代替物の劣化吸収と新生骨の形成を考慮した骨組織再生シミュレーション

安達 泰治，河野 雄二，冨田 佳宏

神戸大学 工学部 機械工学科

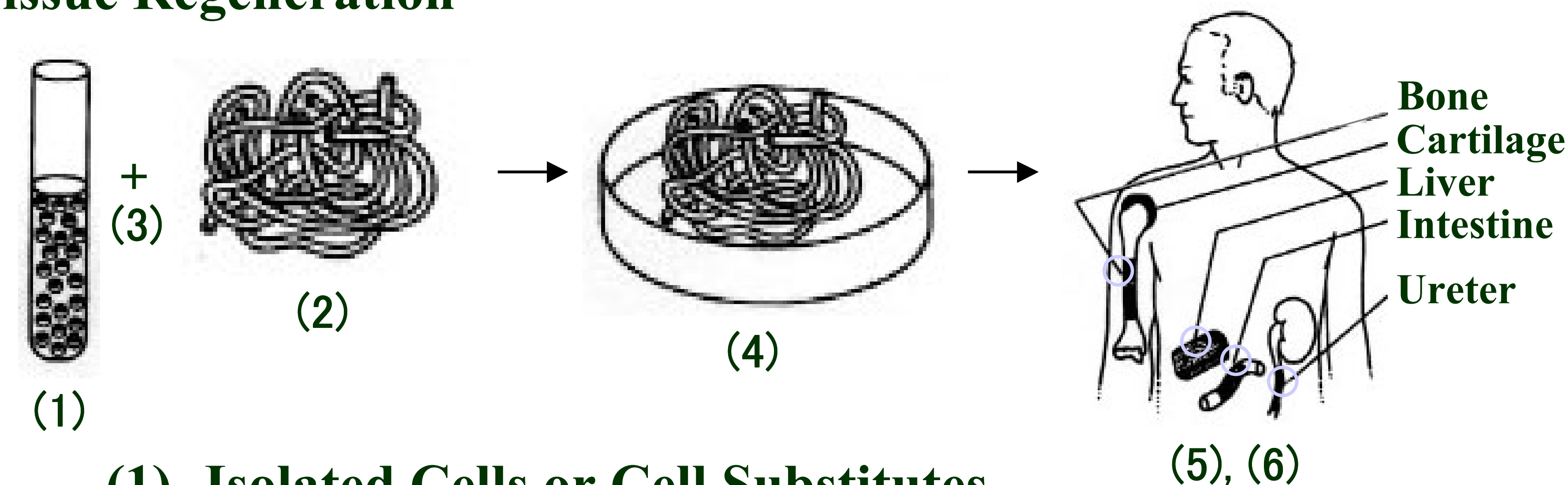
adachi@mech.kobe-u.ac.jp

理研シンポジウム
“生体力学シミュレーション研究”

2001年6月4日(月), 5日(火)
理化学研究所･鈴木梅太郎記念ホール

Introduction: Tissue Engineering (Langer & Vacanti, 1993)

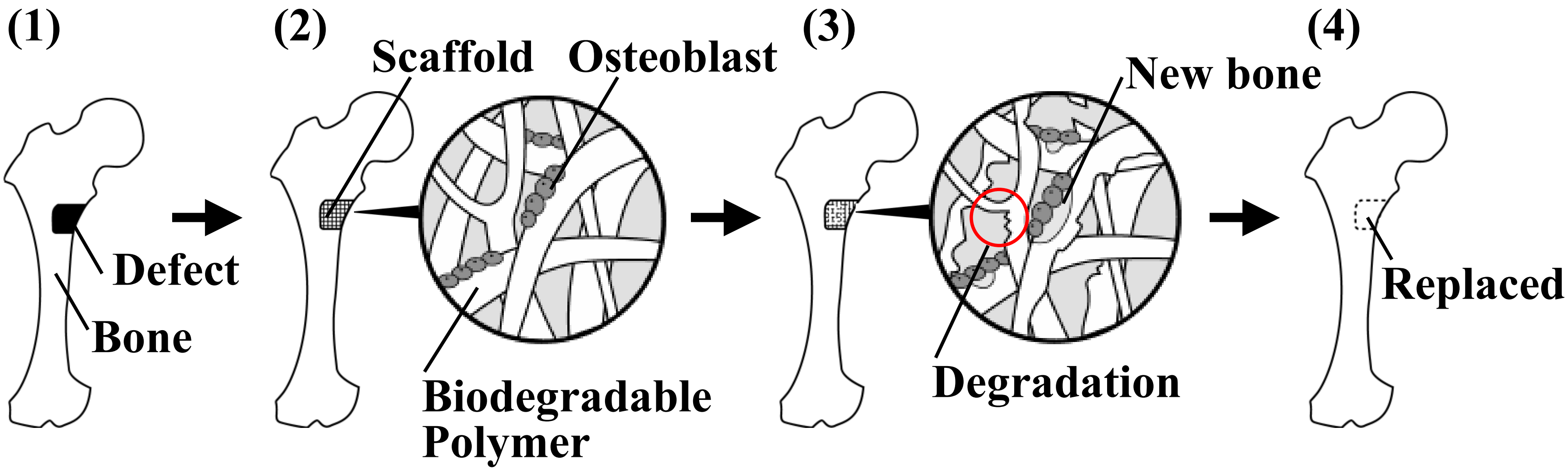
Tissue Regeneration



(1) Isolated Cells or Cell Substitutes
(2) Biodegradable Polymer Scaffold
(3) Cells Placed on or within Matrices (Scaffold)
(4) *In Vitro* Tissue Culture
(5) *In Vivo* Implantation
(6) Degradation of Scaffold, Formation of New Tissue

→ Regeneration: Morphology & Function

Bone Regeneration using Scaffold

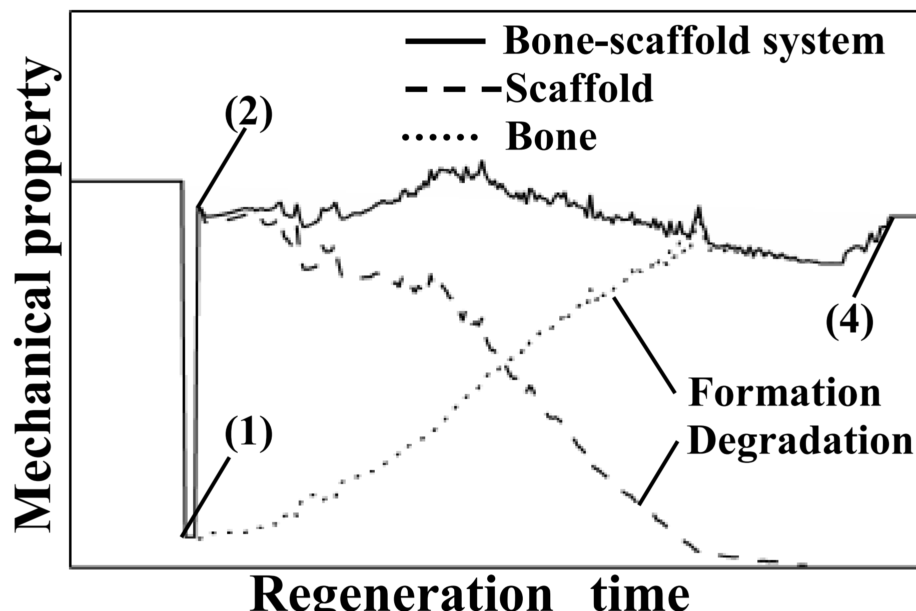


(1) Defect in Bone

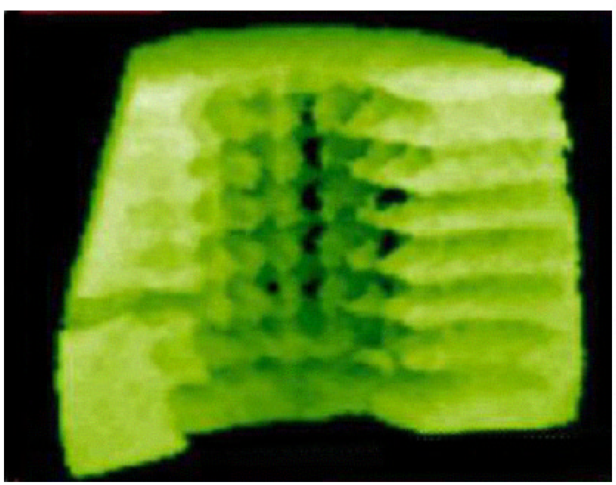
(2) Scaffold Replacement

(3) Scaffold Degradation &
New Bone Formation

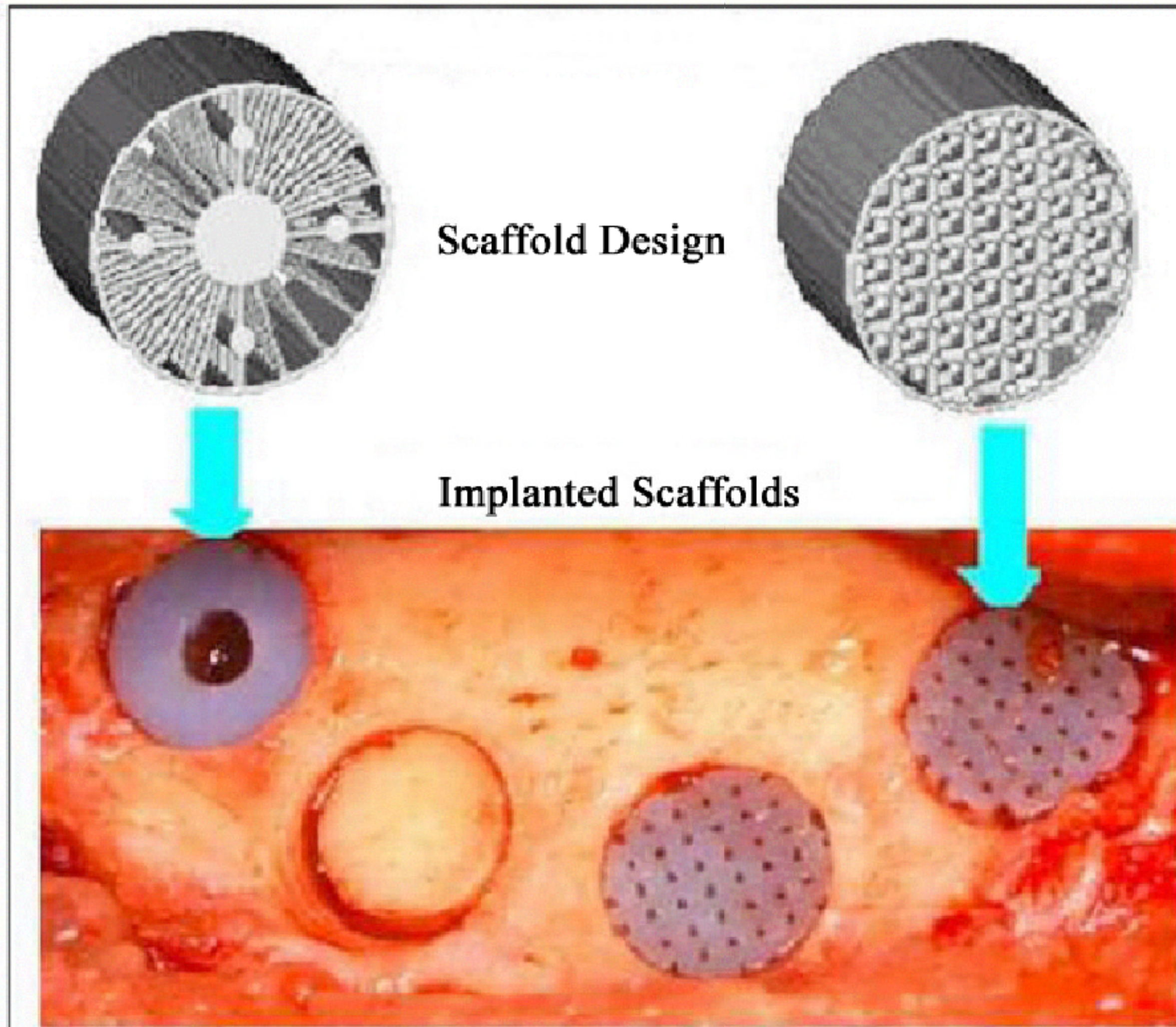
(4) Regenerated



In Vivo Mandible Defect Model



μCT Image of Scaffold

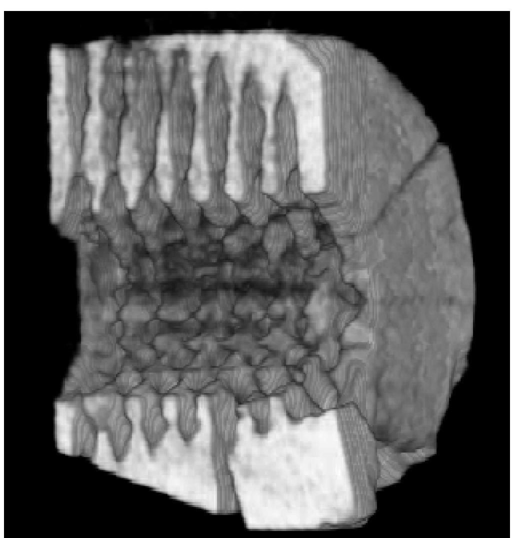


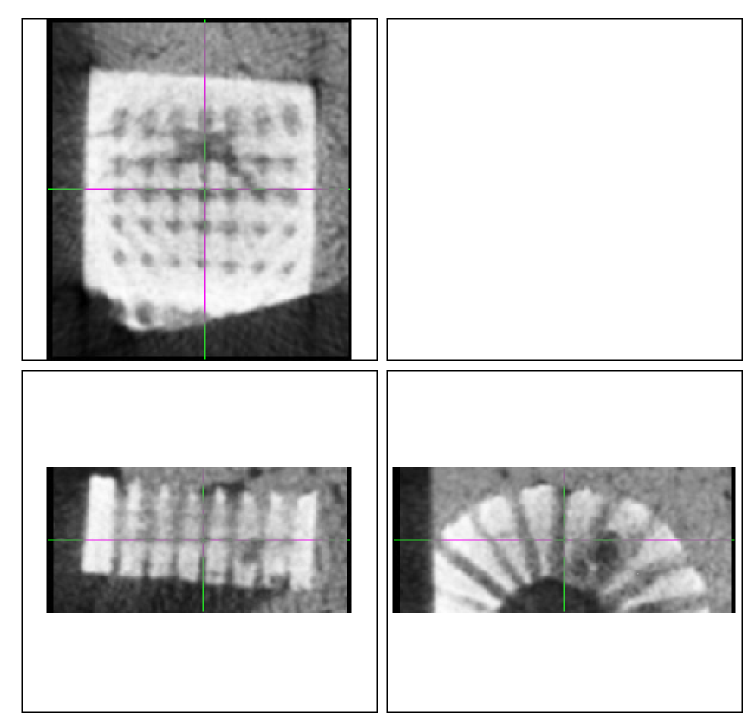
Courtesy of Scott J. Hollister at UM

Structural Design of Scaffold

Functions from Mechanical/Biological Viewpoints:

- compatible with cell ingrowth and migration
- for transportation and diffusion of bioactive factors
- as a transducer of mechanical signal to cells





Present study focuses on:

- **as a mechanical load bearing construct**
- **to consider transition between**

  degradation of scaffold / new bone formation

Purpose

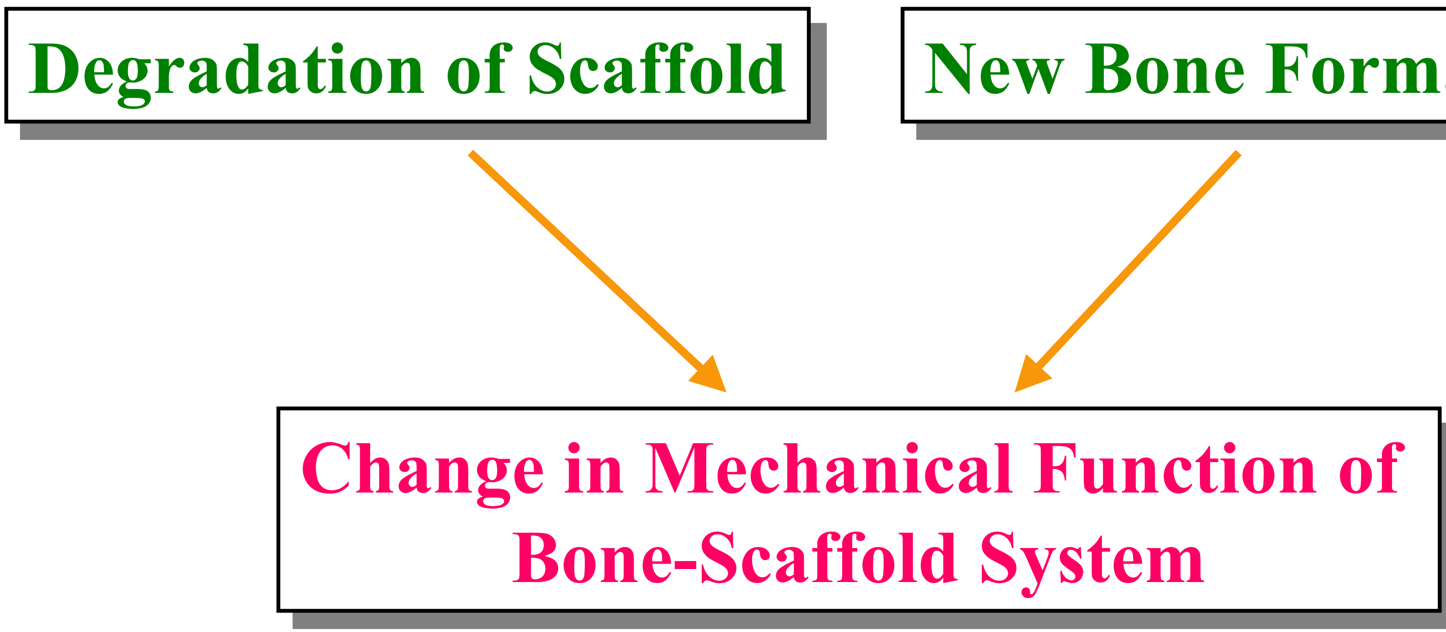
Bone-Scaffold Structure
in Regeneration Process
and Final Replaced Bone

↓

"Design of Scaffold Structure"

1. **Simulation of Bone Regeneration**
2. **Change in Mechanical Integrity of Bone-Scaffold System**
3. **Determine Optimum Scaffold Structure**

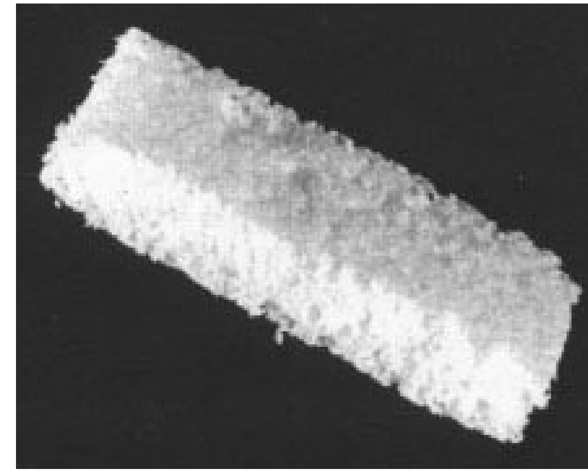
Simulation Model of Bone-Scaffold System



Biodegradable Scaffold for Bone

- **Material**: Poly Lactic Acid (PLA)
  Poly Glycolic Acid (PGA)

- **Properties**: Biodegradable Material
  Biocompatible Material
  Porous Microstructure



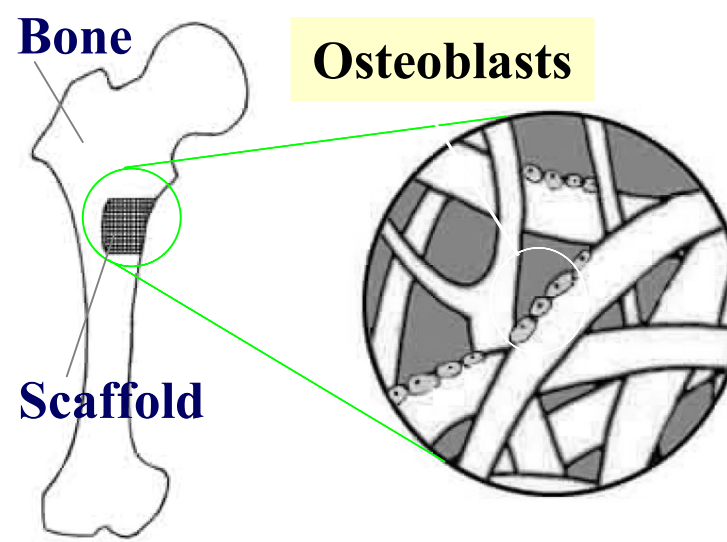
Size: 12 × 30 × 6.5 mm
Apparent Density: 0.085
Mass: 200mg (Brekke, 1996)

Bone Scaffold

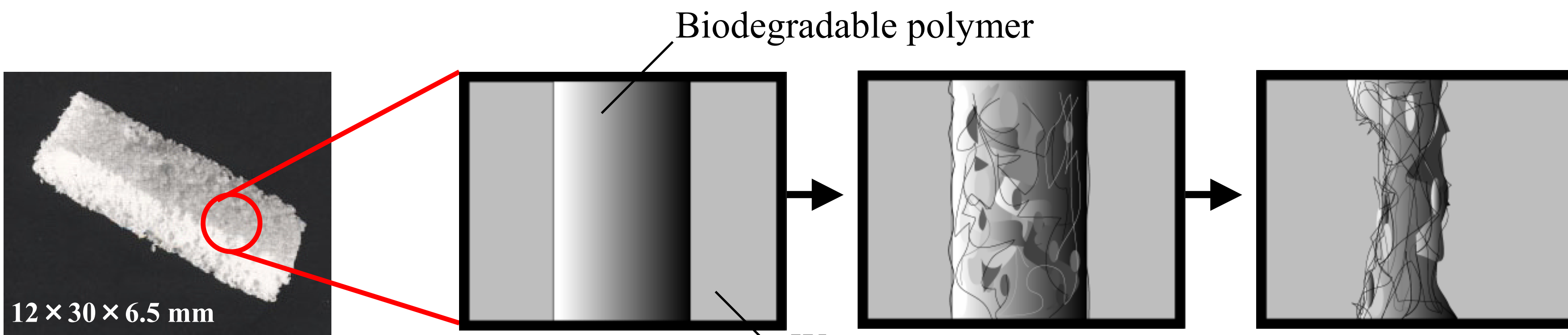
⇩

Mechanical Factors

**e.g. Load Bearing Structure,
Mechanical Stimuli for Osteoblasts**

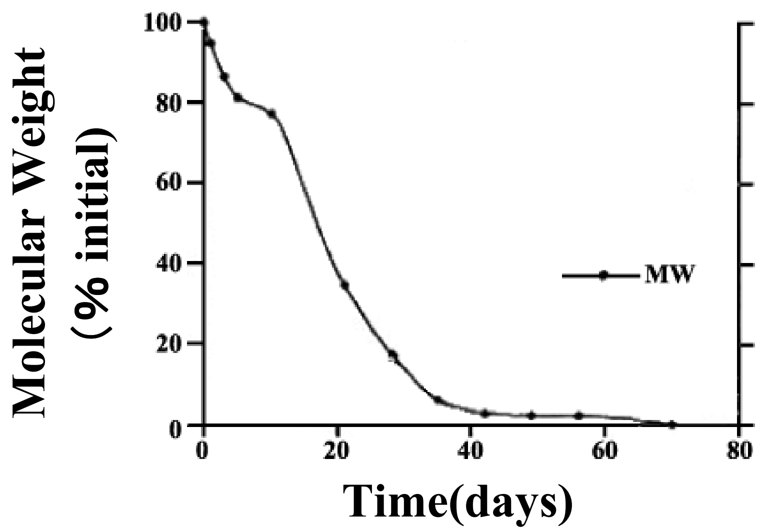


Biodegradable Polymers

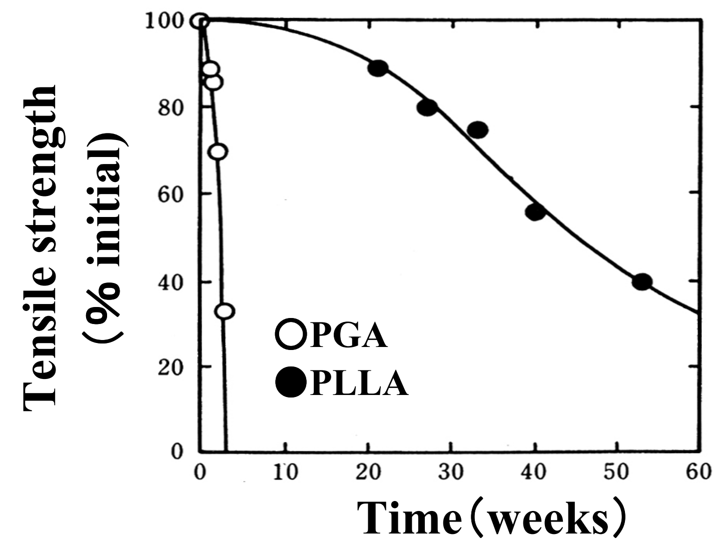


(Brekke, 1998)

Degradation of Biodegradable Polymers

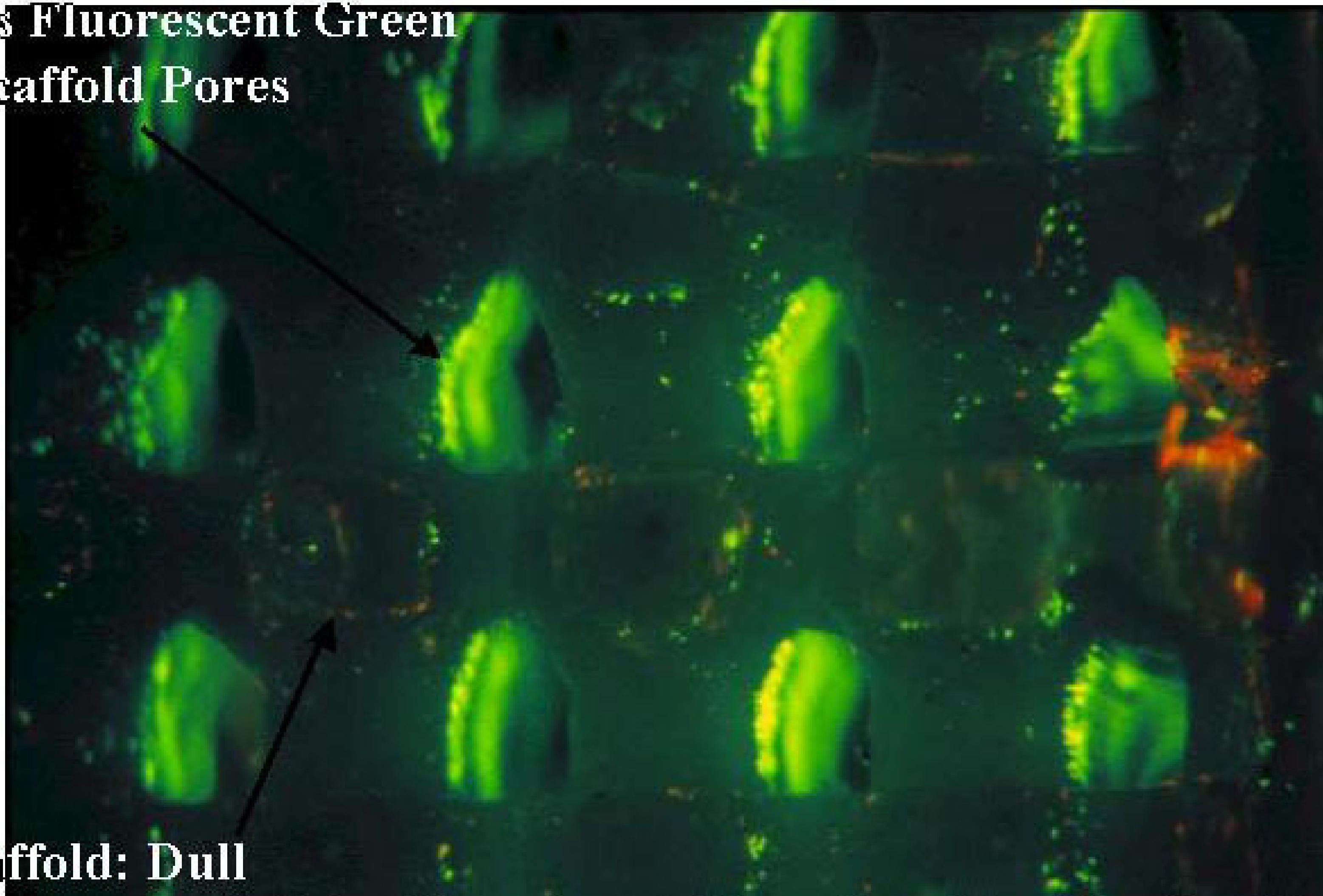


Change in Molecular Weight in Time
(Mooney et al., 1995)



Change in Strength in Time
(Mochizuki, 1995)

Cell/Scaffold Integration



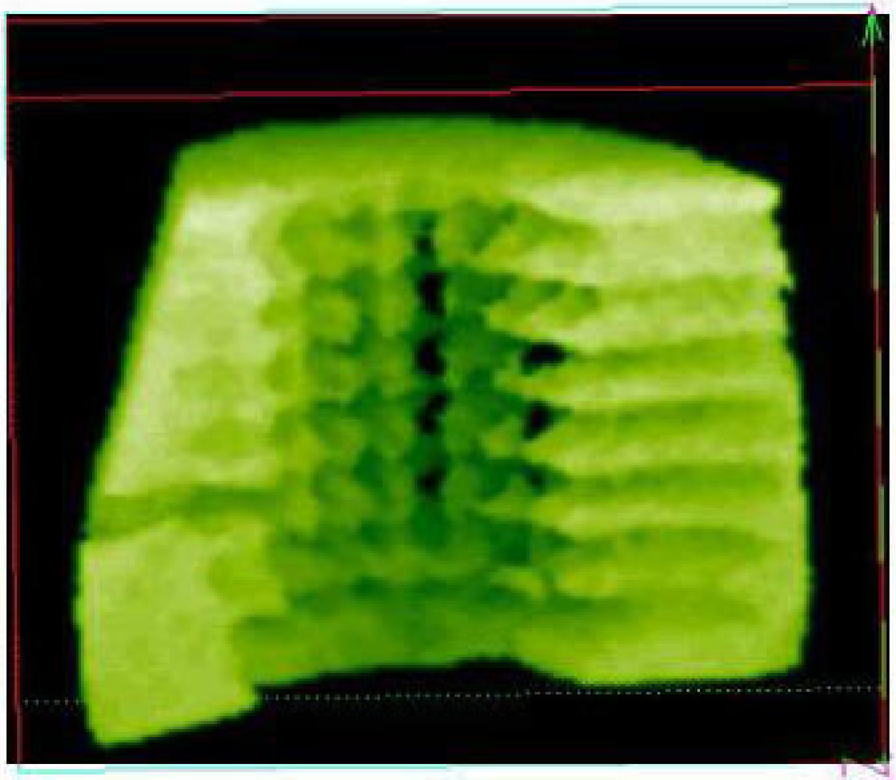
Cell Seeding: <u>Juan Taboas/Jennifer Zieg/David Orton</u>

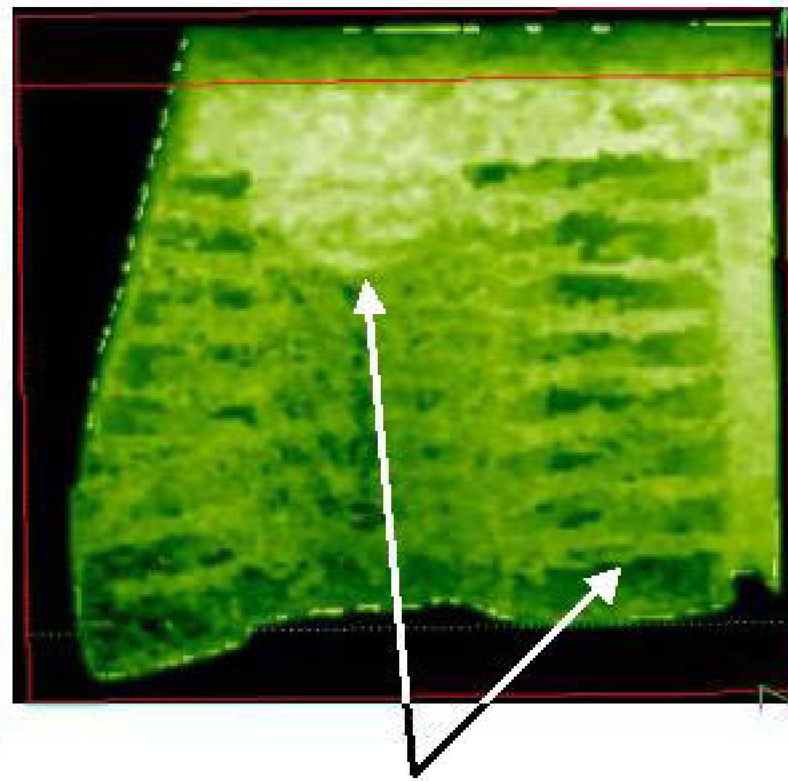
<u>Paul Krebsbach</u>

/ Scott J. Hollister at UM

3D Tissue Ingrowth Architecture

Courtesy Ralph Mueller





Bone Follows pore structure

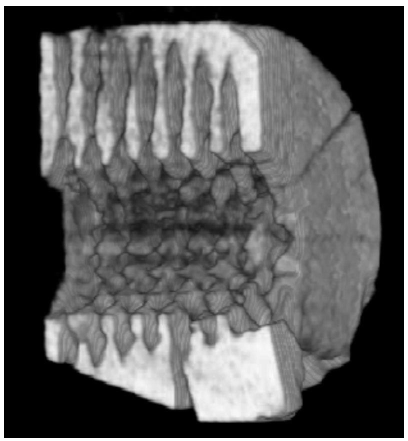
3D Scaffold Structure

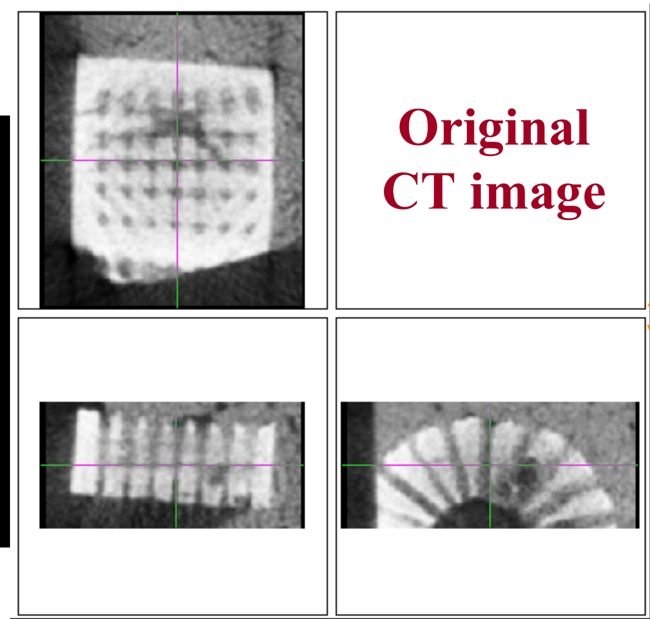
3D Bone Structure

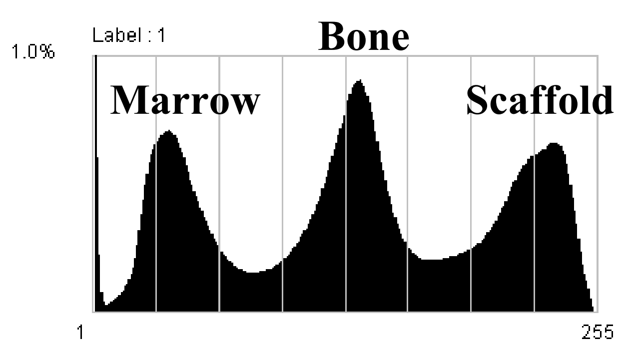
9 weeks in minipig mandible – shows tissue will follow design

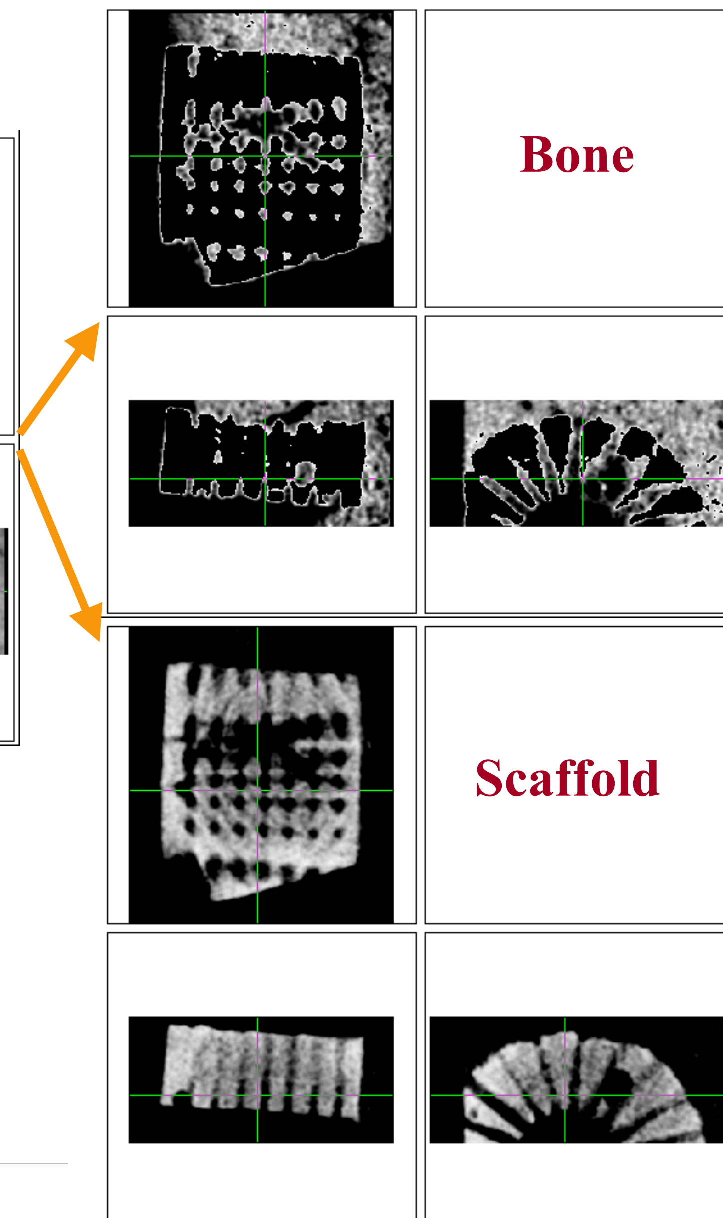
/ Scott J. Hollister at UM

New Bone Ingrowth and Formation



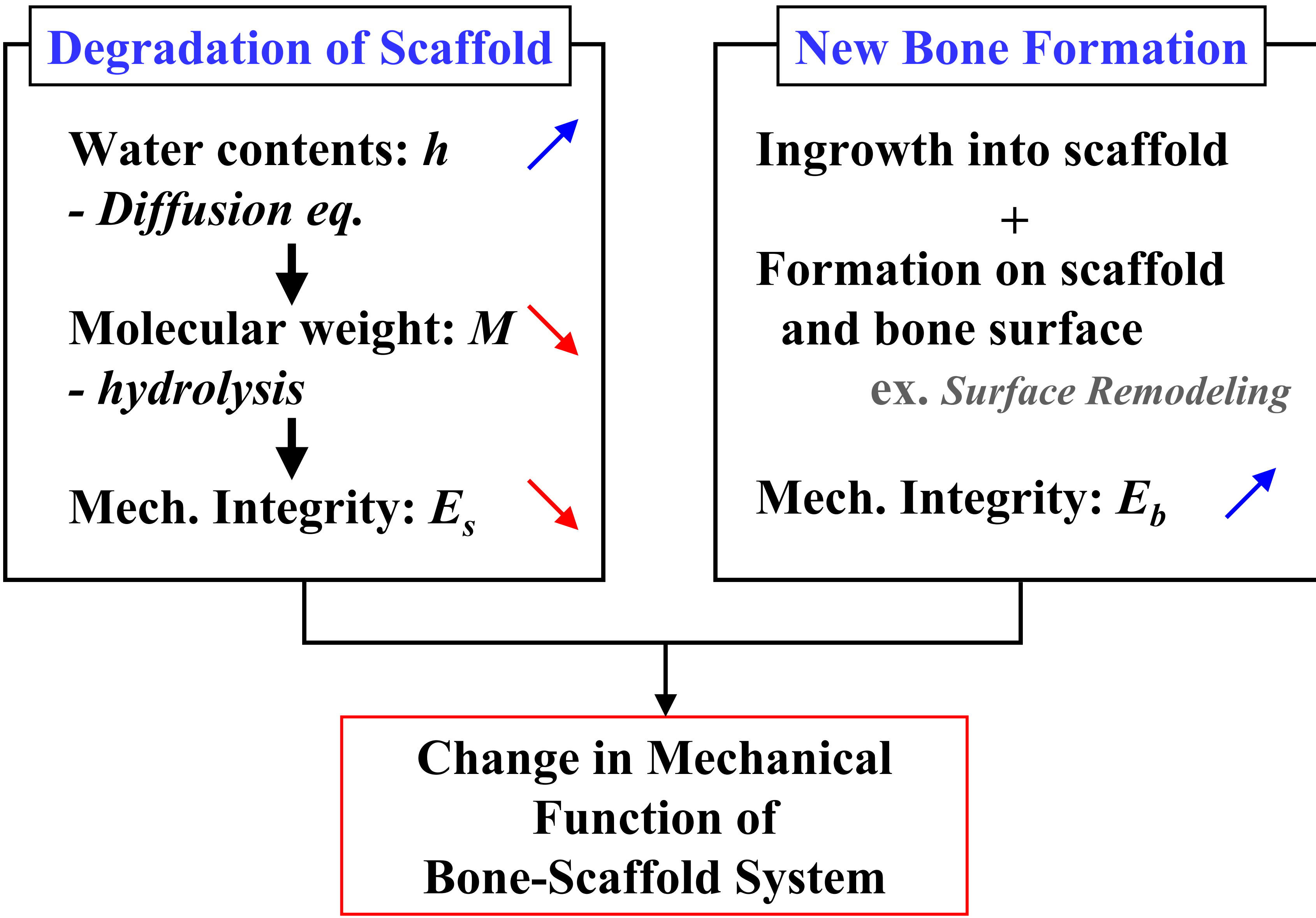






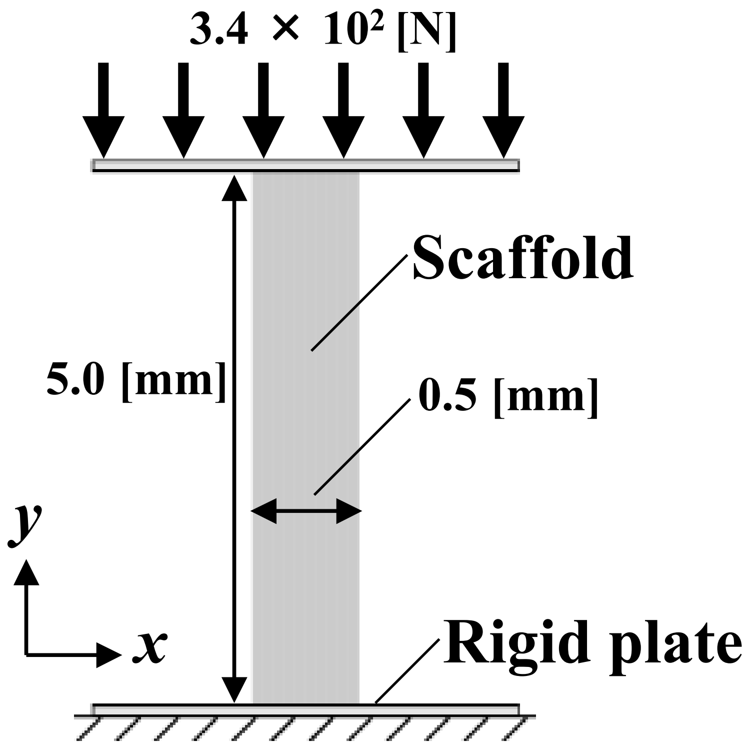
Original Data: Courtesy Scott J. Hollister

Simulation Model of Bone-Scaffold System



Simple Simulation Model

Compressed by constant load

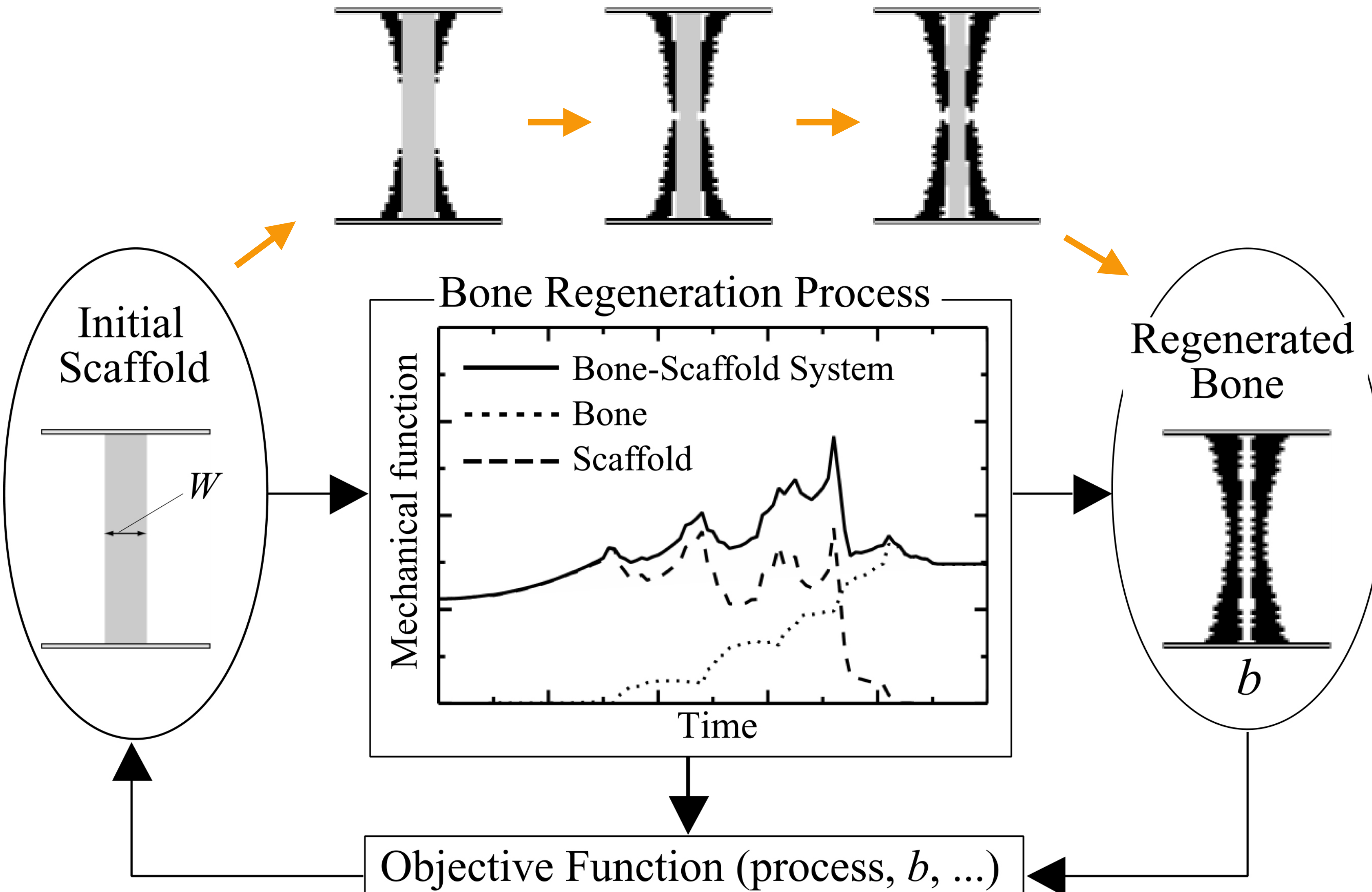


50 × 50 pixels

$E_S = 20$ GPa, $\nu_S = 0.3$

$E_B = 20$ GPa, $\nu_B = 0.3$

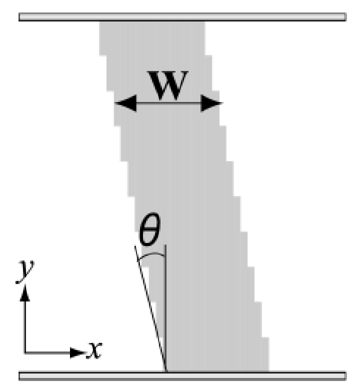
Simulation of Bone Regeneration Process



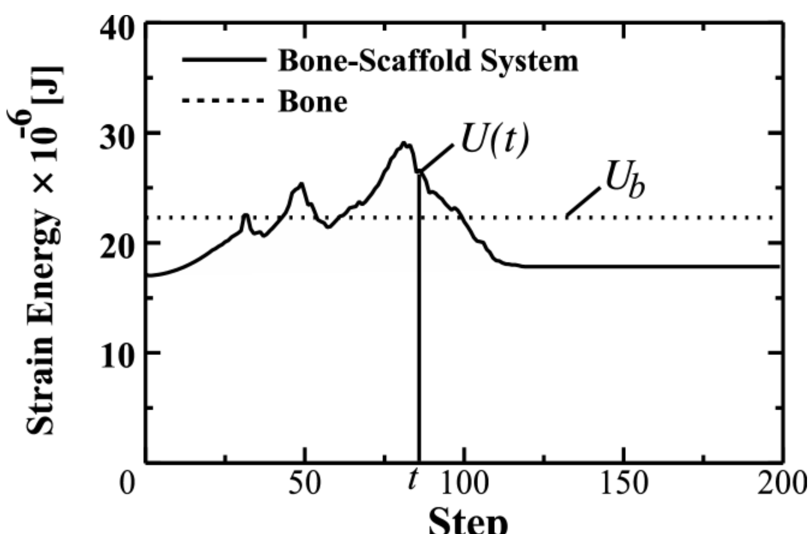
Design Valuables and Objective Function

- Initial Scaffold Shape

W : width
θ : angle



- Objective Function



$$\Phi_p = \int_0^T \frac{|U(t) - U_b|}{T} dt$$

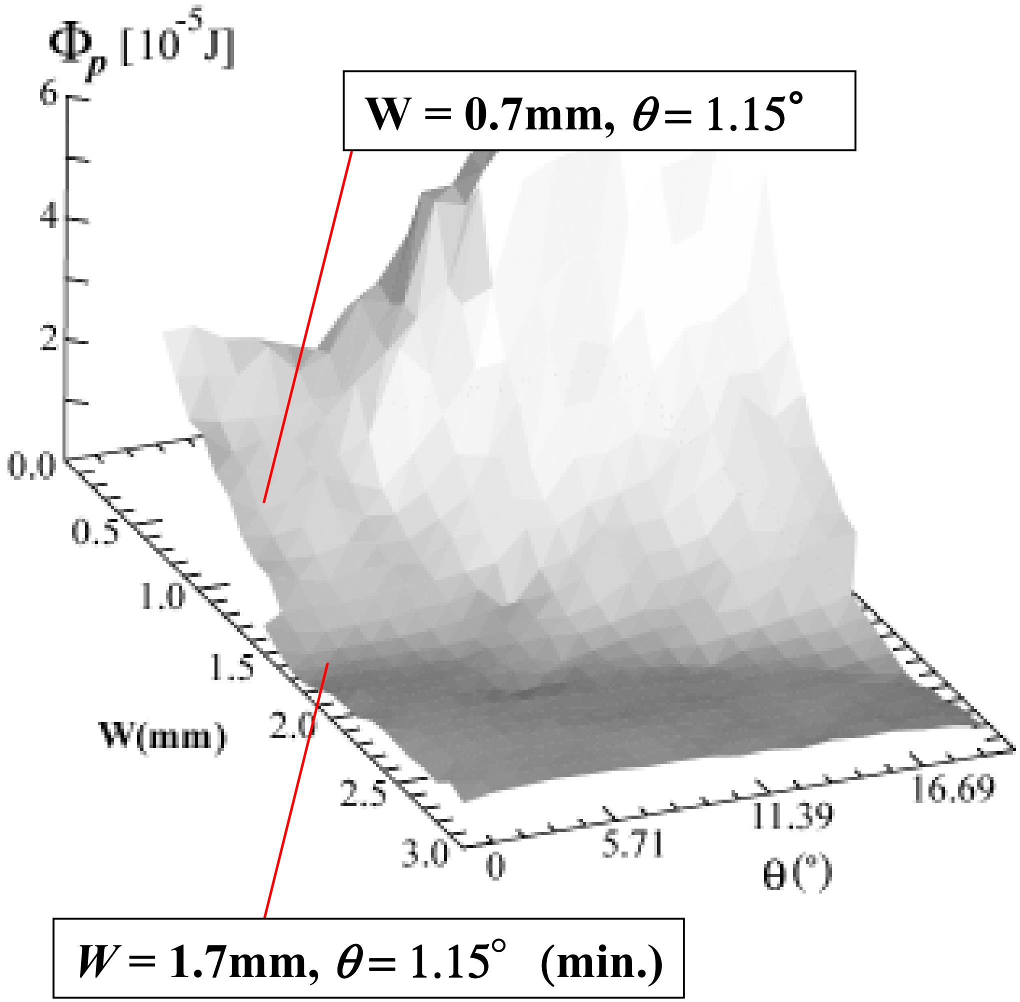
Strain Energy: *U*

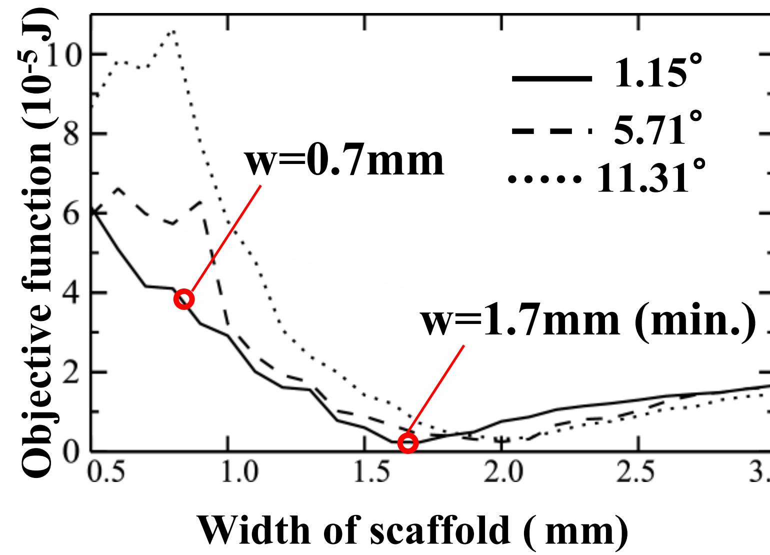
$U(t)$: Bone-Scaffold System

U_b : Ideal Bone

Time at Equilibrium: *T*

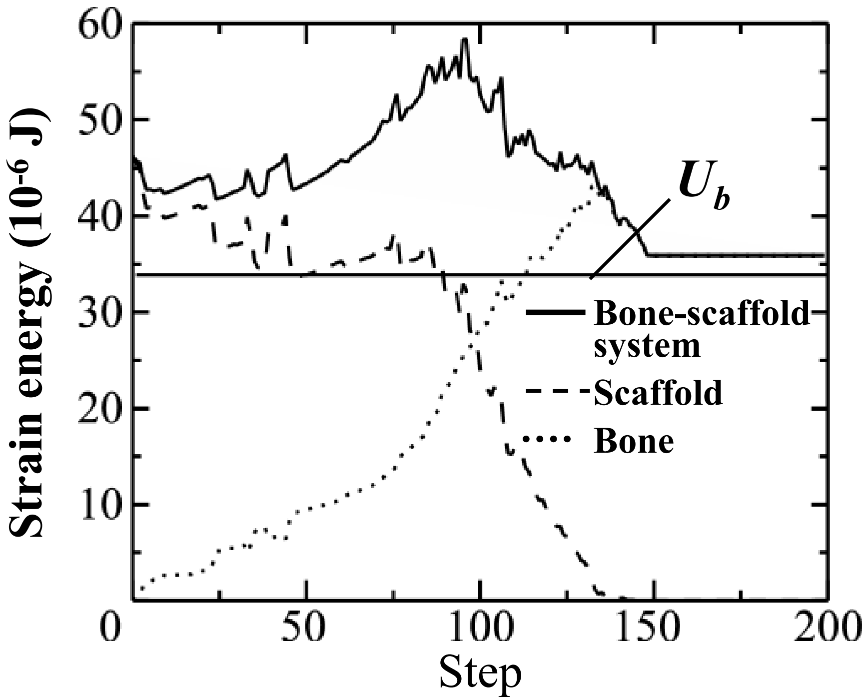
Objective Functions Depending of Initial Shape



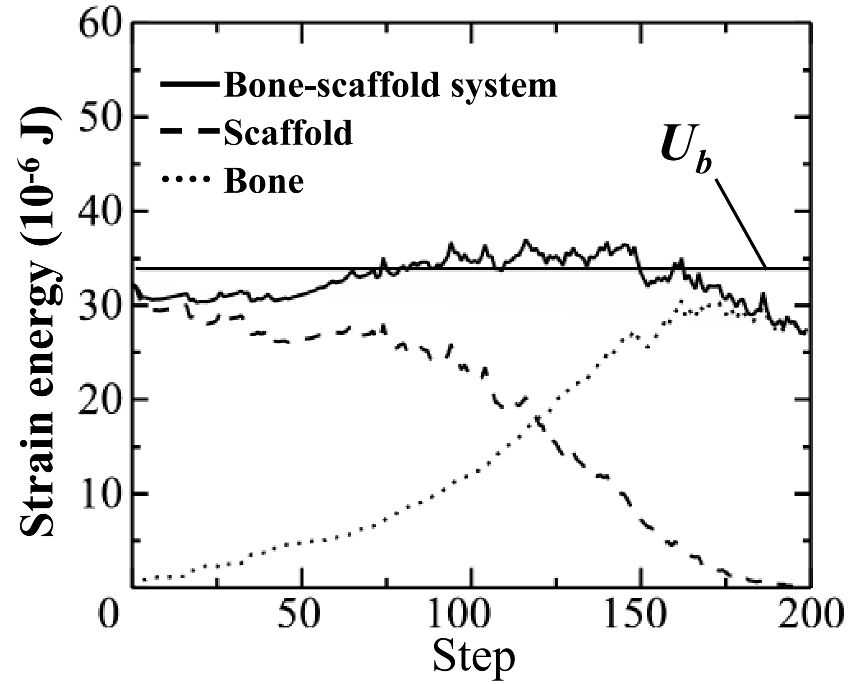


Φp with constant angle

Change in Structural Properties

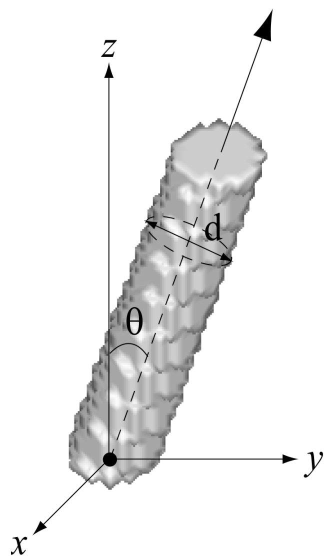


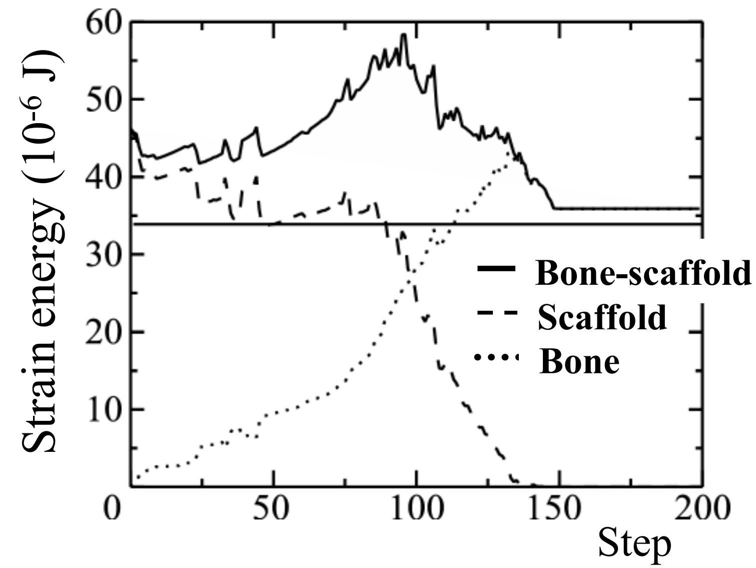
w = 0.7mm, θ = 1.15deg.

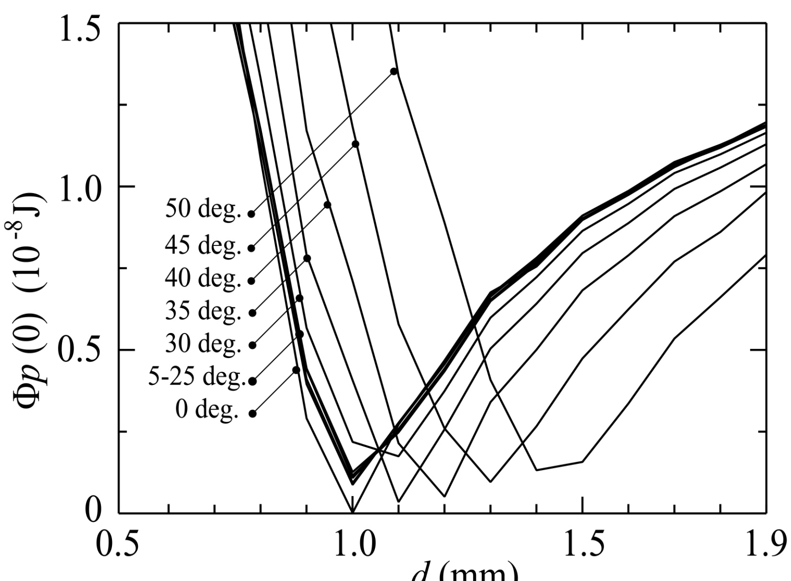


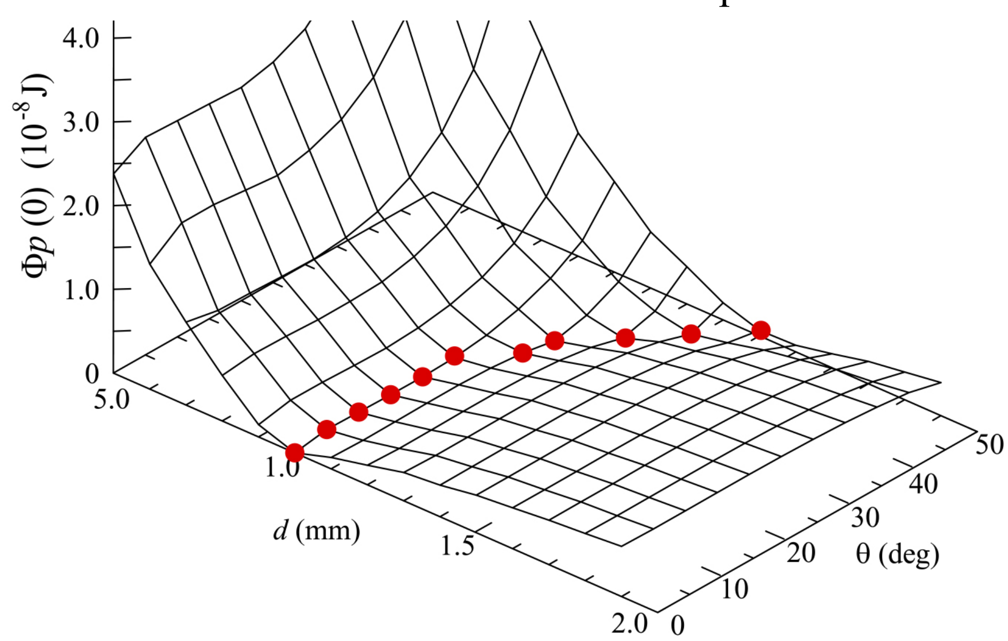
w = 1.7mm, θ = 1.15deg
(minimum)

Minimum Objective Function at Initial

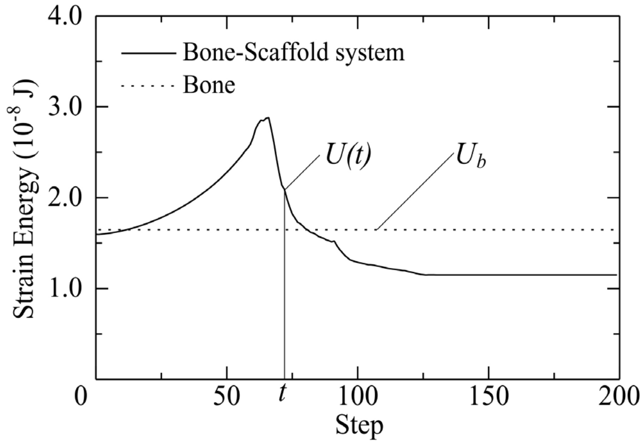


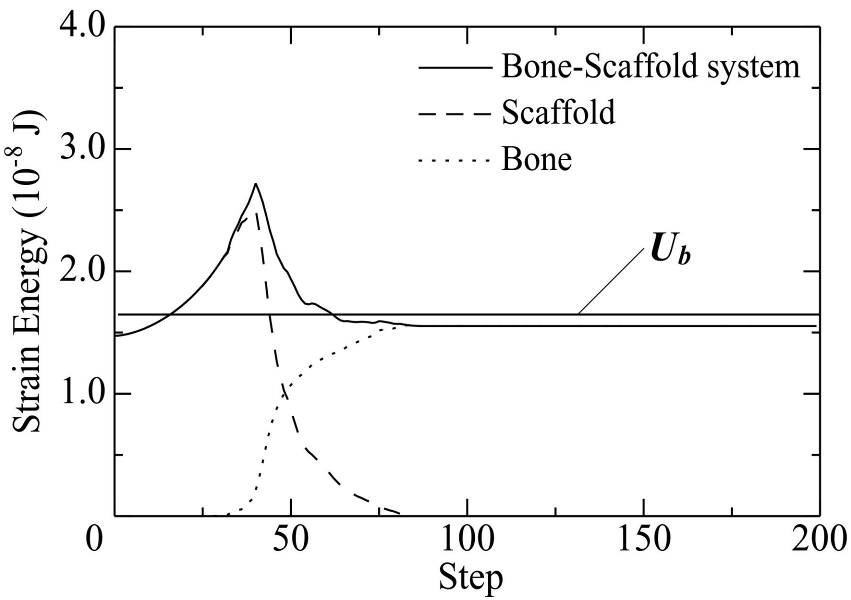




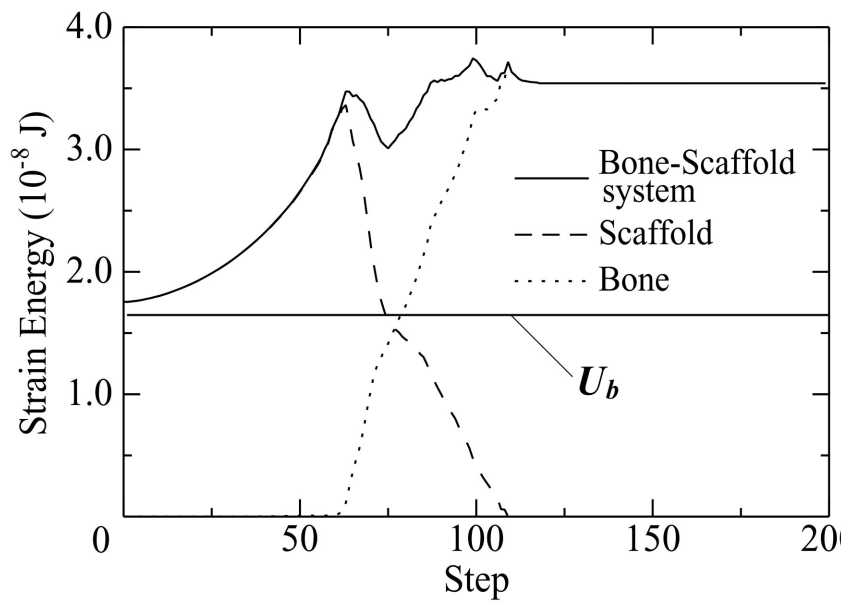


3D Simulation of Bone Regeneration





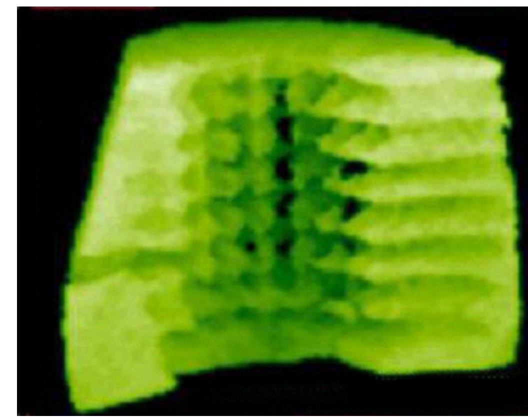
α = 2000, θ = 30[degree]
d = 1.1 mm



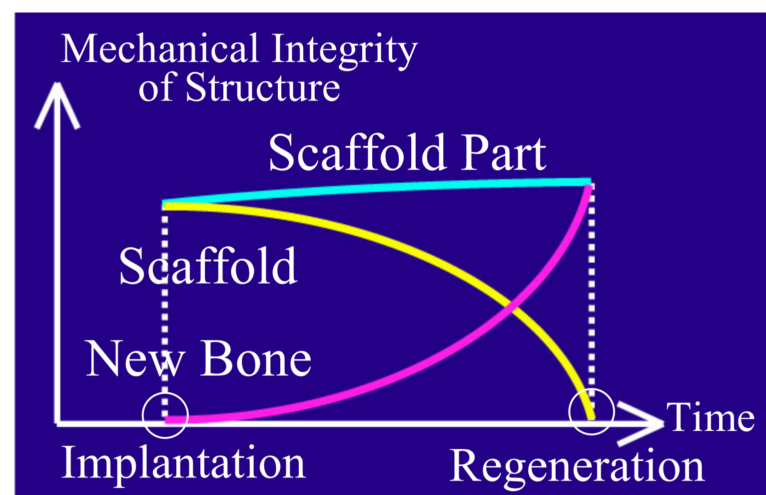
α = 1500, θ = 10[degree]
d = 1.0 mm

Summary

- **Design of Scaffold Degradation**
  - Shape (ex. W, d, θ): Microstructure / Macro shape / size
    w/ constraint depending on objective function
  - Material: E = Stiffness
    α = Degradation rate



- **Bone Formation (bio+mech)**
  - Ingrowth rate (bulk effect)
  - Formation rate
  - Remodeling rate



Future Direction

1. **Extension to a complex structure with large-scale**

2. **Rate equations of bone ingrowth and formation**

3. **Fabrication … and … comparison with experiment.**