骨のリモデリングの計算バイオメカニクス
-階層的モデルとその応用-

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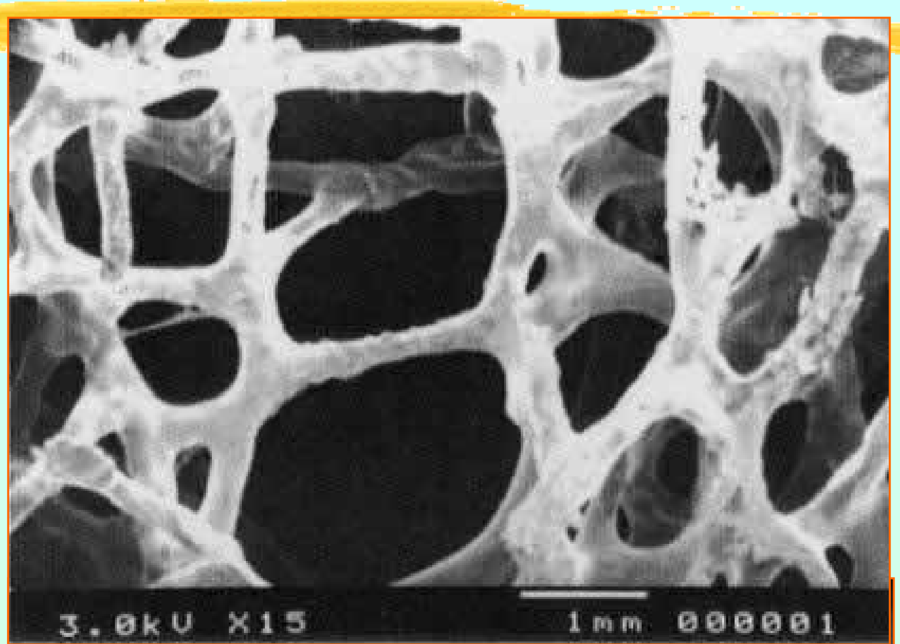
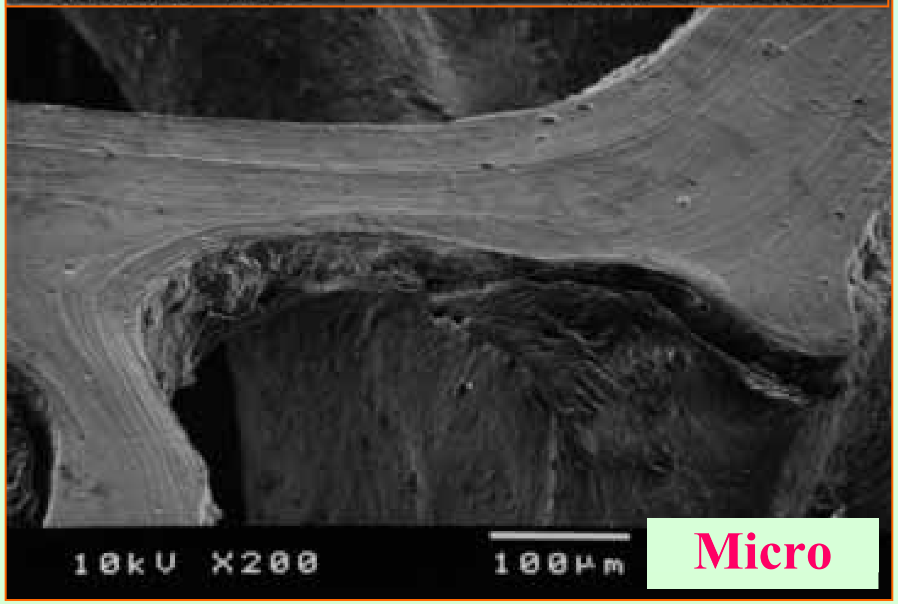
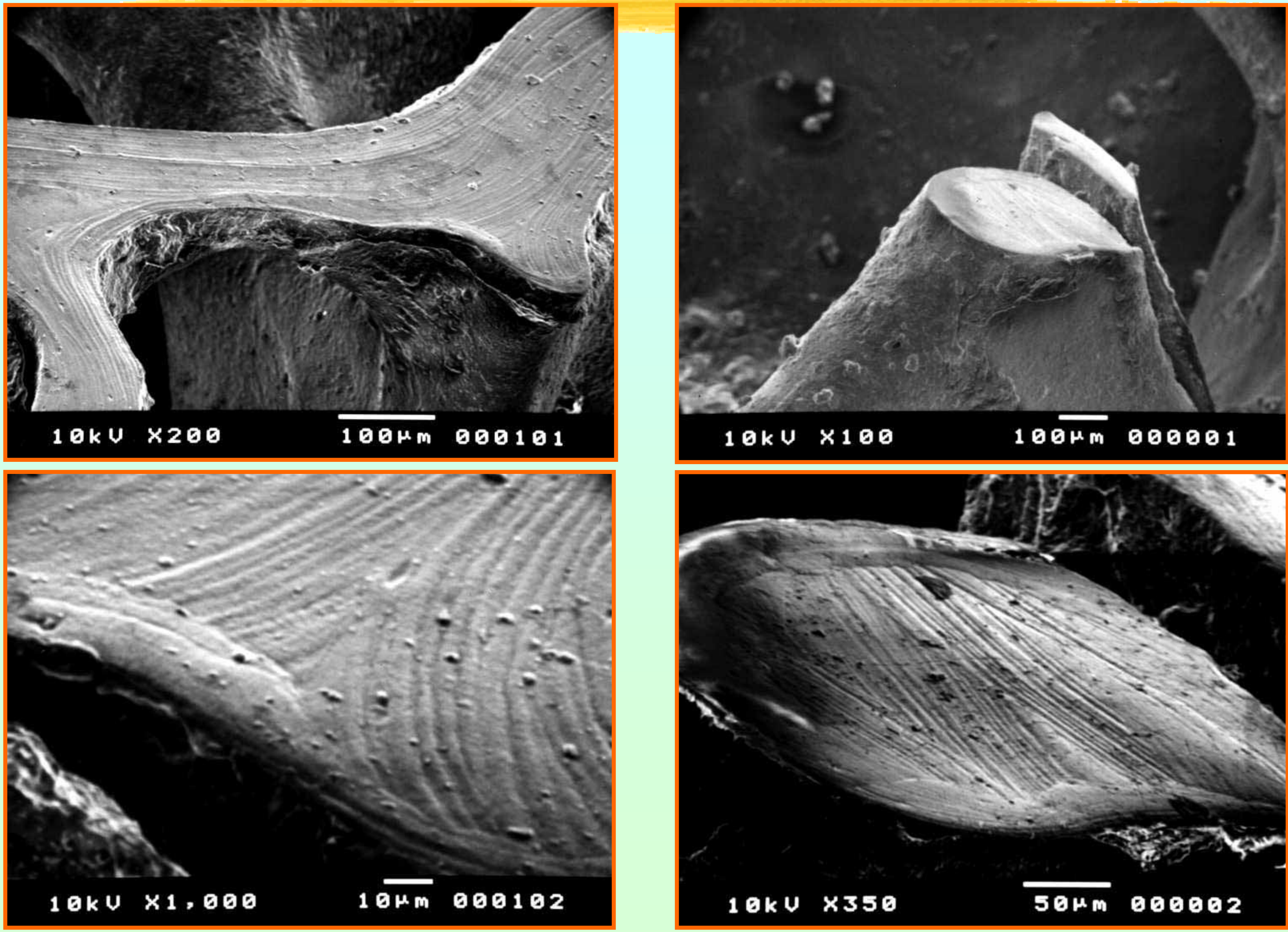
Hierarchical Structure of Bone

Macro

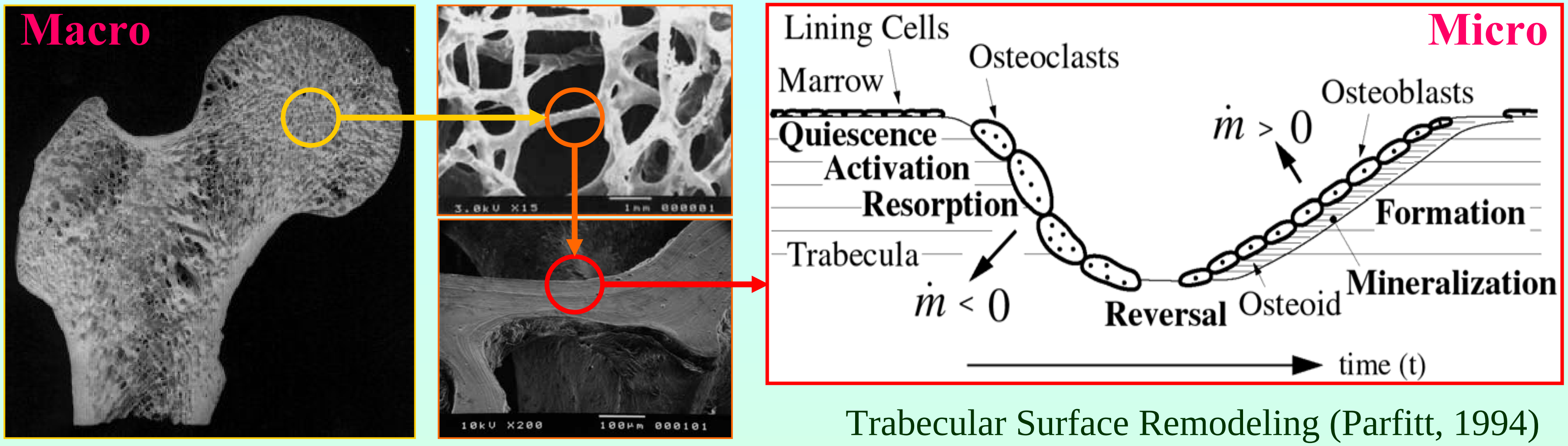




Internal Structure of Trabeculae



Introduction: Trabecular Surface Remodeling



Trabecular Surface Remodeling (Parfitt, 1994)

- Trabecular microstructure of cancellous bone
  - changing / maintained by remodeling, mechanical factors
- Adaptation to mechanical environment
  - regulated by Oc / Ob activities on trabecular surface
- Surface movement by cellular activities lead to
  - macroscopic changes of trabecular architecture

Introduction: Computational simulation

- Theoretical models & Computational simulations

Macroscopic Phenomena	Microscopic Mechanism
Cowin76, Carter87, Huiskes87, Beaupre90, Weinans92	Cowin92, Sadegh93, Mullender94

- Microscopic resorption and formation (Parfitt84)
- Local mechanical signals play an important role
  (e.g. Guldberg97)

- Trabecular level mechanical stimulus
  → related to morphological changes of trabecular architecture

Macroscopic Model: Huiskes *et al.*

Internal Remodeling (Huiskes87)

$$\frac{d\rho}{dt} = C_I(S - S_0)$$

External Remodeling :

$$\frac{d\boldsymbol{X}}{dt} = C_E(S - S_0)$$

ρ : Apparent Density
$\boldsymbol{X}$: Coordinate of Surface Point
S : Mechanical Stimulus
S_0 : Reference Value of S
C_I, C_E : Remodeling Constant

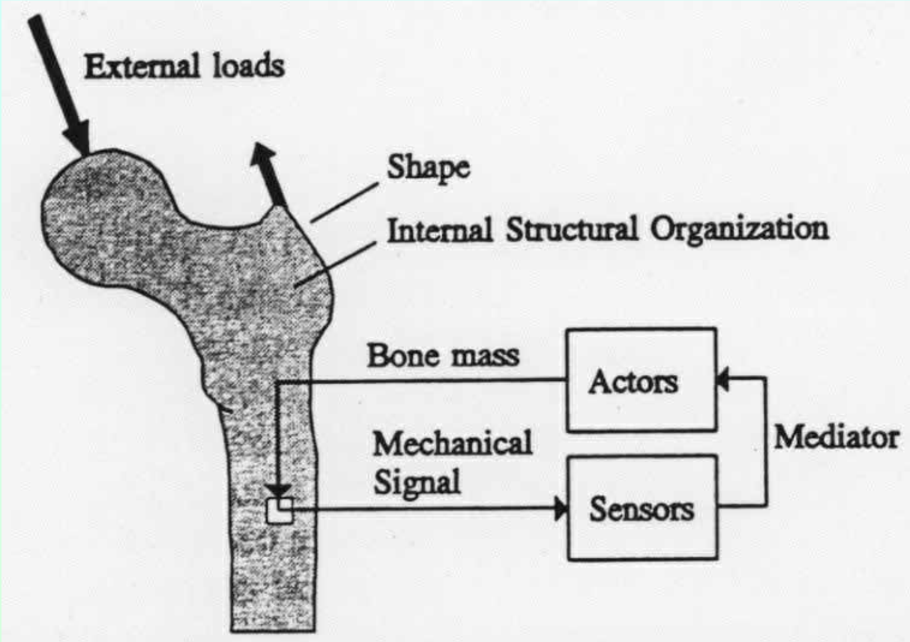


Fig. Feedback Mechanism of Remodeling (Huiskes & Hollister, 1993)

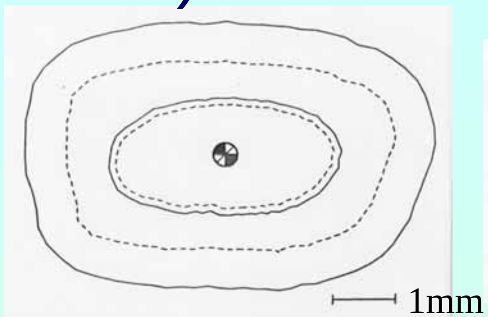
Macroscopic Model and Simulation

- Adaptive Elasticity (Cowin85)

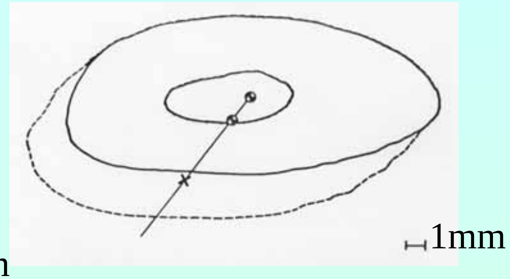
$$U = C_{ij}(Q)[E_{ij}(Q) - E^0_{ij}(Q)]$$

U : Rate of surface movement

- 2D Beam Theory
- Long Bone



(i) Predicted Geometry



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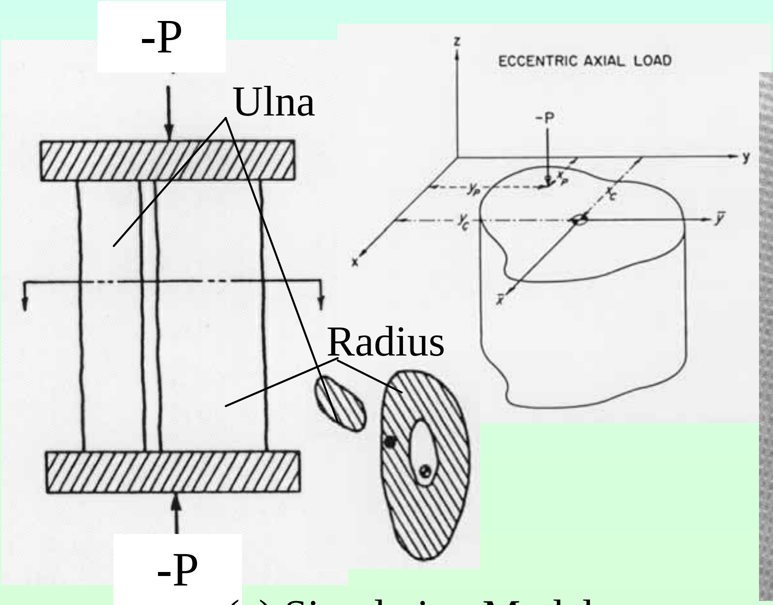
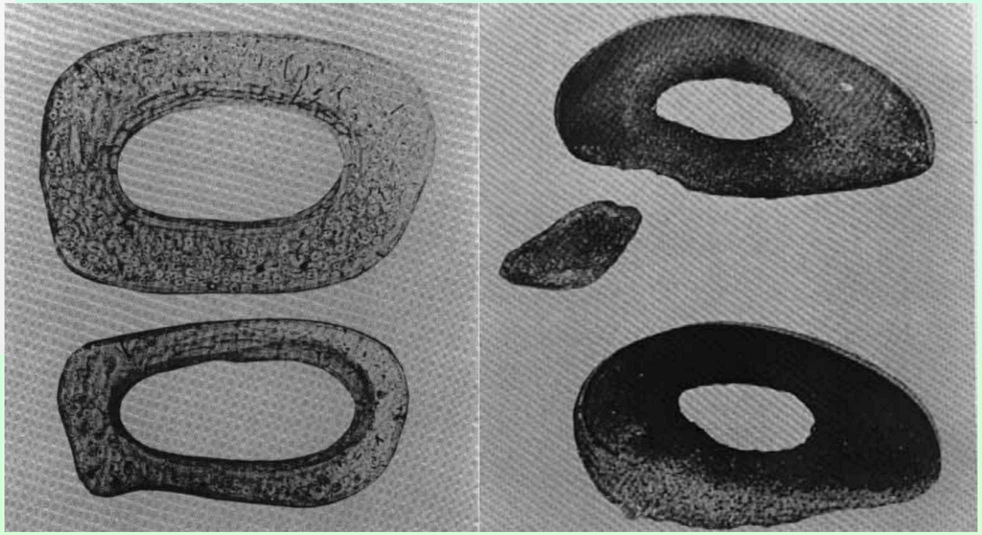


(a) Simulation Model


(ii) Experiment (Uhthoff78) (ii) Experiment (Lanyon82)

(b) Immobilization (c) Ostectomy

Macroscopic Model: Cowin, Carter *et al.*

- Adaptive Elasticity (Cowin76)

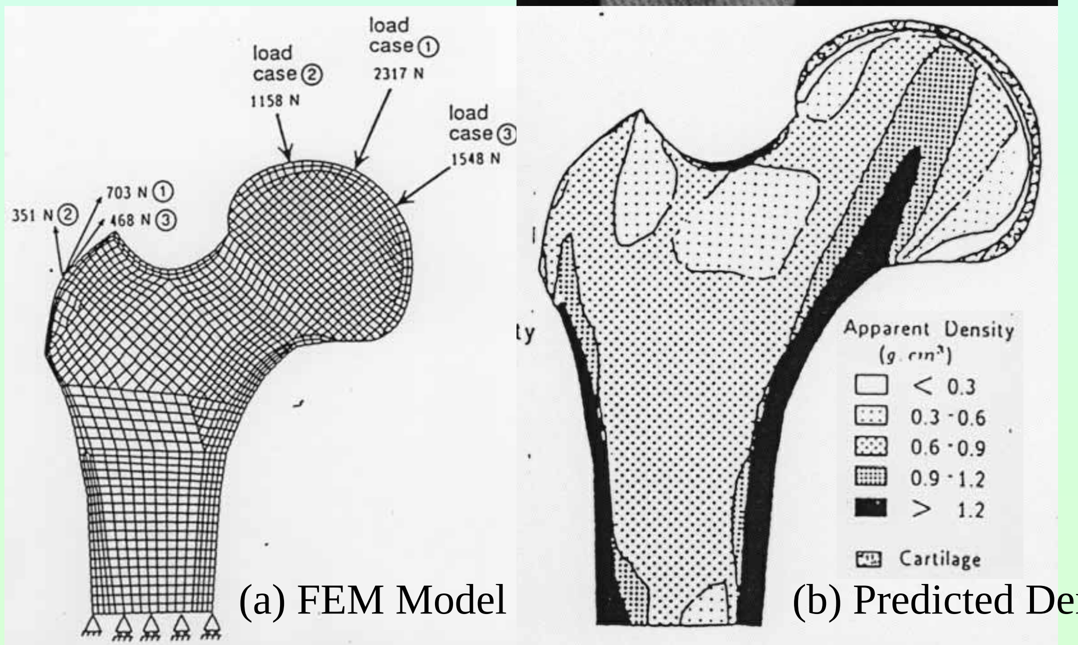
$$\frac{de}{dt} = a(e) + A(e)_{ij}(\varepsilon_{ij} - \varepsilon^0{}_{ij})$$

where $e = \rho - \rho_0$

- Self Optimization Model (Carter87)

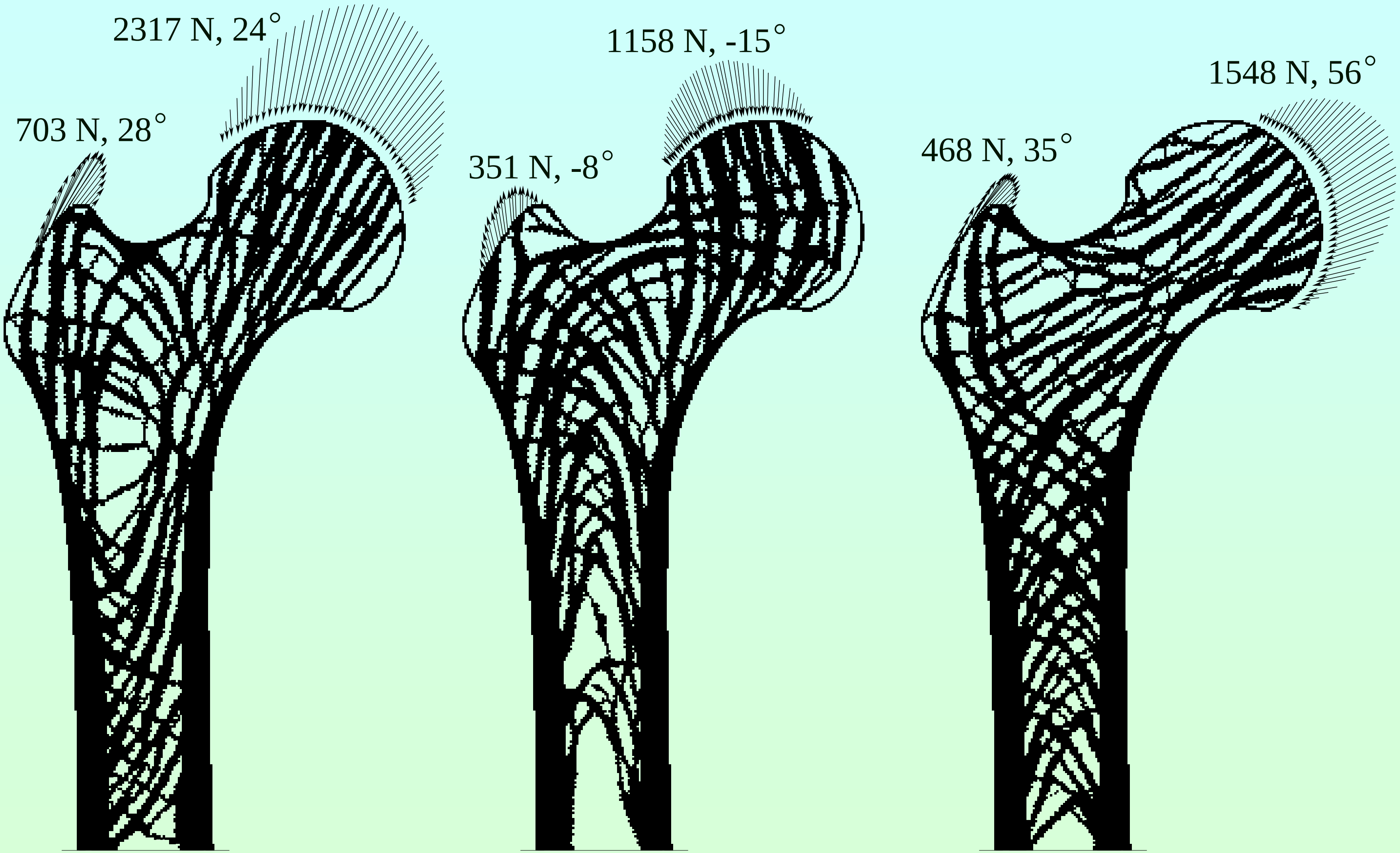
$$\frac{d\rho}{dt} = c(\Psi_b - \Psi_{b\mathrm{AS}})$$

where $\Psi_b = \left(\sum_{i=1}^{N} n_i \overline{\sigma}_{bi}^{\,m}\right)^{1/m}$



(a) FEM Model (b) Predicted Density

Remodeling under Single Load



(a) One-legged stance (b) Abduction (c) Adduction

(Adachi97)

Remodeling under Multi-Loads

Computational Biomechanics of Bone Remodeling

- Purpose: basic understanding & application
  - To understand mechanism of adaptive bone remodeling
  - To predict remodeling, around bone-implant interface
  - To design implant, screw …
  - To apply in bone tissue engineering, design scaffold …
- Approaches:
  - Phenomenological modeling and simulation “Macro”
  - down toward mechanism at cellular level “Micro”

Macro- & Microscopic Viewpoints

Macro　力学負荷 → 外形状・密度変化：巨視的連続体

階層的，微視構造 → 巨視的力学特性

特性変化

Micro　力学刺激 → 骨梁形状・構造変化：微視的連続体

骨リモデリングの連続体モデル？

微視的力学刺激を反映できない

微視レベルでの直接的モデル？

巨視的力学負荷を反映できない

- 微視的な力学刺激を巨視的力学負荷と関連付けるモデル
- 微視構造を考慮した巨視的連続体モデル

Approaches: Model & Simulation

- *Lattice Continuum Model of Bone*
  - Mechanics and Remodeling
  - Cosserat Continuum
  - Hierarchy of structure in continuum
    - cf. Homogenization and localization method

- *Trabecular Surface Remodeling*
  - Microstructural changes

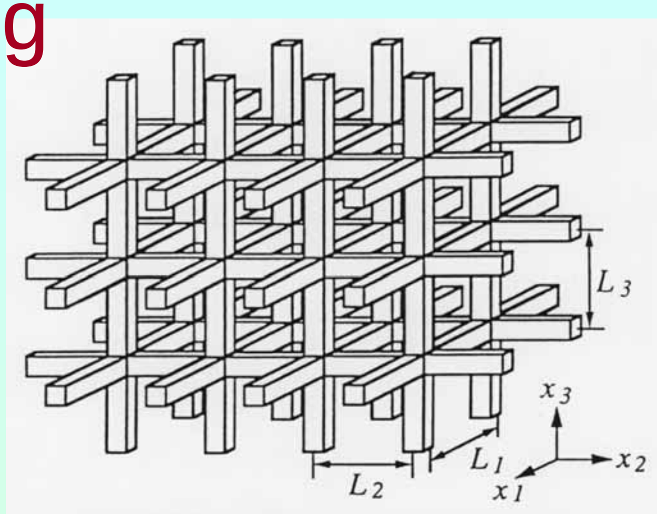
    --> Macro structural and mechanical properties
  - Voxel finite element model

Lattice Continuum Model

- Mechanics and Remodeling

Macroscopic Constitutive Eq.

$$\mathbf{T} = \mathbf{E}\,\boldsymbol{\varepsilon},\quad \mathbf{E} = \mathbf{E}(\rho, \mathbf{H}, \mathbf{S}, \cdots)$$



- Macro- Remodeling Rate Eq. $\dot{\mathbf{E}} = f(\mathbf{T}, \boldsymbol{\varepsilon}, \cdots)$

$$\boxed{\mathbf{T}, \boldsymbol{\varepsilon}} \xrightarrow{\text{S: Structure}^{\text{micro}}} \boxed{\mathbf{T}^e, \boldsymbol{\varepsilon}^e}$$

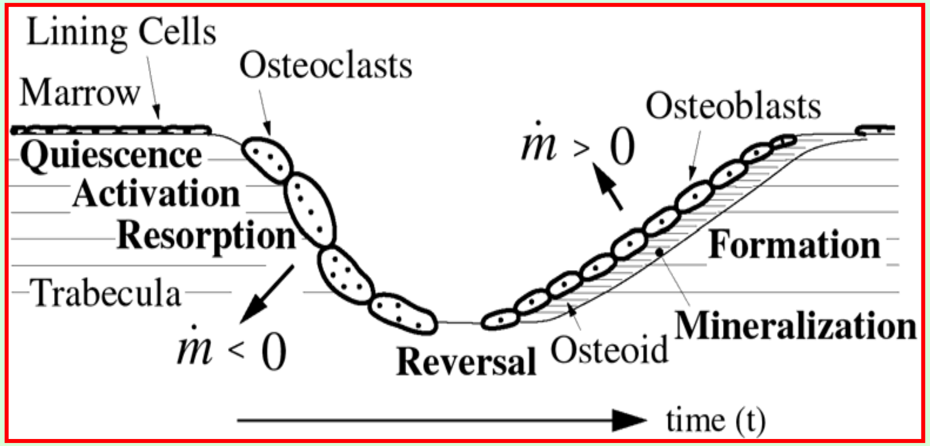
- Micro- Remodeling Rate Eq.

$$\dot{\mathbf{E}} = f(\dot{\mathbf{S}}),\ \dot{\mathbf{S}} = f(\mathbf{T}^e, \boldsymbol{\varepsilon}^e, \cdots)$$

Trabecular Surface Remodeling

Remodeling at trabecular level: microscopic level

- Rate Equation: Microscopic
  - Approach to Cellular level mechanism
- Simulation: Microscopic
  - --> Structural changes in Macro
  - --> Change in Apparent Mechanical Properties



Rate of trabecular surface movement

$$\dot{M} = F(\Gamma)$$

Γ : microscopic mechanical stimulus

3D Simulation Model Using Voxel Micro FE

(Adachi *et al.*, 1997; Tsubota *et al.*, 1998)

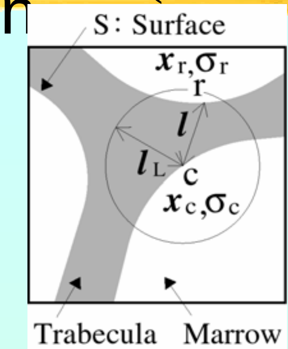
- Uniform Stress Criterion

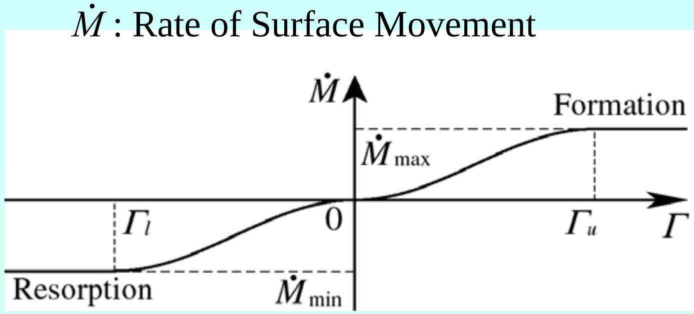
Representative Stress

$$\sigma_d = \int_S w(l)\sigma_r dS \Big/ \int_S w(l) dS$$

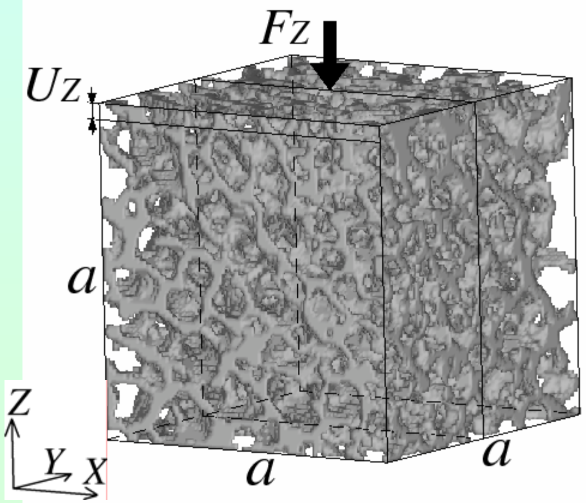
Driving Force

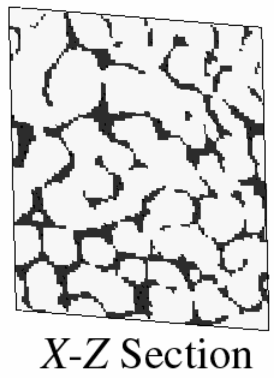
$$\Gamma = ln(\sigma_c / \sigma_d)$$



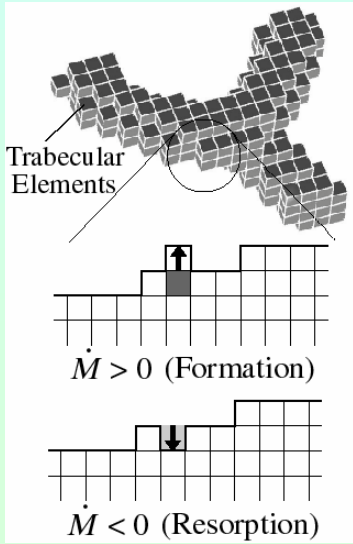


- μCT Image-Based Cancellous Bone Model





- Dimension of Cube a : 5mm, Voxel : 50 µm
- Applied Force: F_Z
- Displacement: U_Z
- Apparent Stress σ_Z: $F_Z/a^2 = 1.24$ MPa
- Apparent Strain ε_Z: U_Z/a



Trabecular-Level

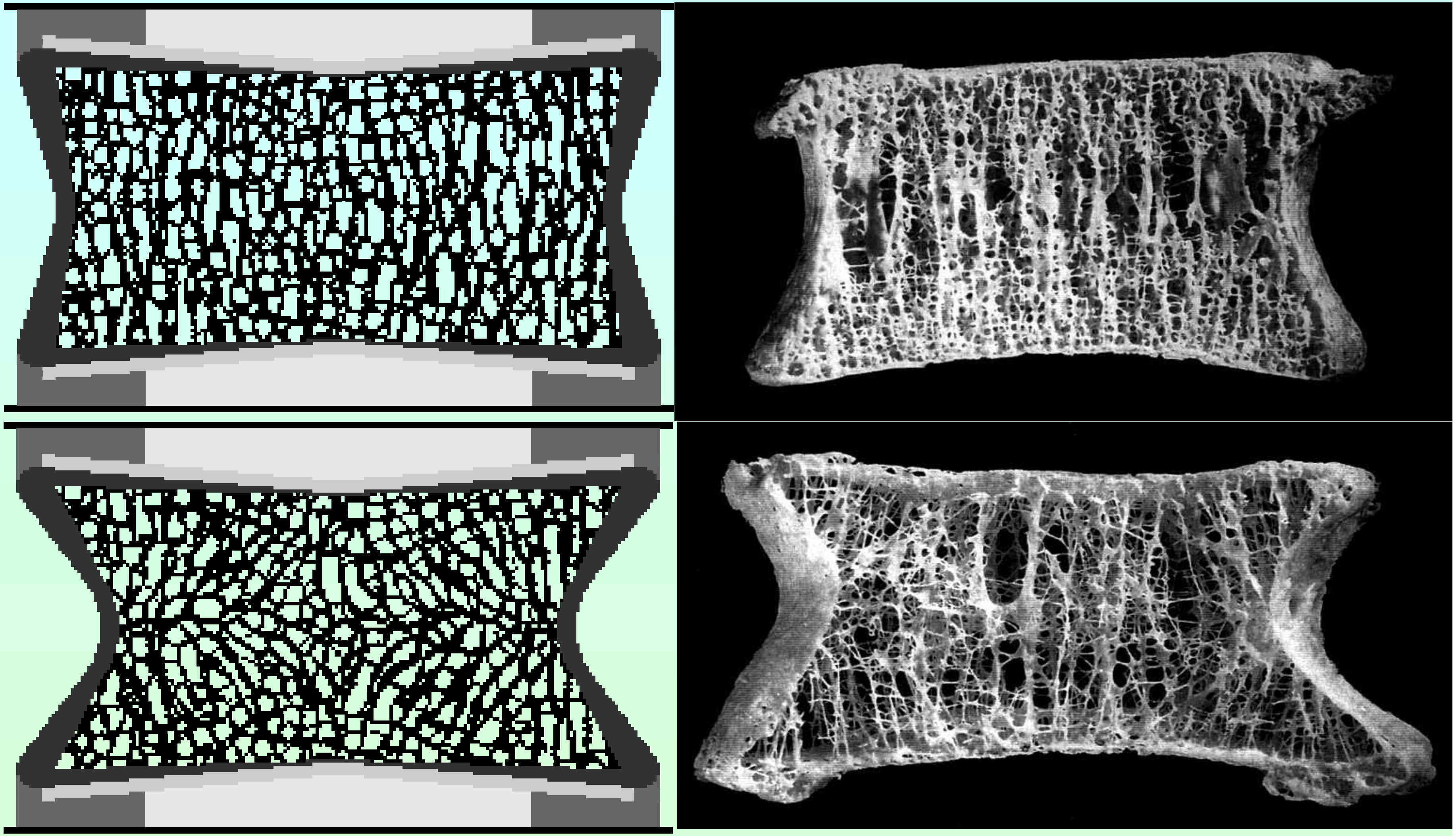
Macroscopic Phenomenon	**Mechanical Stimulus** ↔ **Morphological Change**	Cellular-Level Mechanism

Application:

Computational Biomechanics of Bone Remodeling

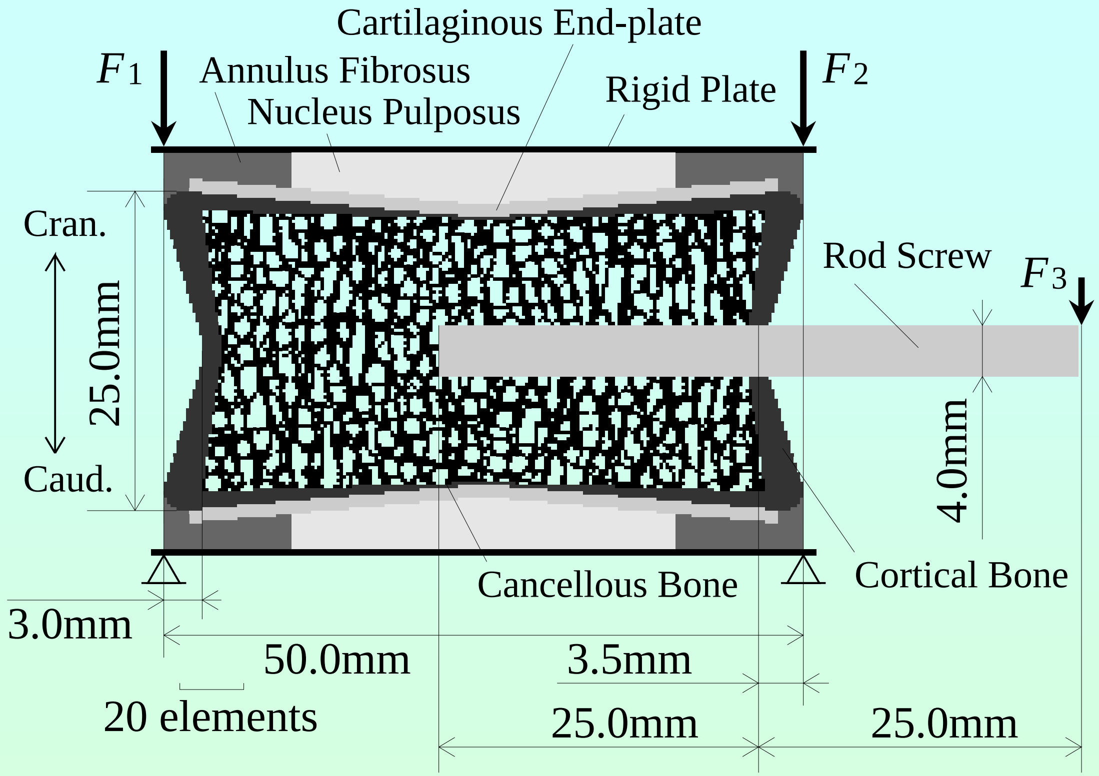
- Evaluation and prediction of bone remodeling around artificial joint, implant, artificial joint, ...
- Design of implant, screw, joint considering remodeling
- Design of scaffold structure in tissue engineering
- Scaffold & new bone ingrowth
  - mechanical function and biochemical degradation

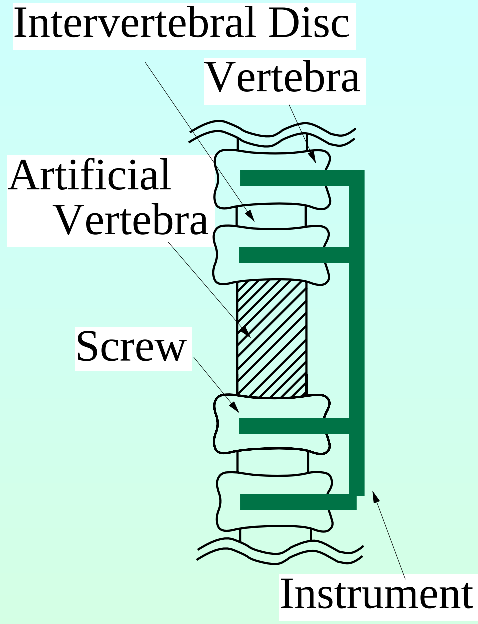
Comparison



(Mosekilde 1990)

Vertebral Body with a Rod Screw





(Ikebuchi K. *et al.* 1995)

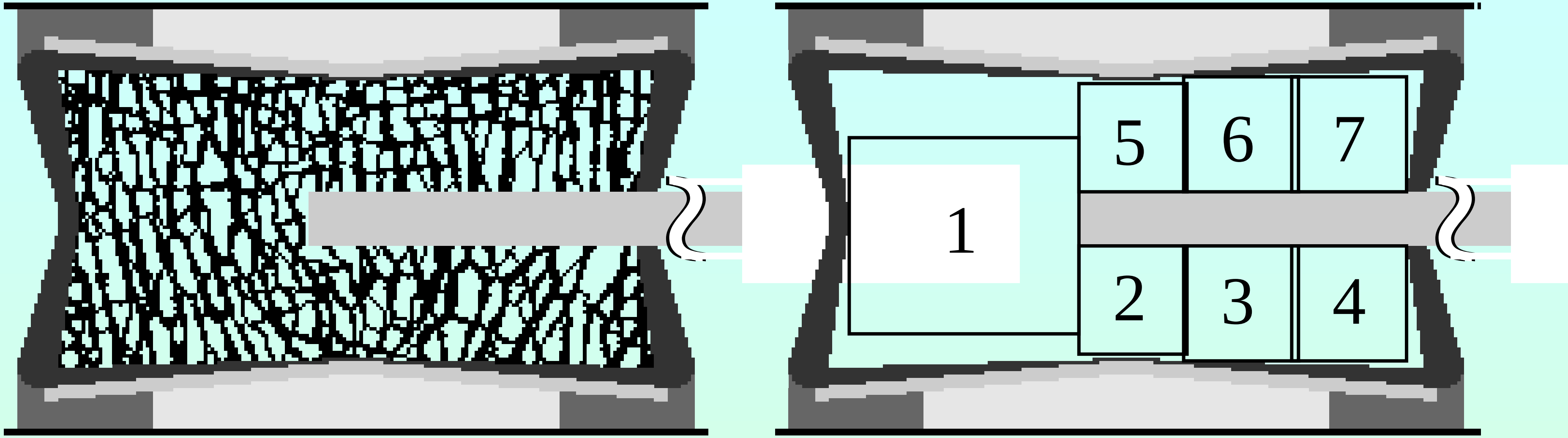
Applied Load to Rod Screw

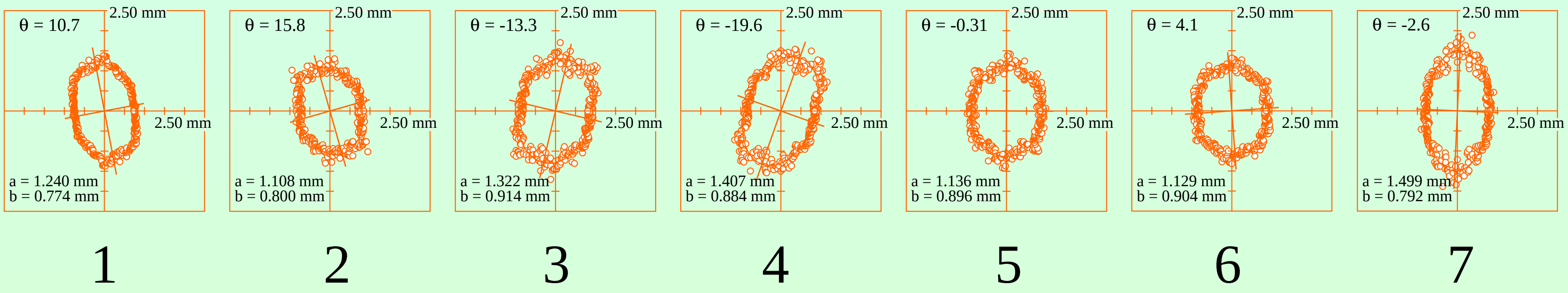
$$F_3 = 58.8\text{N}$$
$$= (F_1 + F_2)/10$$

290×128 elements

$$l_L = 1\text{mm}$$
$$\Gamma_l = -5,\ \Gamma_u = 4.0$$

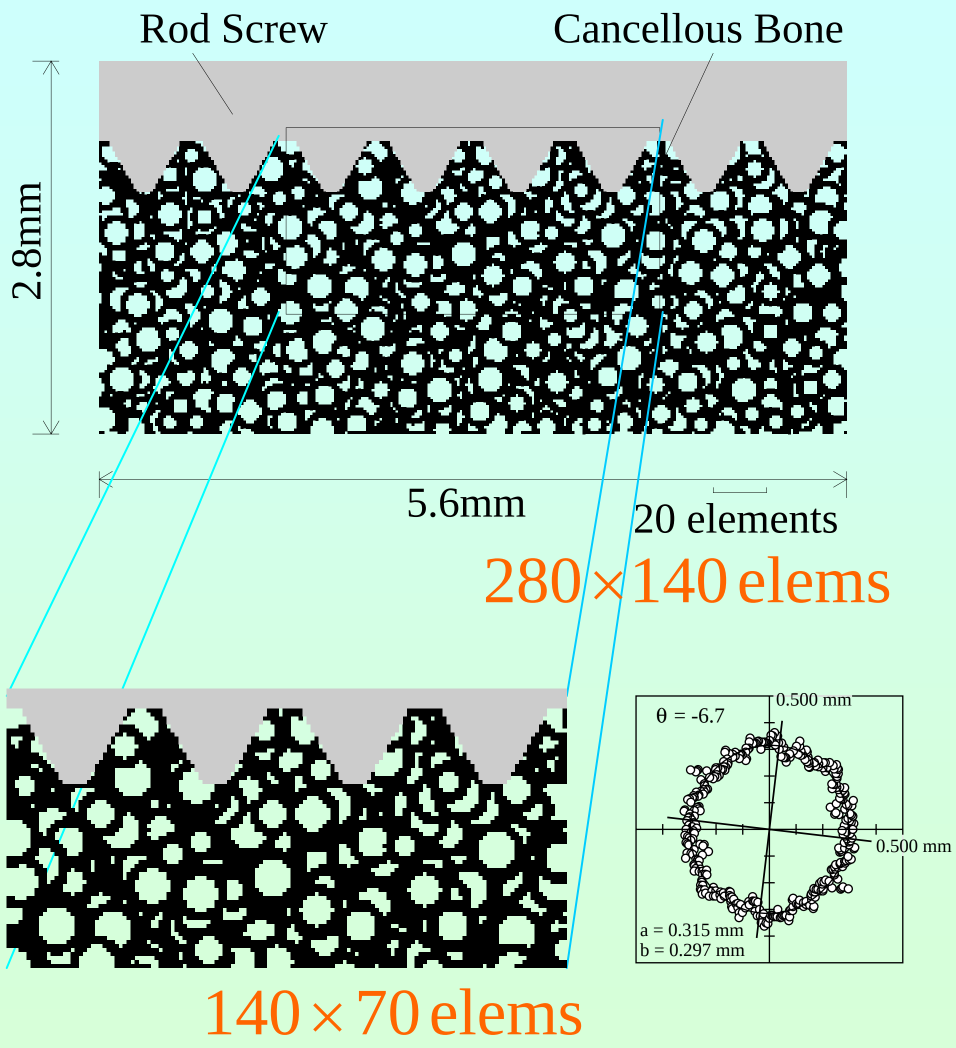
Remodeling: With a Rod Screw

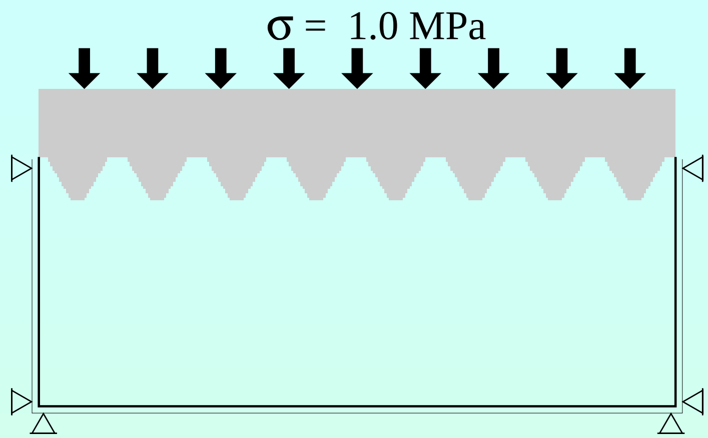




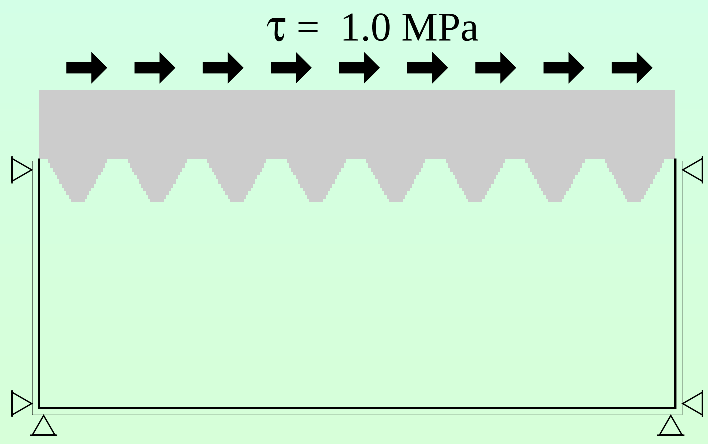
→ **Remodeling Rod Screw Interface**

Model around Rod Screw Interface





Compression: Case Sc



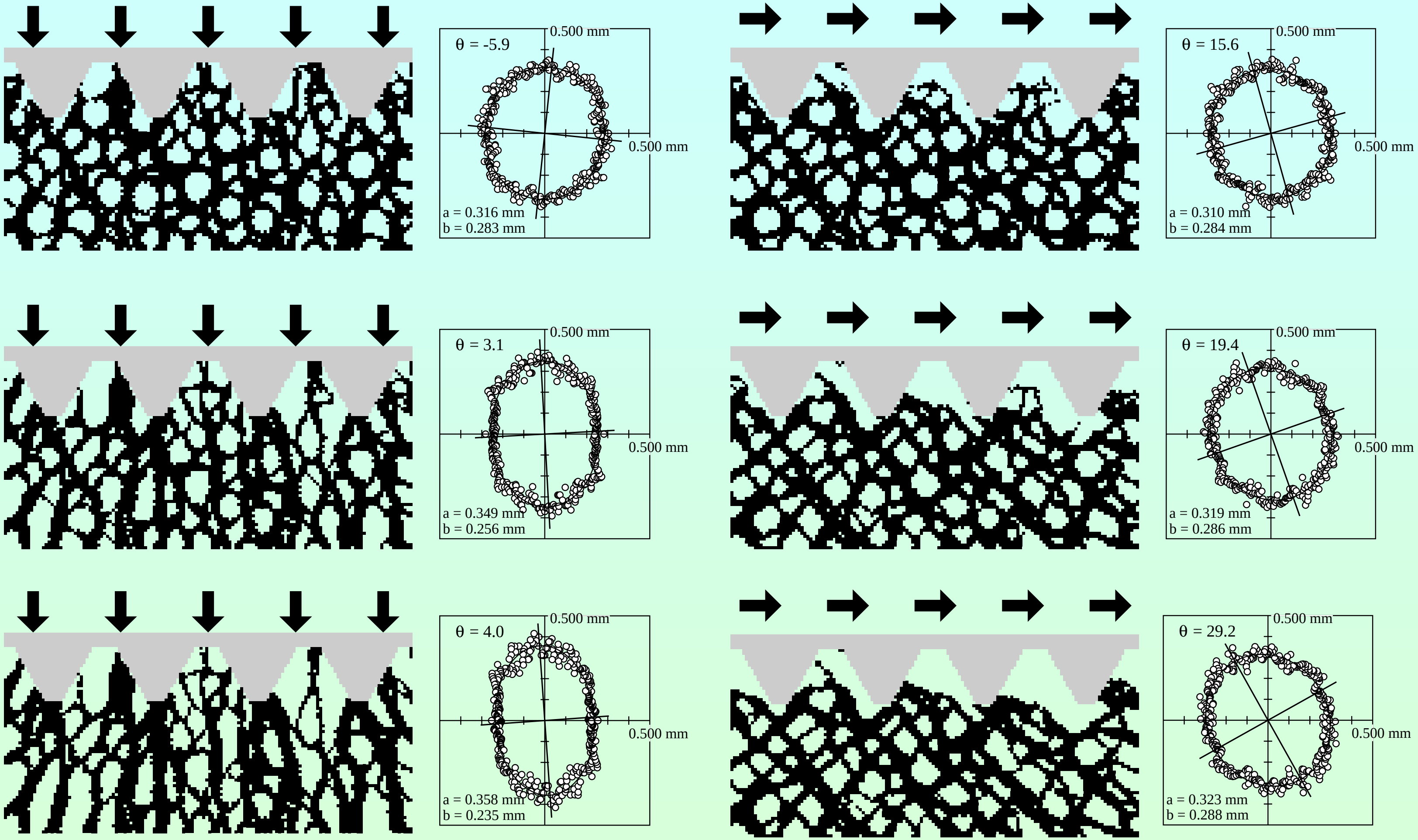
Shear: Case Ss

Remodeling around Rod Screw Interface

4th step

12th step

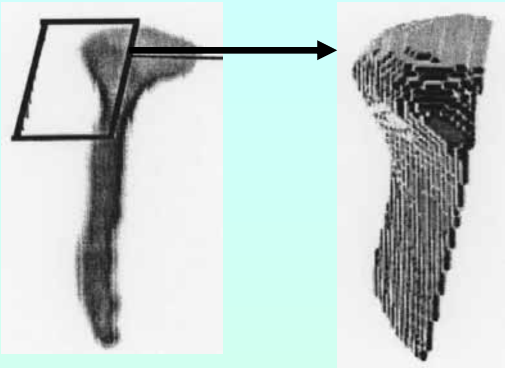
20th step



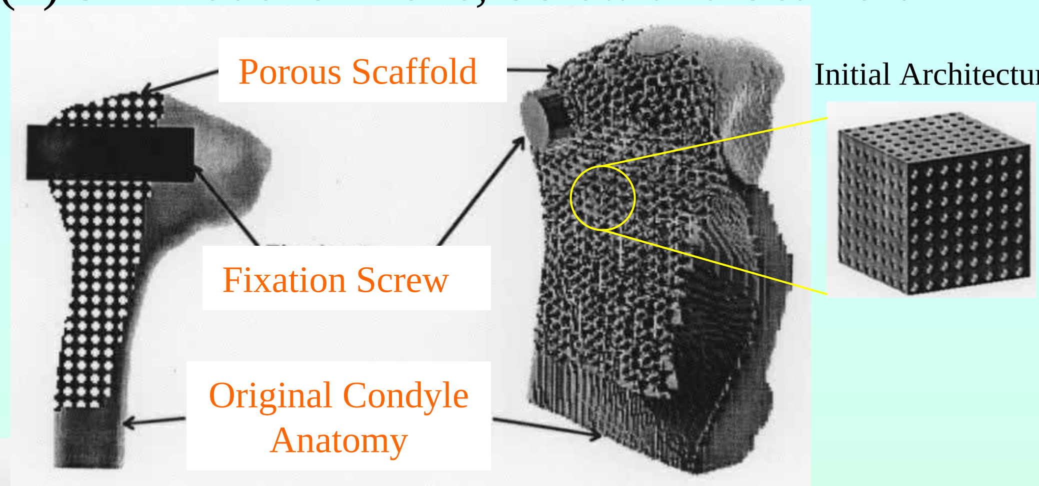
Compression: Case Sc **Shear: Case Ss**

Application: Bone tissue engineering

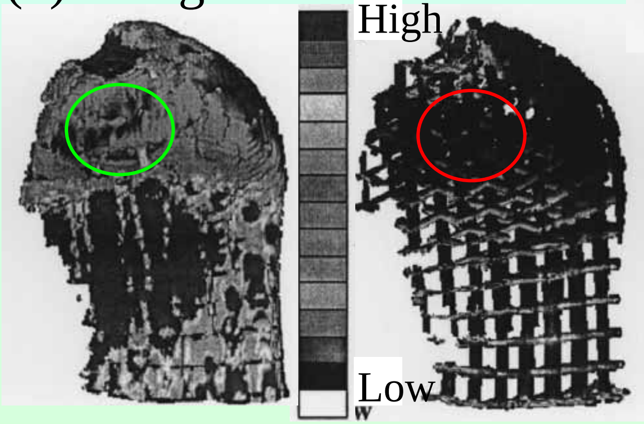
(1) Digital Image



(2) 3D Model of Bone, Screw and Scaffold



(3) Design of Scaffold



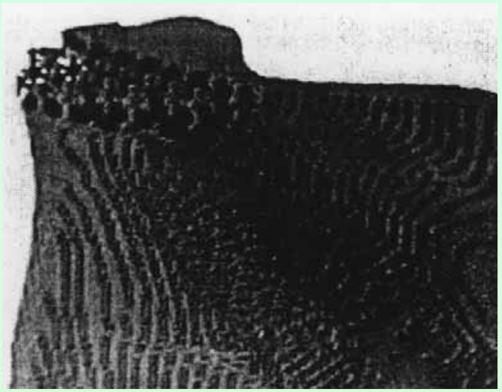
Von Mises Stress in Scaffold

Strain Energy Density in Tissue

Topology Optimization

- Structural analysis of Scaffold
- Mechanical Bone Remodeling

(4) SFF Manufacture Directly or by Casting

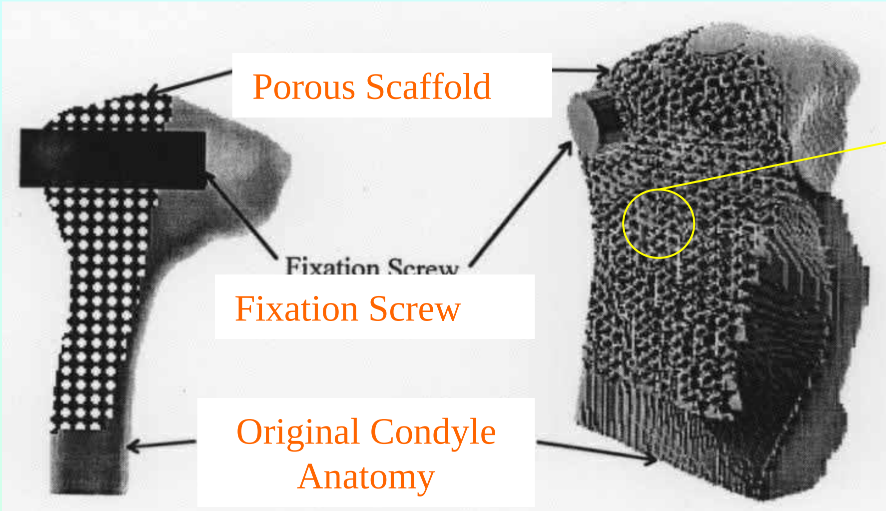


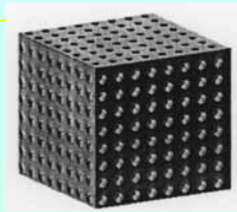
Manufactured Condyle with Scaffold

Rendering of CT Image

(Hollister *et al*., 1998)

Application: Design structure of scaffold





(Hollister *et al*., 1998)

- as a load bearing construct
- compatible with cell ingrowth and migration
- as a transducer of mechanical signal to cells
- to consider transition between
  - degradation of scaffold
  - new bone formation and remodeling

Conclusions

Computational biomechanics in bone remodeling

- Macro- and Micro- Hierarchy
  - in Bone mechanics and remodeling
- Basic science --> Application