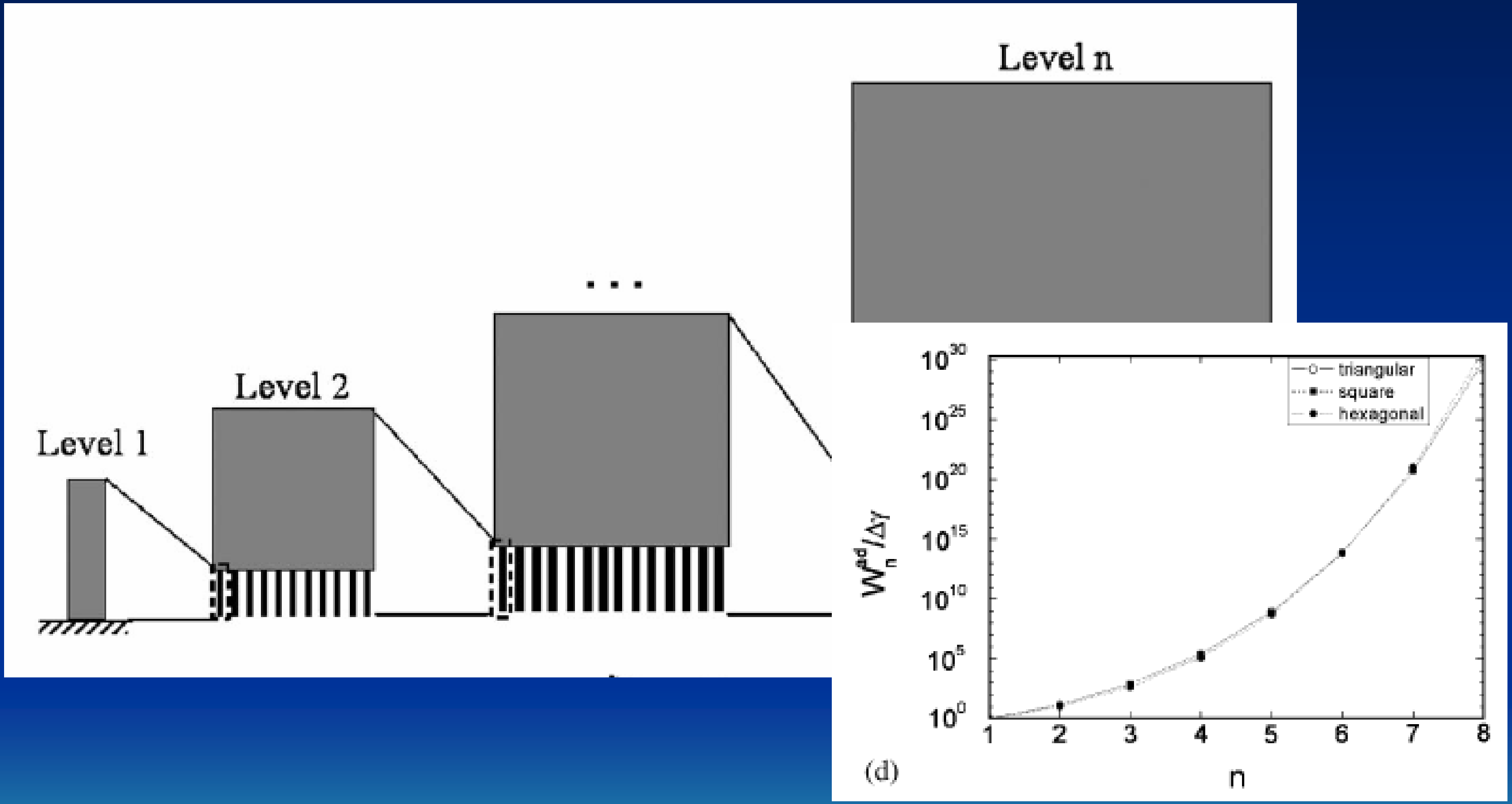


$$J_c = \varphi\Delta\gamma + \underline{L\int \sigma\varphi d\varepsilon} = \varphi\Delta\gamma + \frac{L\sigma_c^2\varphi}{2E}$$

$$\frac{J_c}{\varphi\Delta\gamma} = 1 + \frac{\sigma_{th}}{2E}\boxed{\frac{L}{\delta}}$$

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

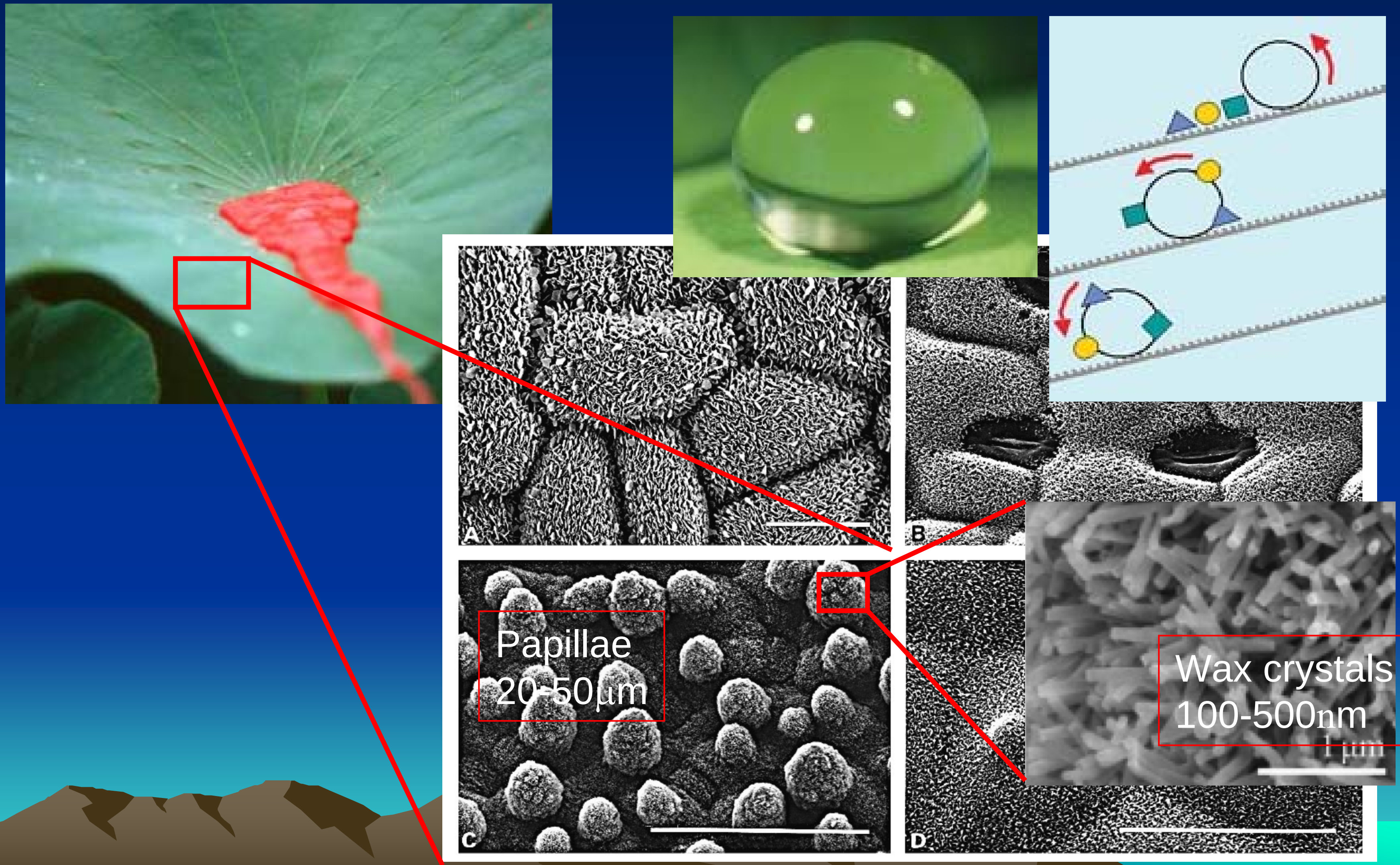
Hierarchical design



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

H. Yao and H. Gao, 2006, JMPS 54, 1120

Water-Repellent Plant Leaves

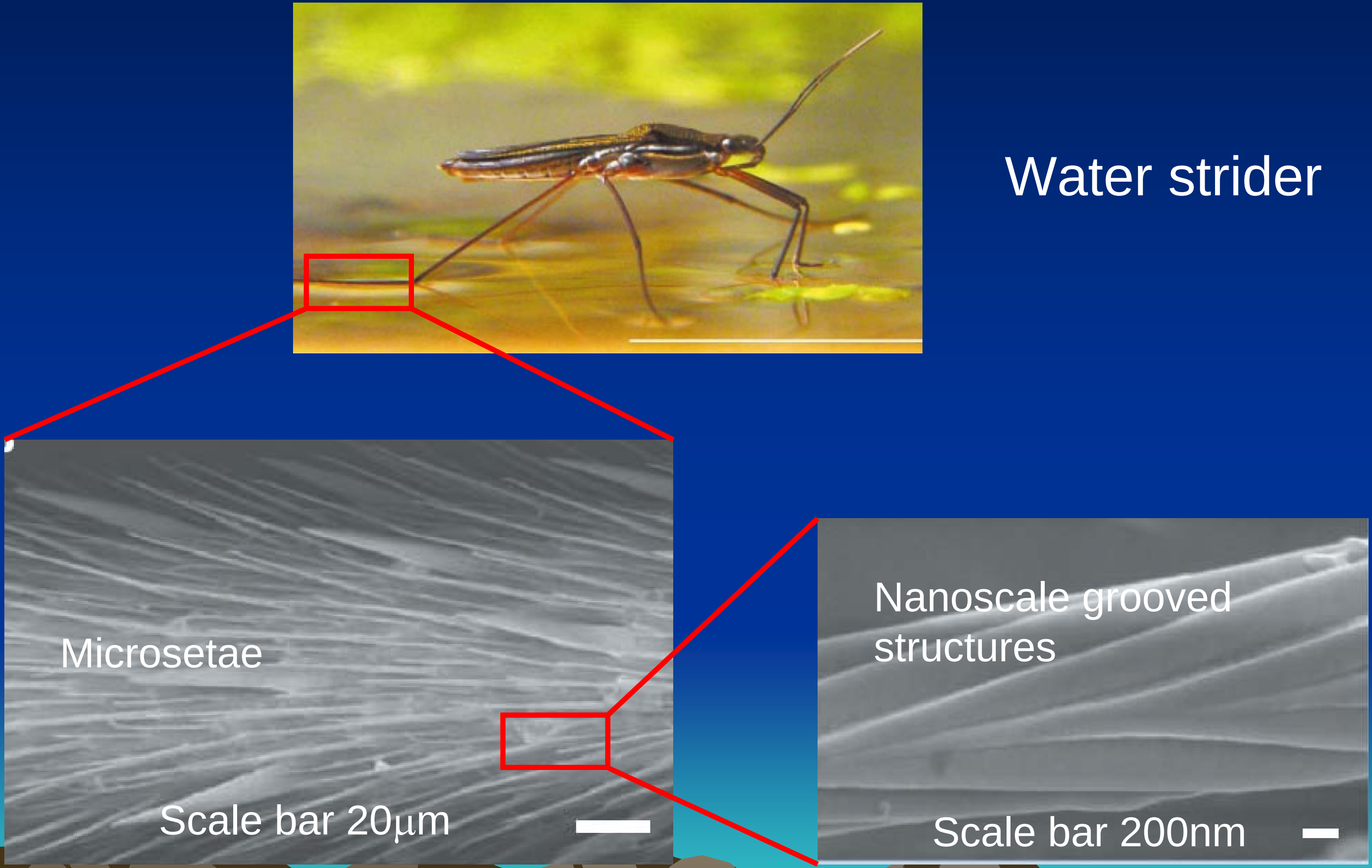


Papillae
20-50µm

Wax crystals
100-500nm

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

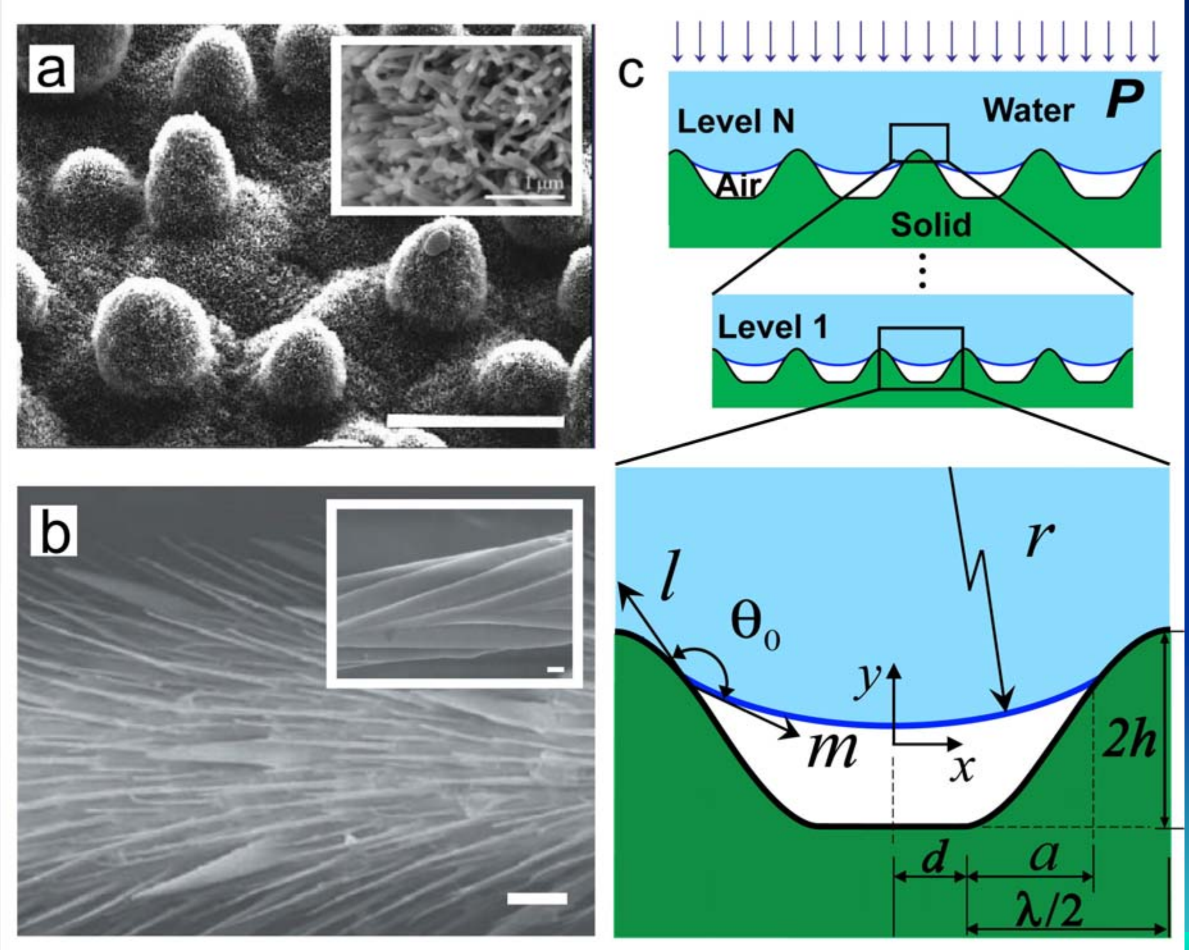
Water-Repellent Insects



Water strider

Jiang, Nature 2005

A theoretical model for hierarchical biological surface structure for low adhesion



Y. Su, B. Ji, et al., submited

Summary

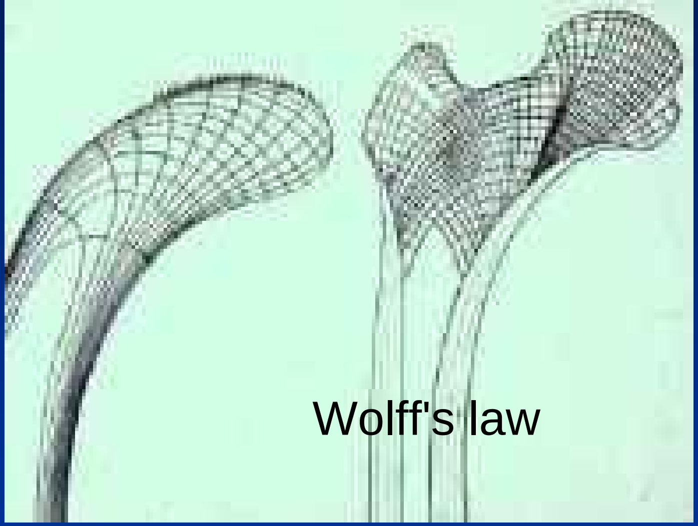
- It seems that Nature use similar strategies, i.e., with hierarchical design from nanoscale, to optimize or control different material properties.
- At the nanoscale, the structure is not sensitive to flaws, achieving maximum strength of the materials.
- Hierarchical structures are designed for the 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.

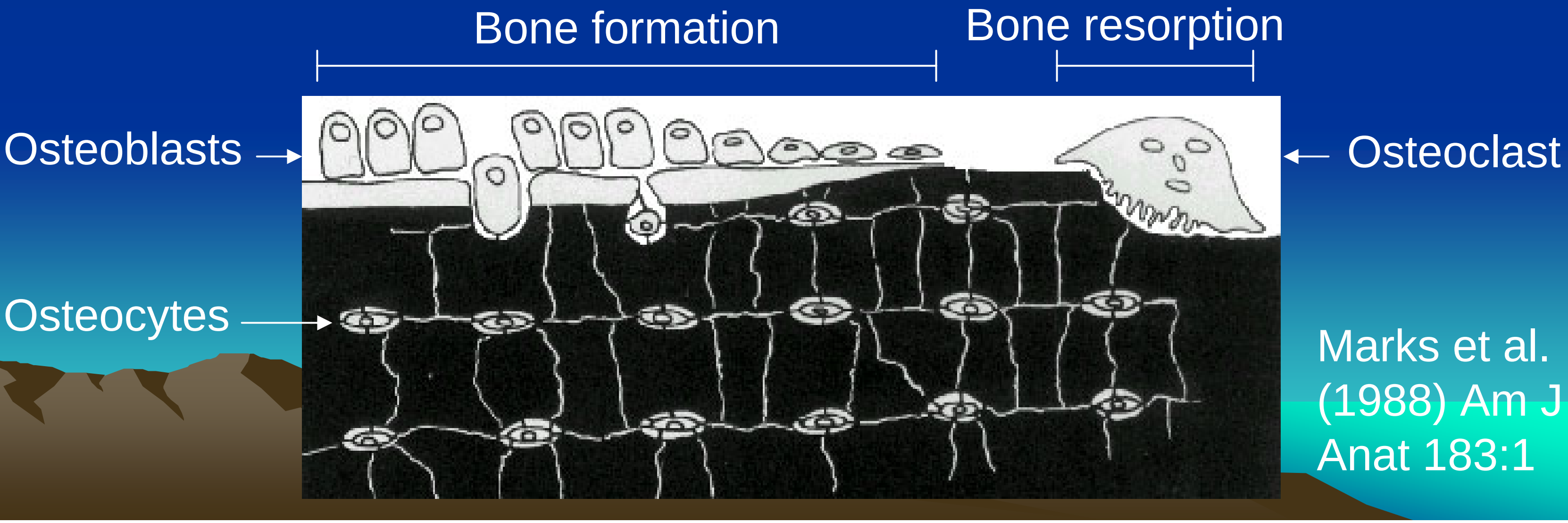
“Smart” biological materials

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.





Marks et al. (1988) Am J Anat 183:1

Part II

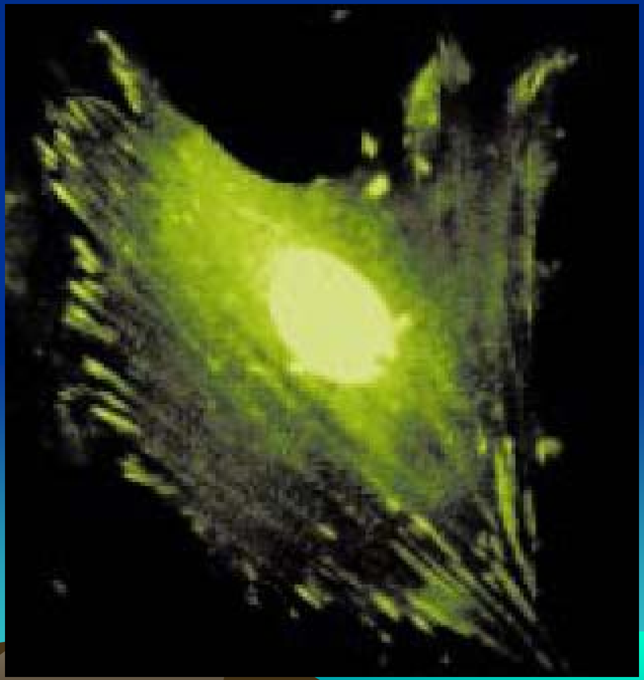
Modeling of cell adhesion: from molecular level

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…



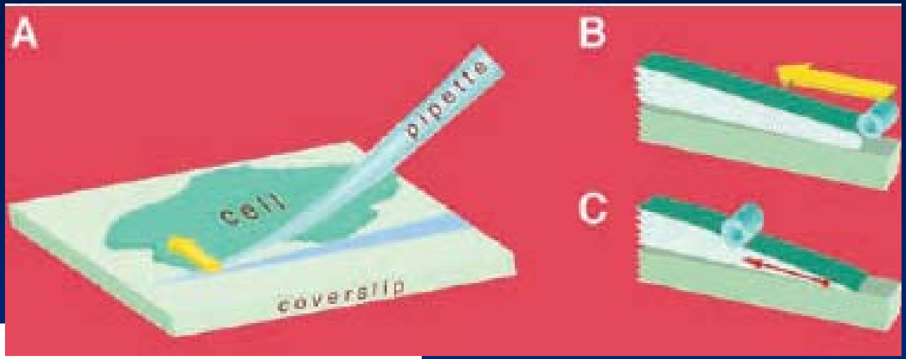
细胞黏附与疾病

诸如：血栓形成，动脉粥样硬化，肿瘤的侵润和转移…

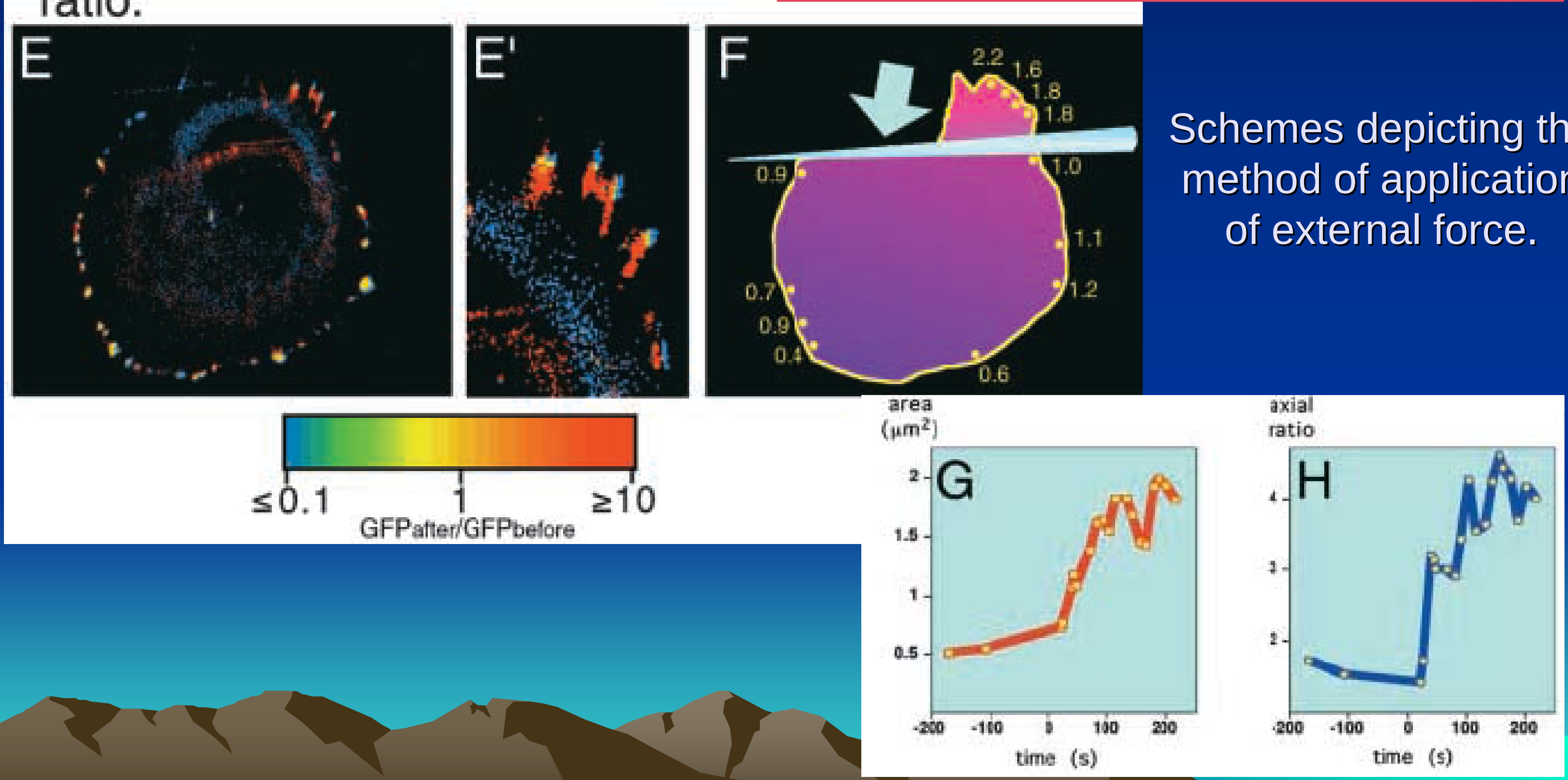
A time to experiment, and a time to theorize (Bershadsky et al., 2006)

- Cell Movement Is Guided by the Rigidity of the Substrate (Engler et al., 2006, Cell 126, 677; Lo et al. 2000. Biophy. 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

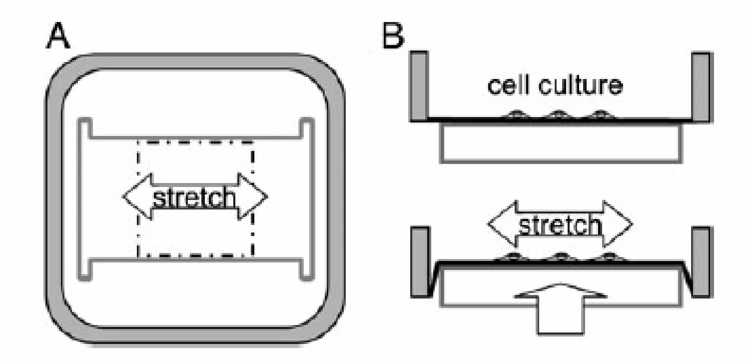


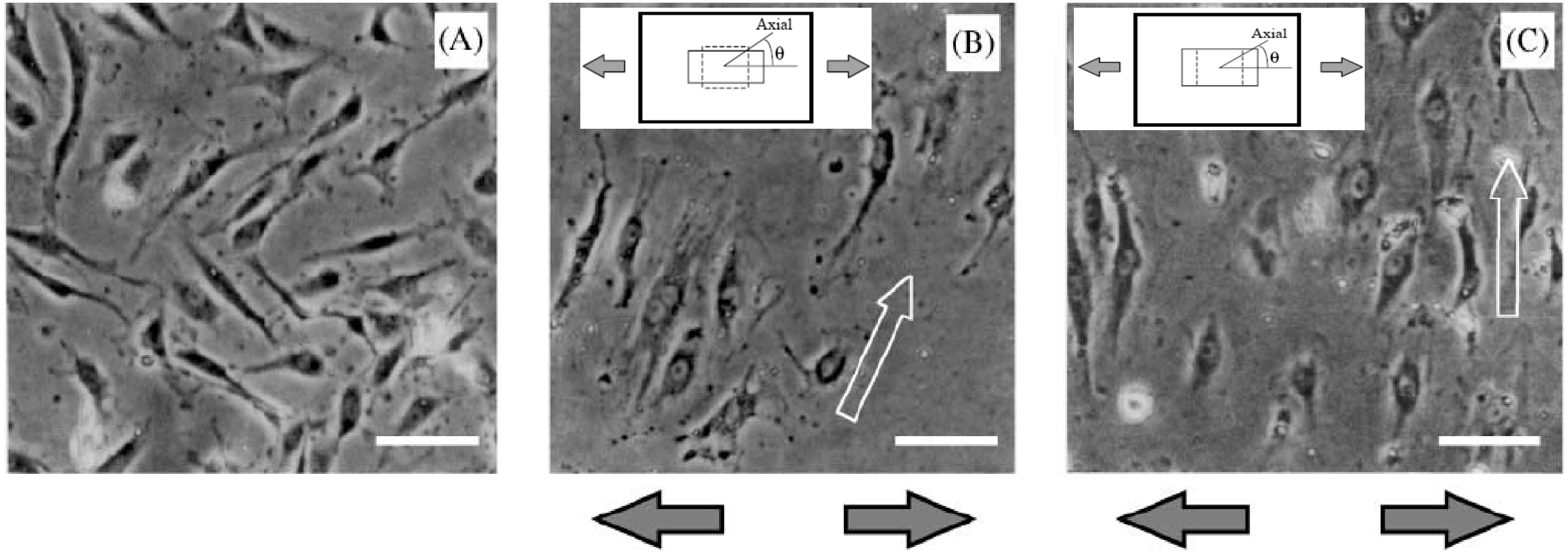
Schemes depicting the method of application of external force.



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

Cell reorientation under cyclic strain

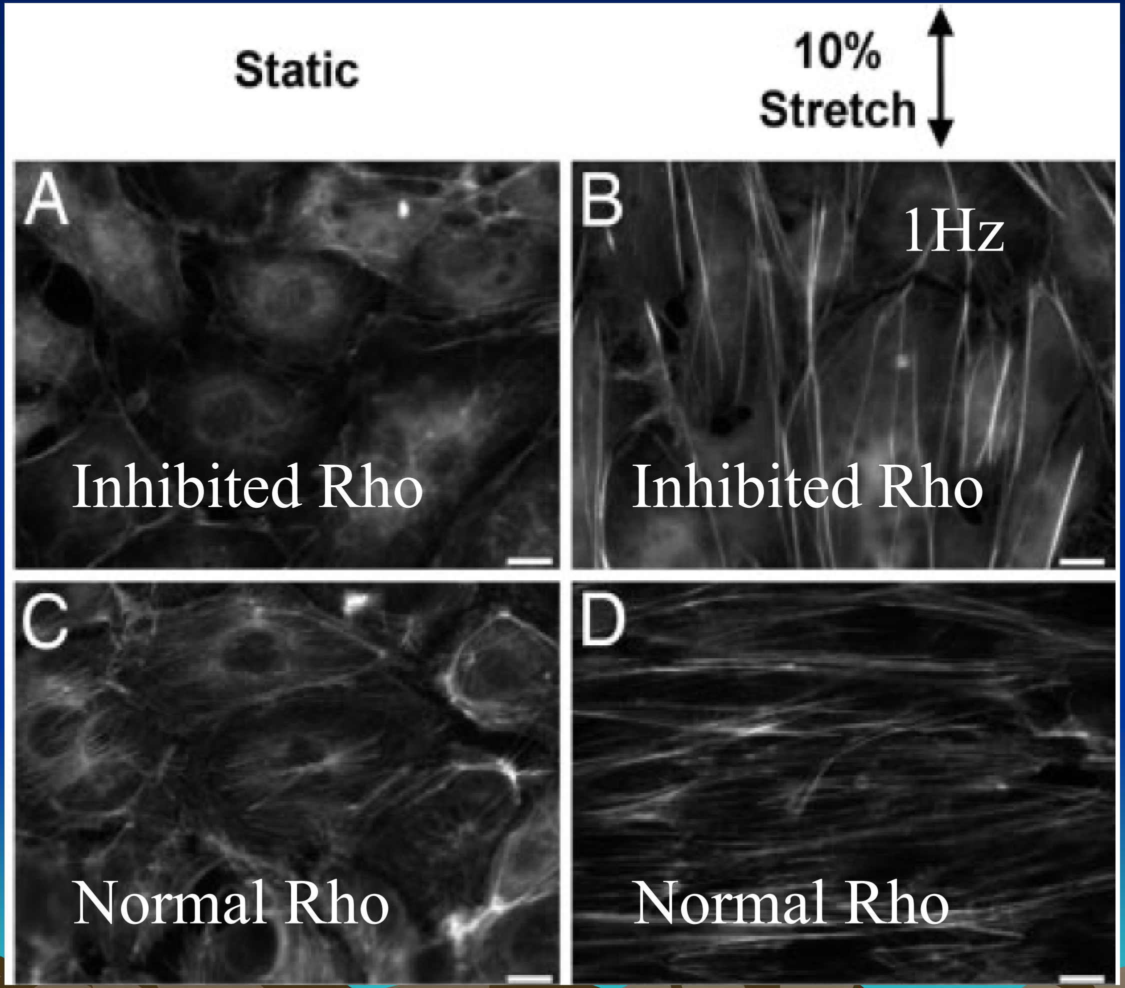


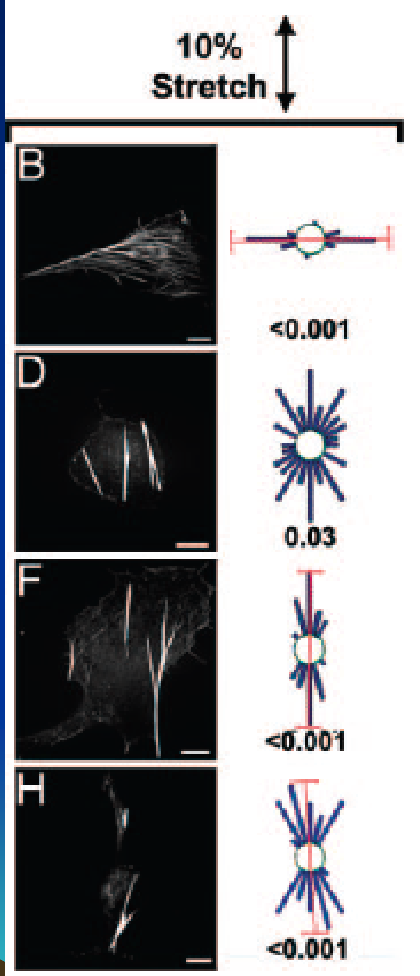


Representative phase contrast microphotographs of endothelial cells: unstretched (A), after 3 h of simple elongation (B), and after 3 h of pure uniaxial stretching (C).

Wang et al., 2001, J. Biomech. 34, 1563

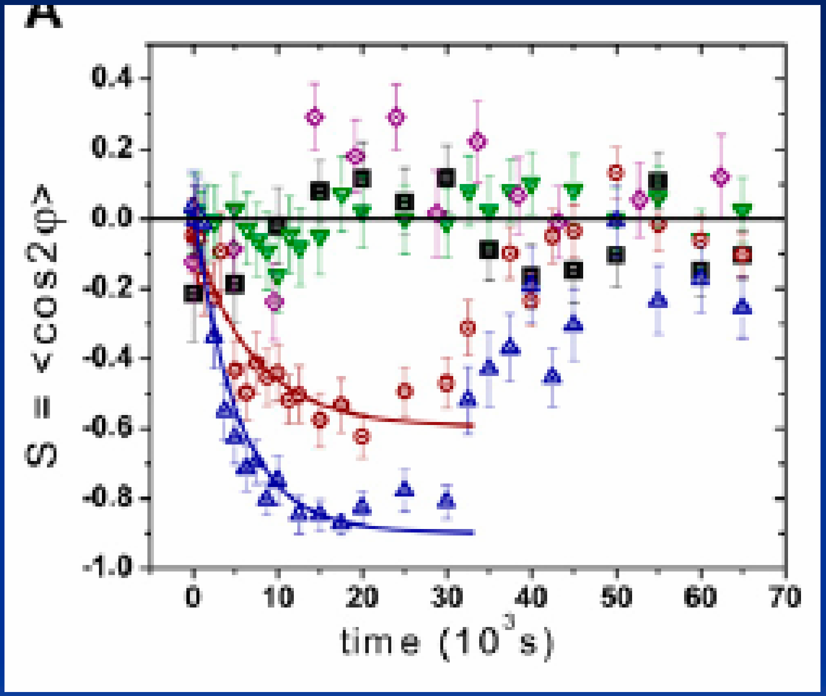
Cell reorientation under cyclic strain



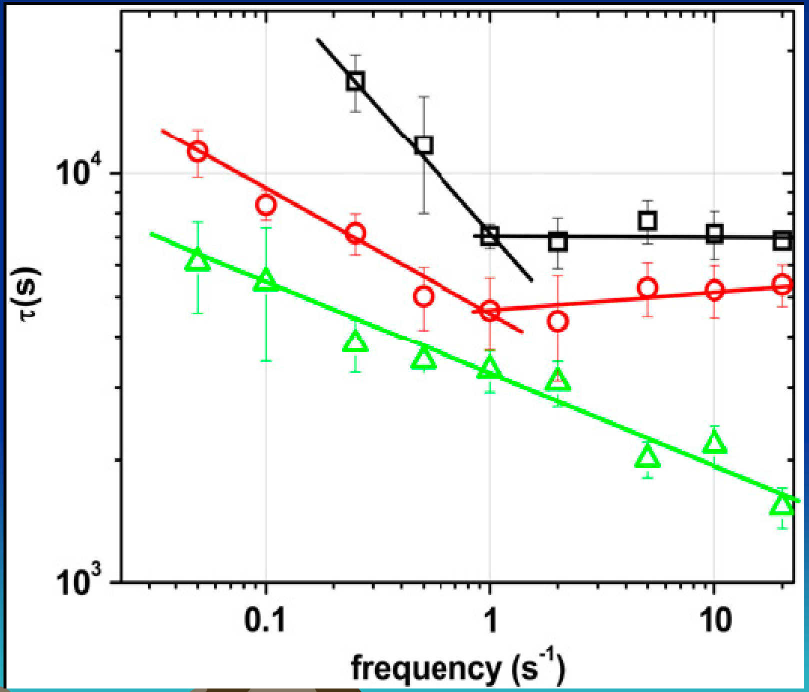


Kaunas et al. 2005. PNAS 102, 15895

Frequency-dependent Cell reorientation under cyclic strain



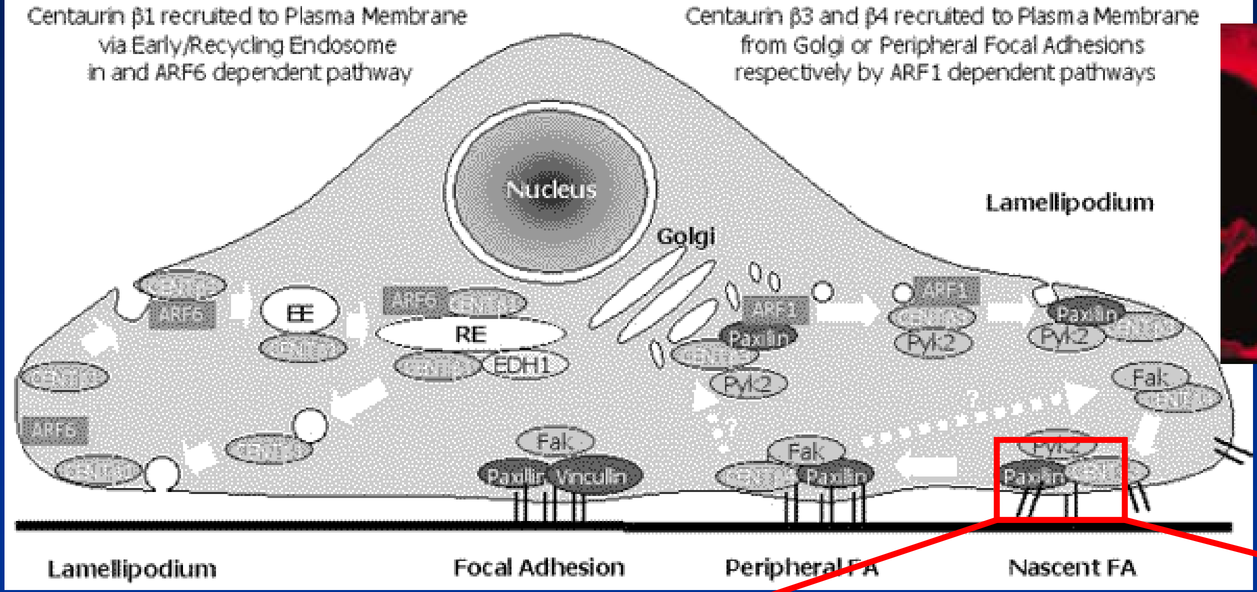
Biphasic characteristics of dynamic cell reorientation

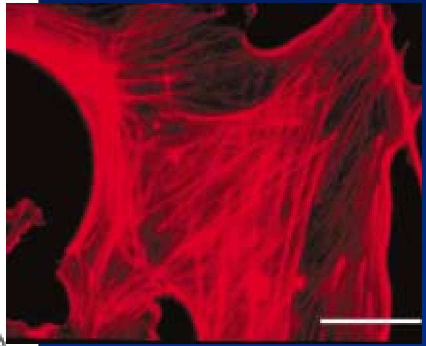


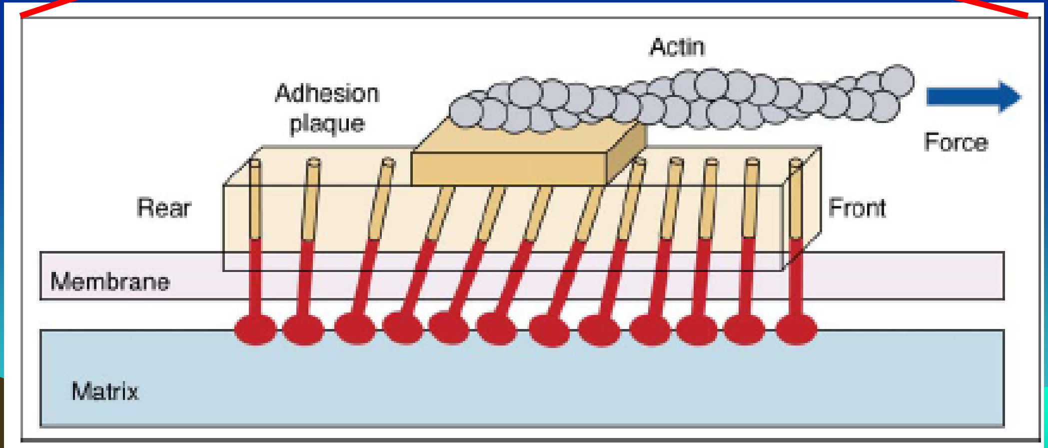
Exponential decrease of the order parameter S from a random orientation to a saturation value at different stretching frequencies

Jungbauer et al. 2008. Biophys. J 95, 3470

Focal adhesion

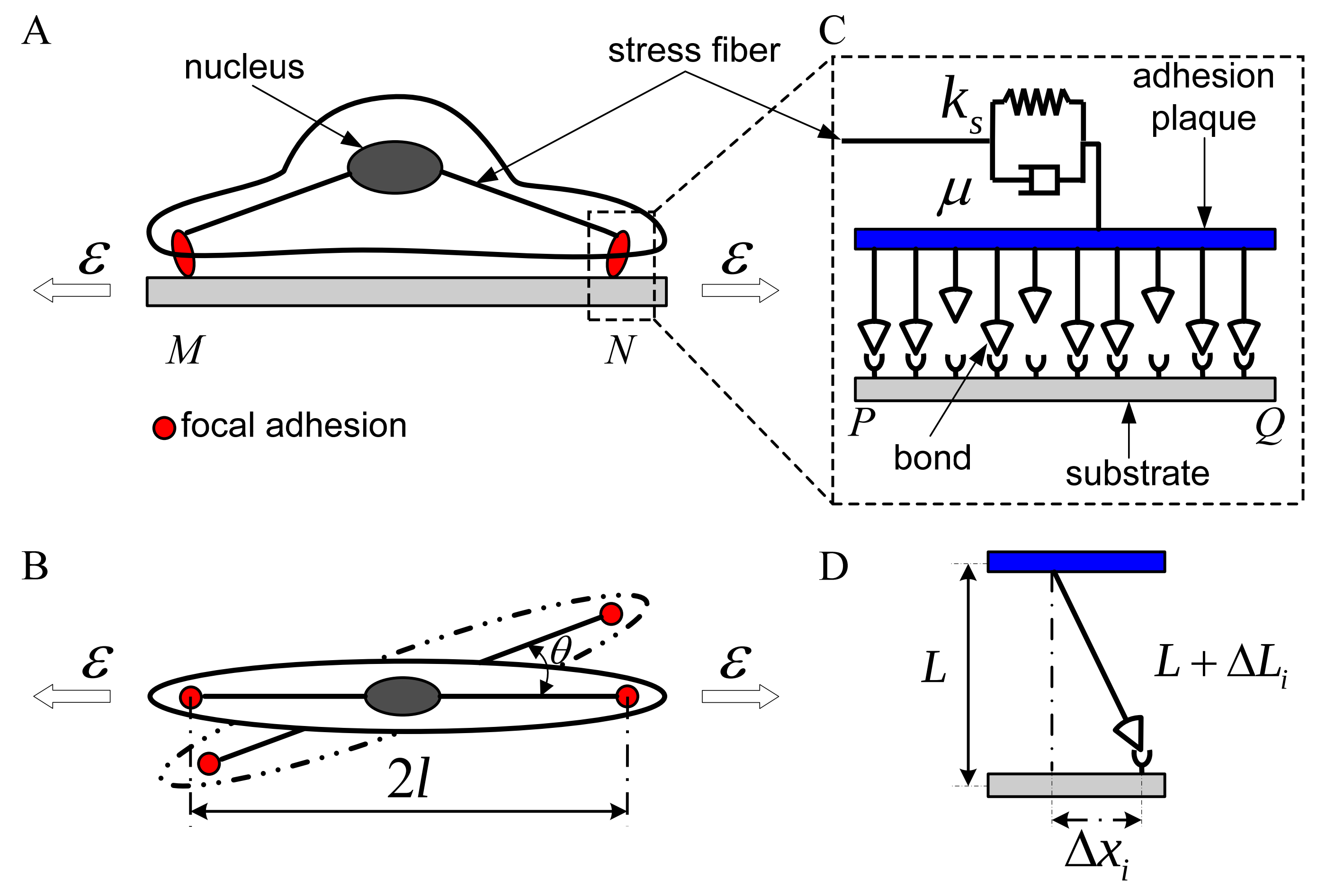






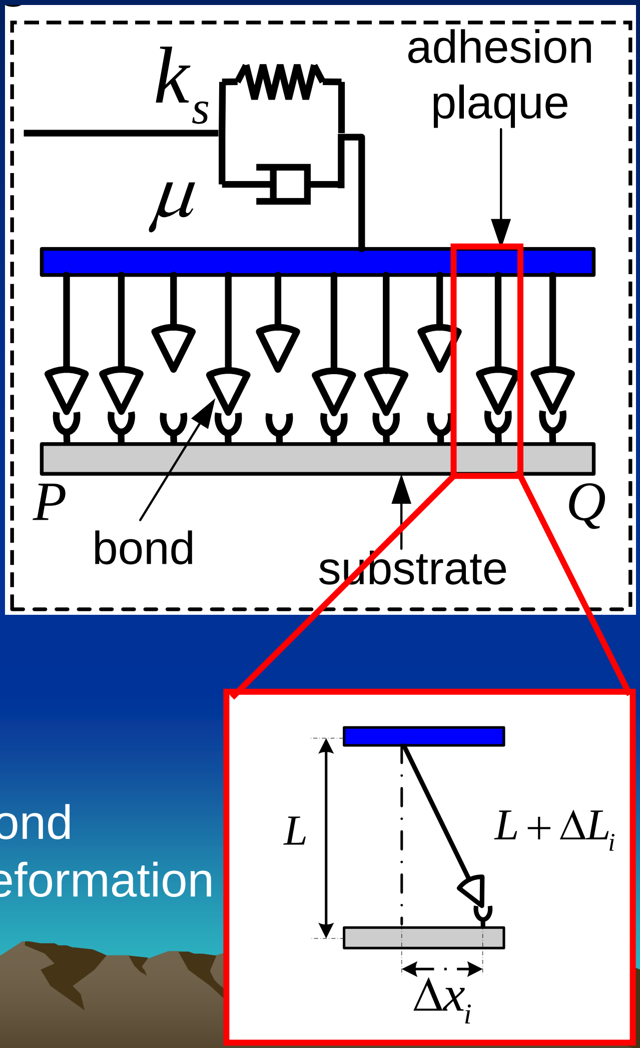
Bershadsky et al., 2006, Curr. Opin. Cell Biol. 18, 472

A microscopic model



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

Modeling of adhesion cluster



Bond deformation

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

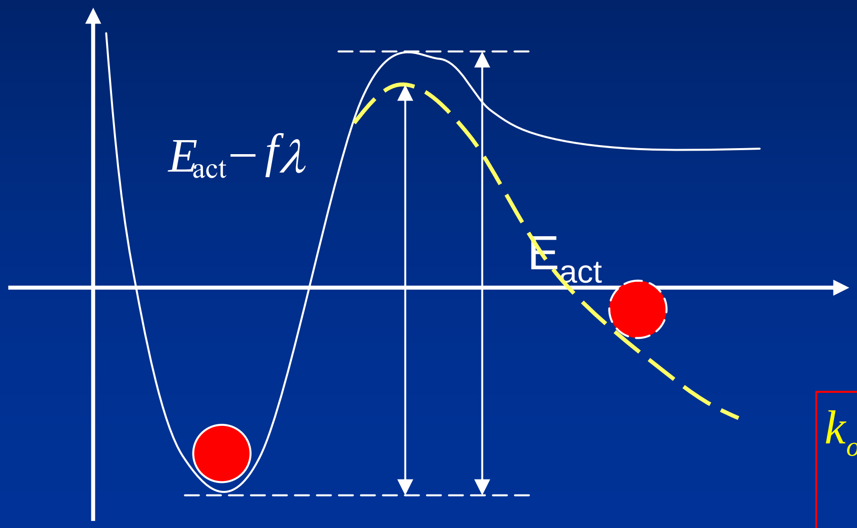
$$s = l\varepsilon(\cos^2\theta - \nu \sin^2\theta)$$

Bond force

$$f = k_b \Delta L$$

Modeling of adhesion cluster (cont.)

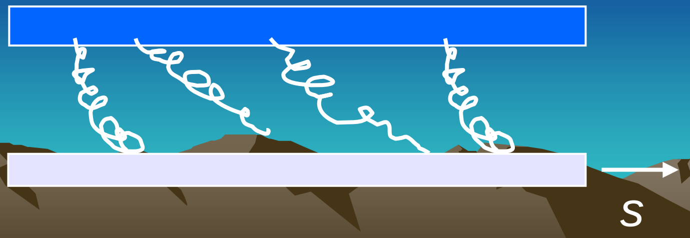
Dynamics of adhesion bonds



$$\mathrm{R + L} \underset{k_{off}}{\overset{k_{on}}{\rightleftarrows}} \mathrm{Bond}$$

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

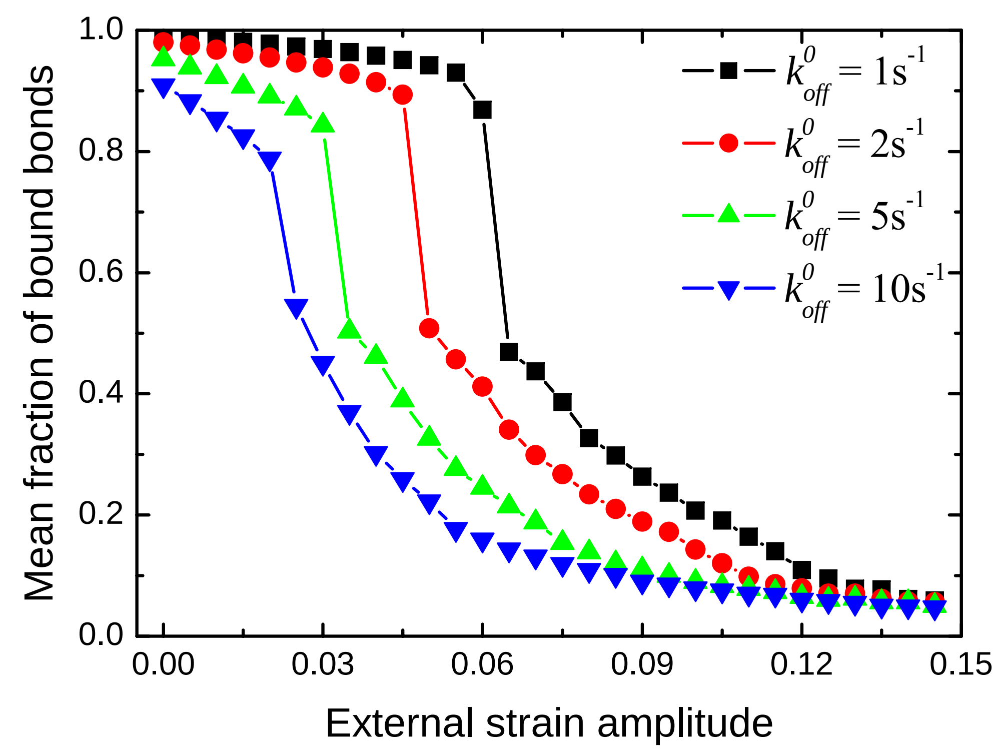
$$k_{on} = k_{on}^{0} g(\tau_c, \tau_b) \quad \& \quad g(\tau_c, \tau_b) = \begin{cases} 1, & \tau_c > \tau_b \\ \tau_c / \tau_b, & \tau_c < \tau_b \end{cases}$$



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

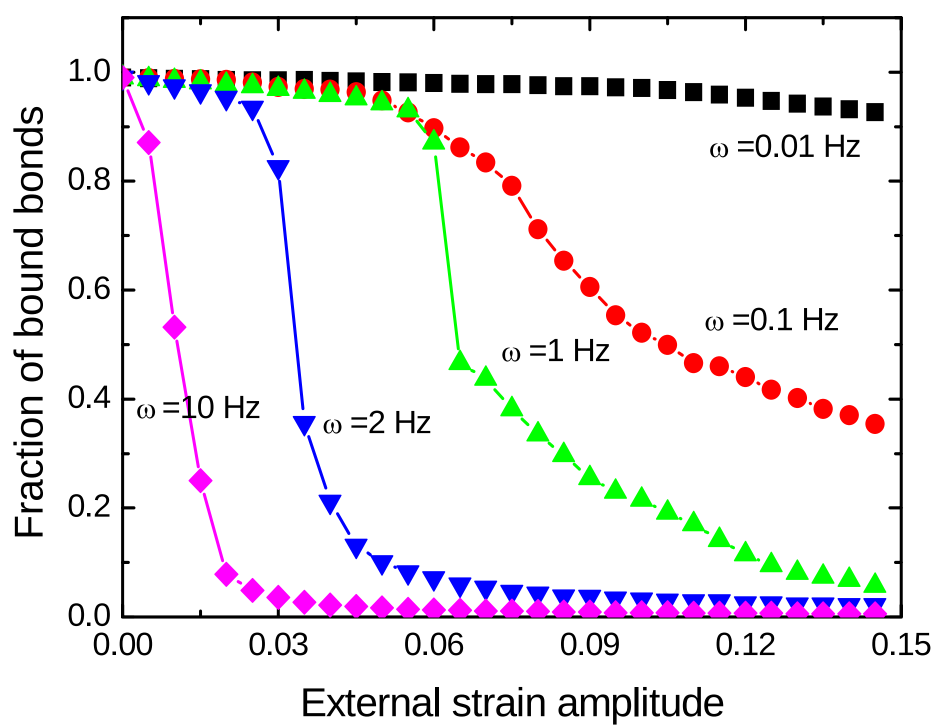
Dartsch and Hammerle, 1986, Eur. J. Cell Biol. 41: 339–346.

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

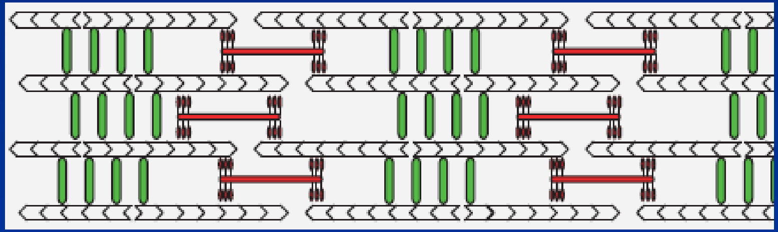
Kong, Ji and Dai, Biophys. J. 2008, 95 4034

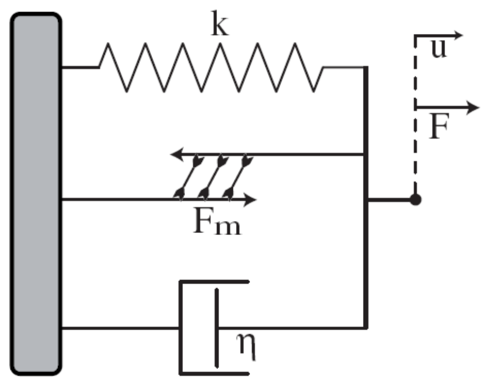
Effect of loading frequency

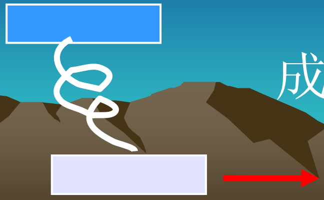


1. 对黏附分子反应的影响

2. 对应力纤维的影响



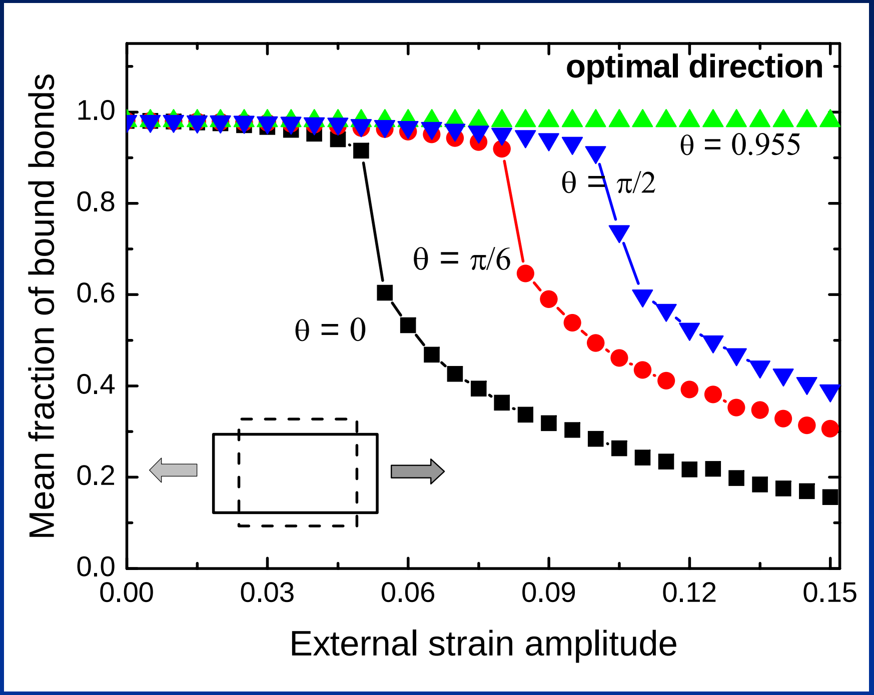




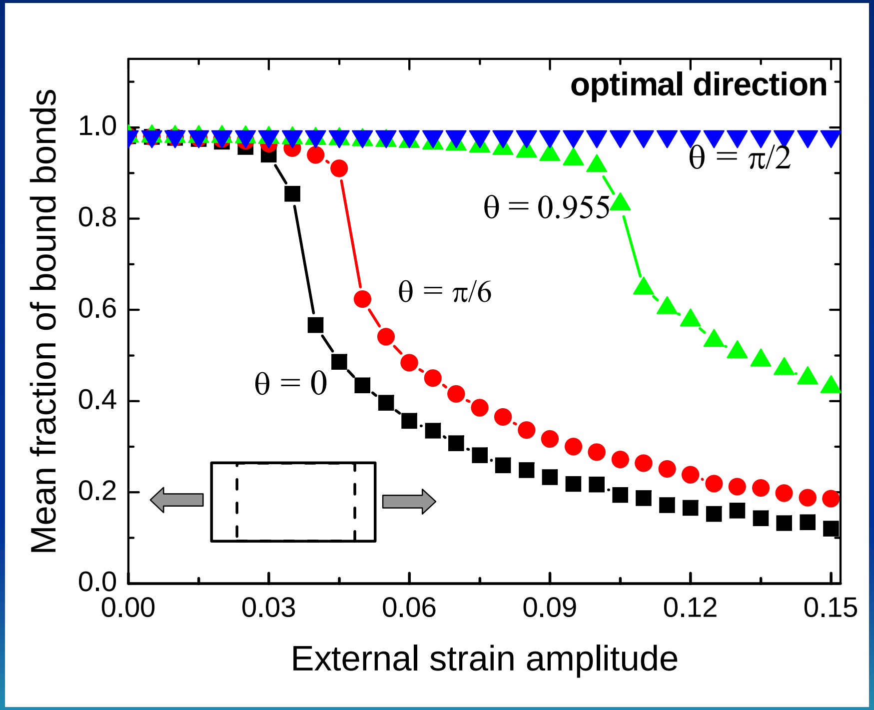
成键时间VS接触时间

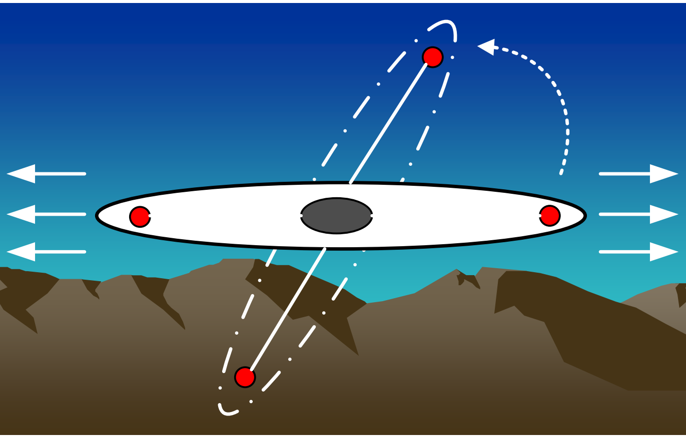
Kong et al., 2008; Besser and Schwarz, 2007

Optimum orientation



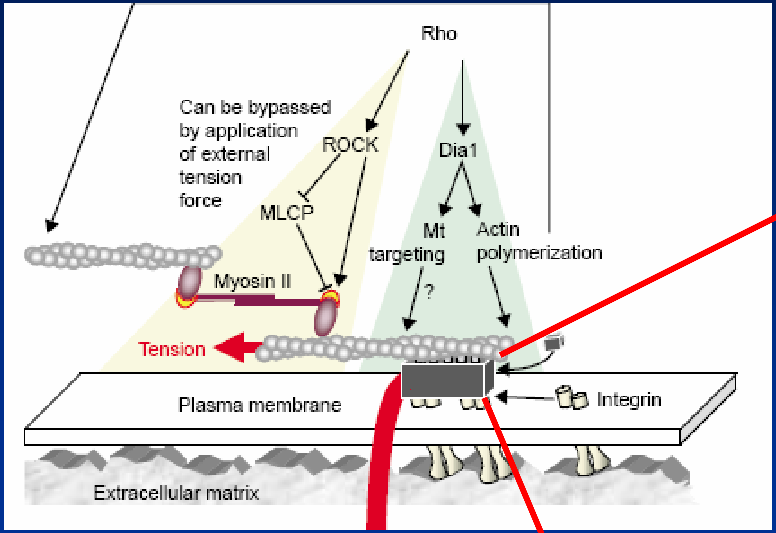
细胞趋向外力最小的方向。



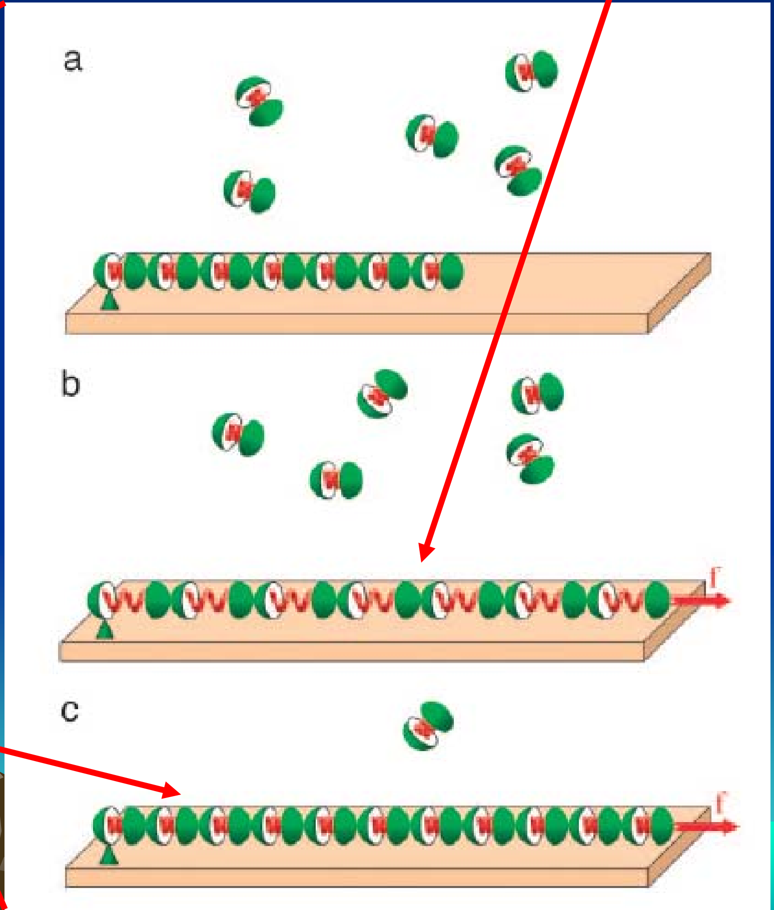


Kong, Ji and Dai, Biophys. J. 2008, 95 4034;
Wang et al., 2001, J. Biomech. 34, 1563

Growth mechanism



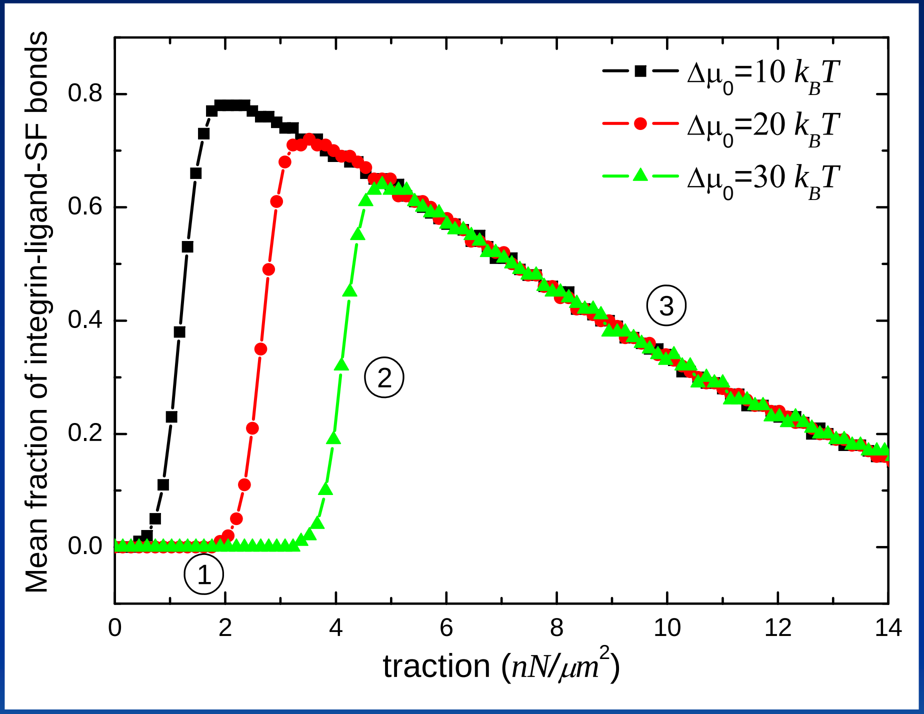
$$\Delta\mu = \Delta\mu_0 - \gamma \cdot l_0$$

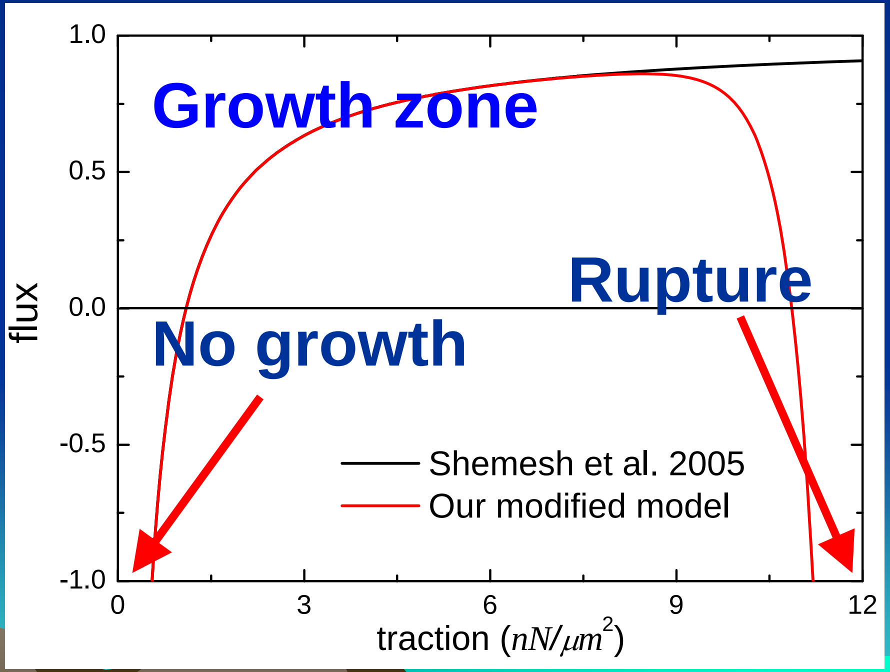


$$g_{on} = g_{on}^{0} \cdot e^{-\Delta\mu / k_B T}$$

A unified model

黏附斑生长 → 黏附斑破坏 → 细胞尺度取向变化

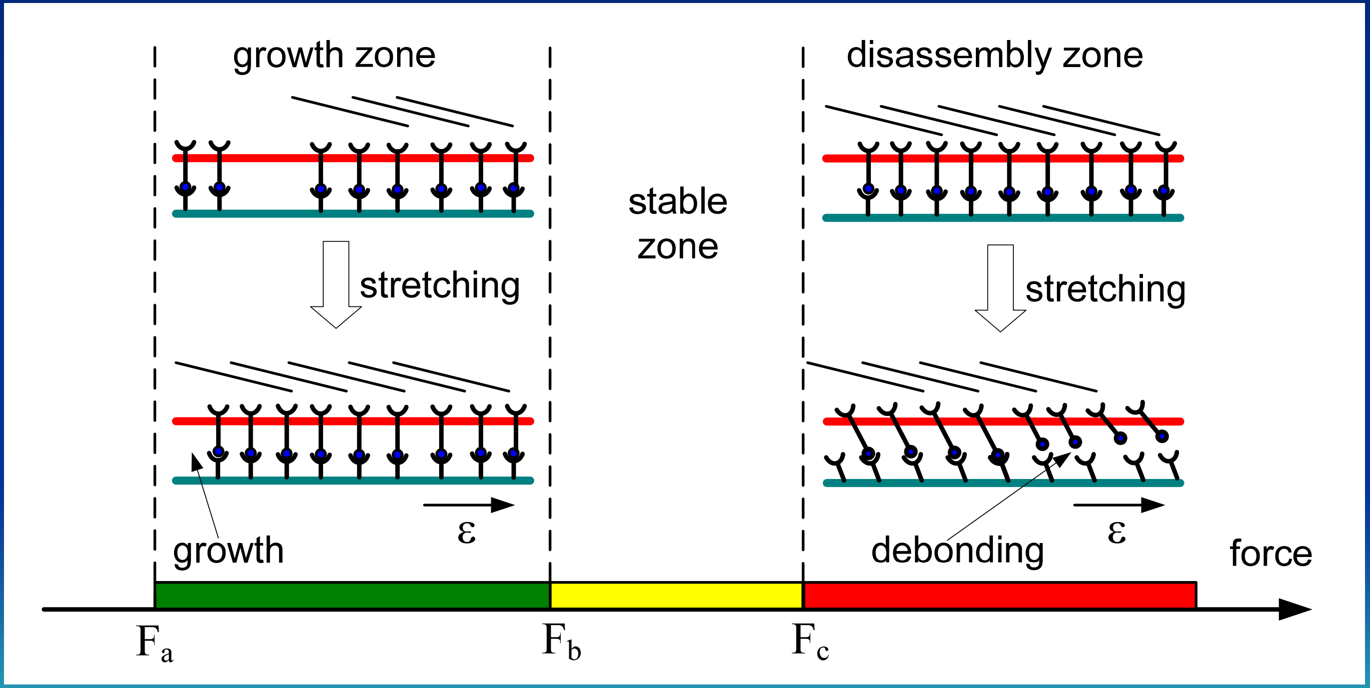




Kong, Ji and Dai, in preparation 2008

A unified model (cont.)

黏附斑生长 → 黏附斑破坏 → 细胞尺度取向变化



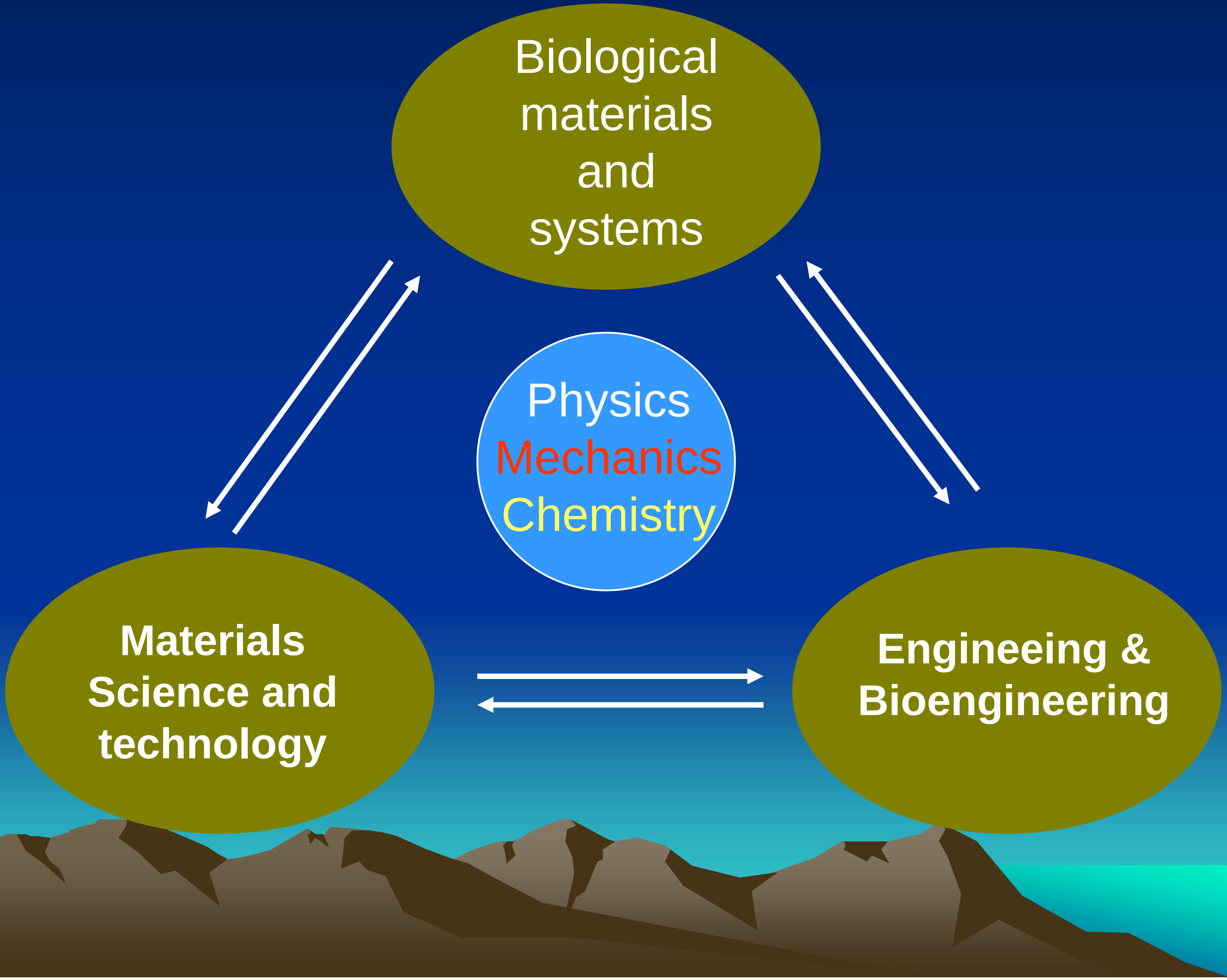
5.5 nN/μ m² < 48nN/μ m²

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



Biological materials and systems

Physics
Mechanics
Chemistry

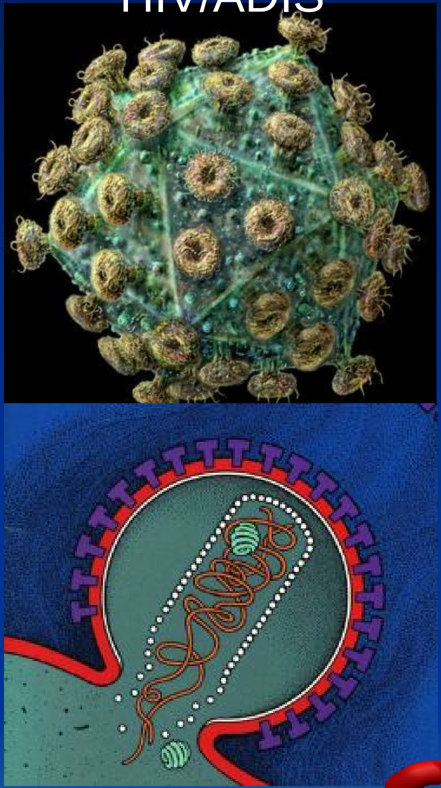
Materials Science and technology

Engineeing & Bioengineering

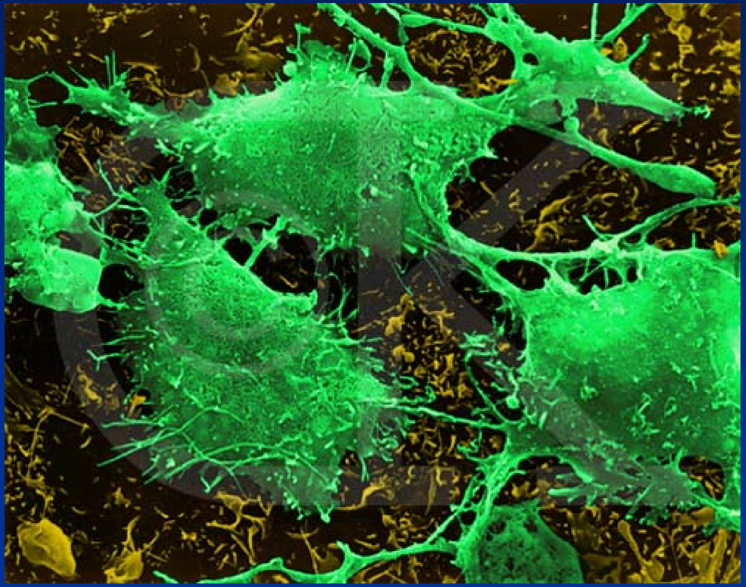
Man-made advanced materials

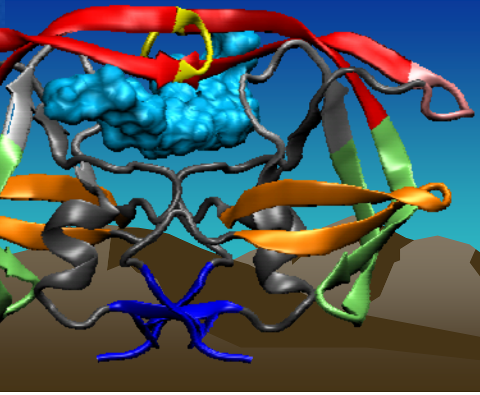
Understanding the mechanisms of the vital diseases and malfunctions

HIV/ADIS



Cancer





Osteoporosis/bone loss

Supports :

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