*French-American Workshop, June 15-16th, 2015, Grenoble*

# Enhancing bone regeneration through capillary forces

A. J. Wagoner Johnson, PhD
Associate Professor
Department of Mechanical Science and Engineering
University of Illinois at Urbana-Champaign

# (this) French-American collaboration made possible by:

tissue engineering and bone

Scaffold and material system

in vivo observations

in vitro test hypothesis

in vivo verify hypothesis

nano SCIENCES FONDATION

*Chair of Excellence award*

LMGP

SIMaP

LiPhy Laboratoire interdisciplinaire de Physique

INSTITUT ALBERT BONNIOT

*Host (C. PICART) and collaborative laboratories*

ILLINOIS UNIVERSITY OF ILLINOIS AT URBANA-CHAMPAIGN

*Release for sabbatical*

# Grenoble - Illinois Connection – Chairs of Excellence

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nano SCIENCES FONDATION

Dillon FONG aims to develop in-situ X-ray synchrotron scattering techniques for the study of oxide thin film growth – down to the atomic-scale. He is at Argonne National Lab in Illinois.

David CEPERLEY is a theoretical physicist. He is a world expert in the area of the development and the application of the Quantum Monte Carlo's methods for the precise calculation of the fundamental state and the spectral properties of models of increasing complexity.

Jian Min ZUO is a materials scientist who works on the development of electron Coherent Diffractive Imaging (CDI) for structure characterization of nanoparticles and carbon nanotubes.


About

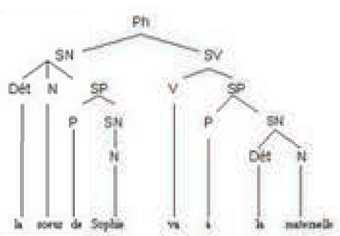
Undergraduate Studies

Graduate Studies

Journals

Centre d'Excellence

- Fellowhips and Opportunities Abroad
- Local and Regional Events of Interest




# French Connections at the University of Illinois

## Animal Sciences

Keith W. Kelley - Professor, Immunophysiology
Project: **Nutrition and Neuroinflammation** - Members: Robert Dantzer, Keith W. Kelley, Rod W Johnson (Professors, UIUC). French Connection: Sophie Laye (Université de Bordeaux II).
Contact: Robert Dantzer click here

David Miller - Associate Professor, Animal Sciences Project: **Function of the oviduct in sperm storage before fertilization** - French connection: Xavier Druart
Contact: David Miller click here

## Anthropology

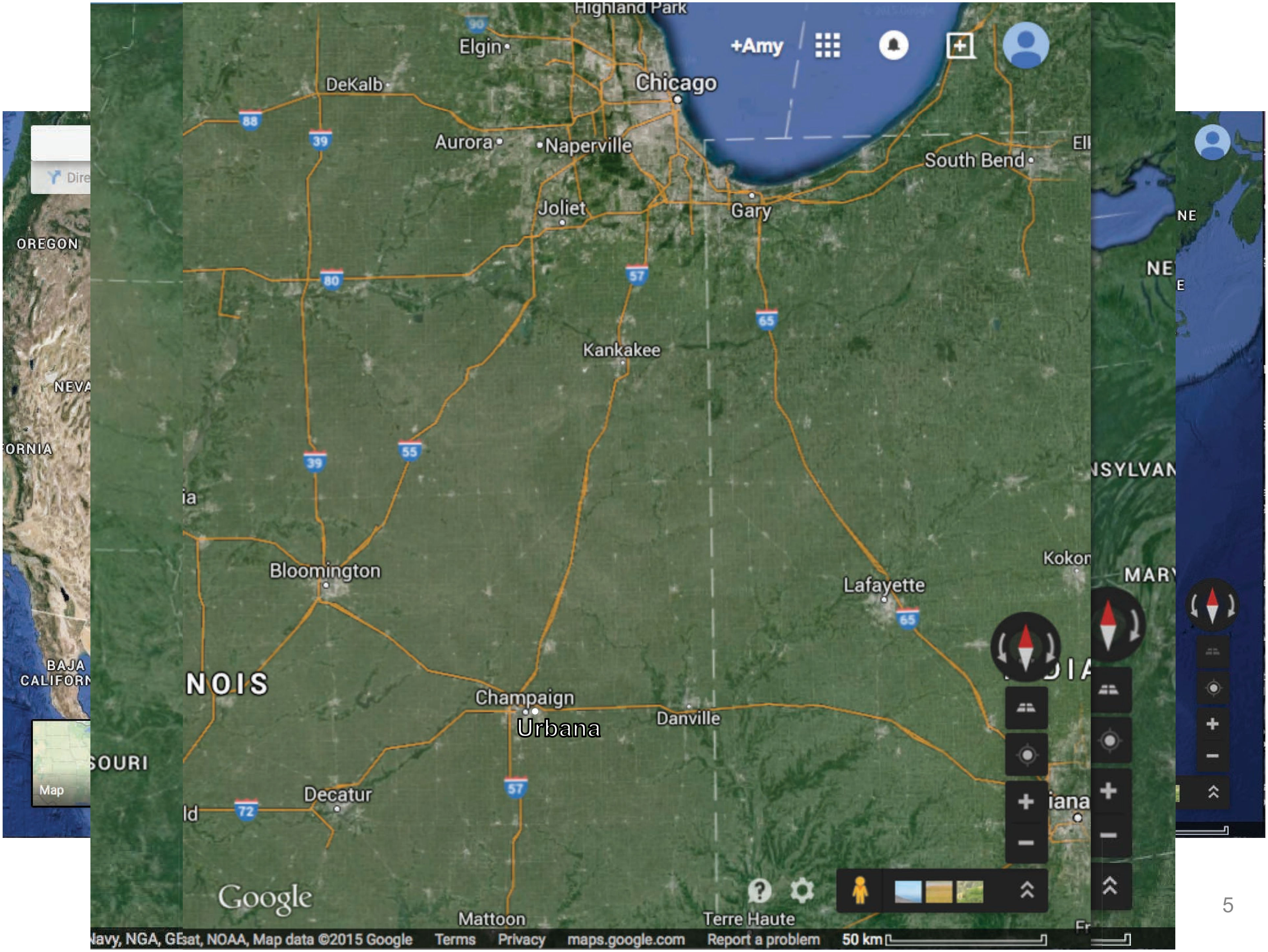
Alma Gottlieb - Professor, Anthropology & African Studies
Project: **Visiting Professor** - EHESS (Ecole des Hautes Etudes en Sciences Sociales) Fall, 2010.
Contact: Prof. Hamit Bazarslan (EHESS) click here

## Chemistry

Thomas Rauchfuss - Professor, Chemistry
Project: **Formal Collaboration** - Frederick Gloaguen, Thomas Rauchfuss.
Contact: Thomas Rauchfuss click here

Deborah Leckband - Professor, Chemistry
Project: **Formal Collaboration** - Team members: Deborah Leckband (Chemical Sciences, UIUC), Paul Braun (Materials Science, UIUC). French Team: Giovanna Fragneto (Institute Laue Langevin, Grenoble); Avraham Halperin (Université de Grenoble).
Contact: Deborah Leckband click here

*www.frit.illinois.edu/french/centre/connections/*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Champaign
Urbana
Danville
Decatur
Mattoon
Terre Haute
OREGON
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ORNIA
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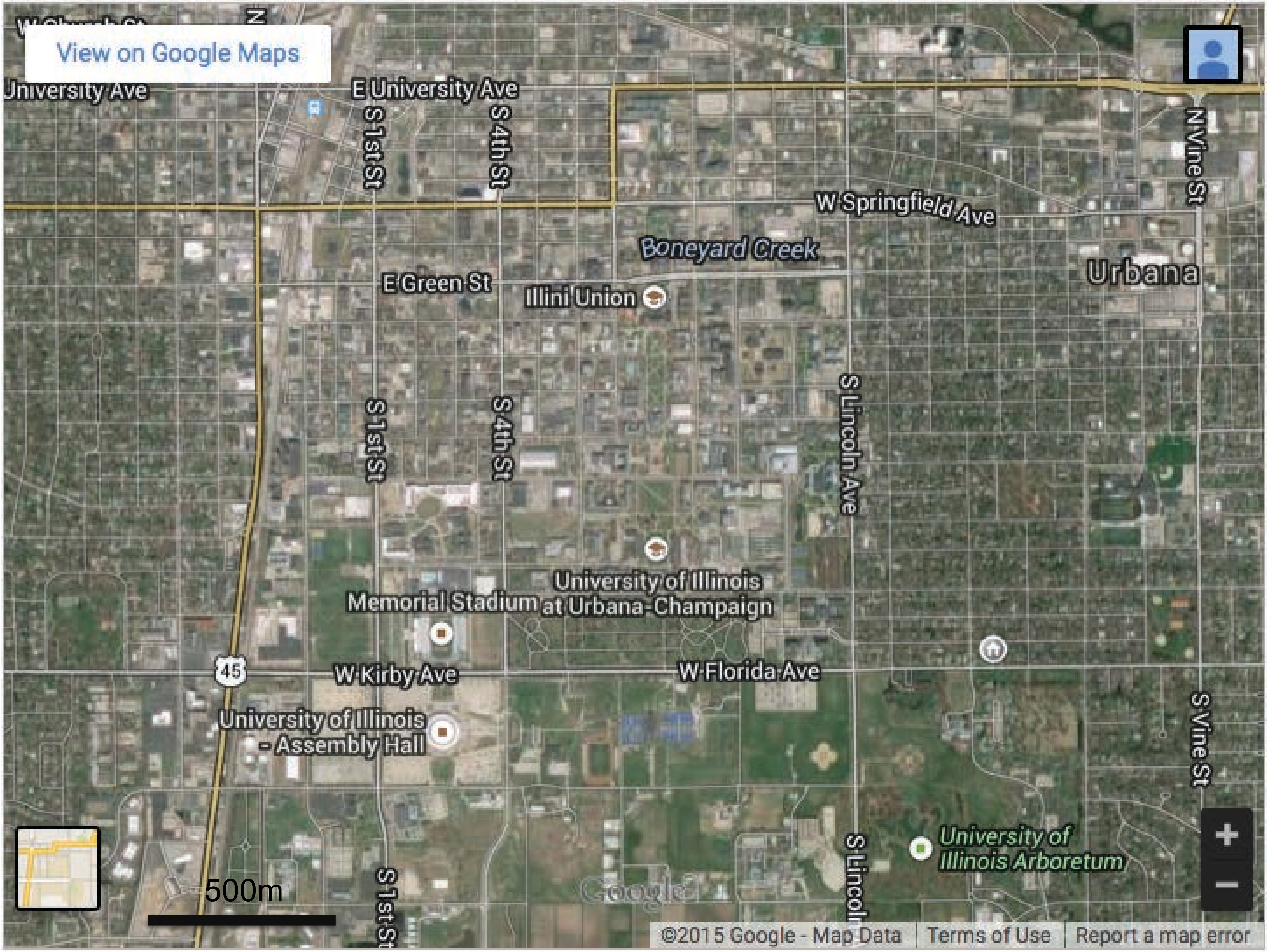
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at Urbana-Champaign
Memorial Stadium
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W Kirby Ave
W Florida Ave
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Téléphérique
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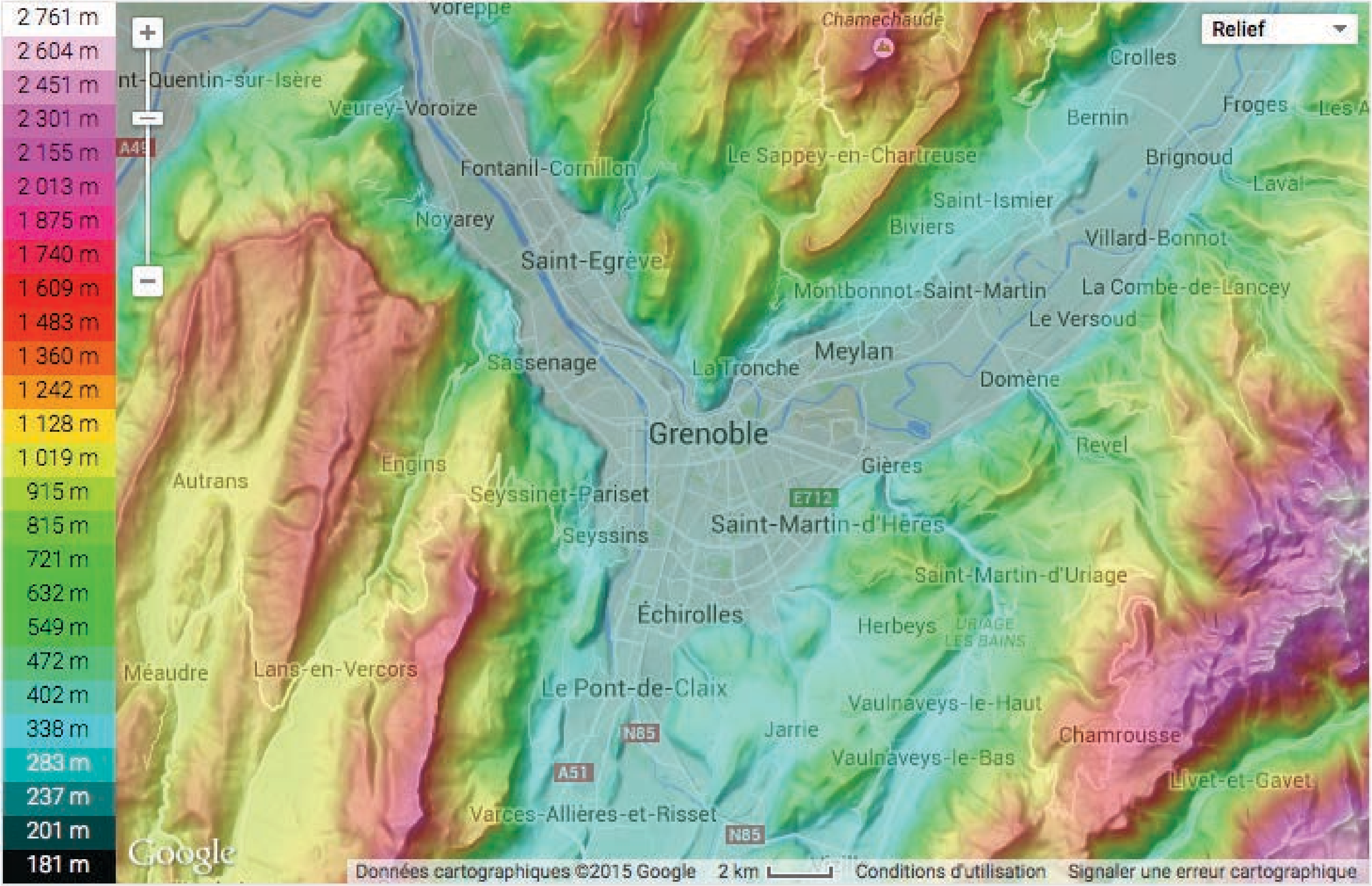
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Fontanil-Cornillon
Laval
Saint-Ismier
Noyarey
Biviers
Villard-Bonnot
Saint-Egrève
Montbonnot-Saint-Martin
La Combe-de-Lancey
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Gières
Engins
Autrans
Seyssinet-Pariset
E712
Saint-Martin-d'Hères
Seyssins
Saint-Martin-d'Uriage
Échirolles
Herbeys
URIAGE LES BAINS
Méaudre
Lans-en-Vercors
Le Pont-de-Claix
Vaulnaveys-le-Haut
Jarrie
Chamrousse
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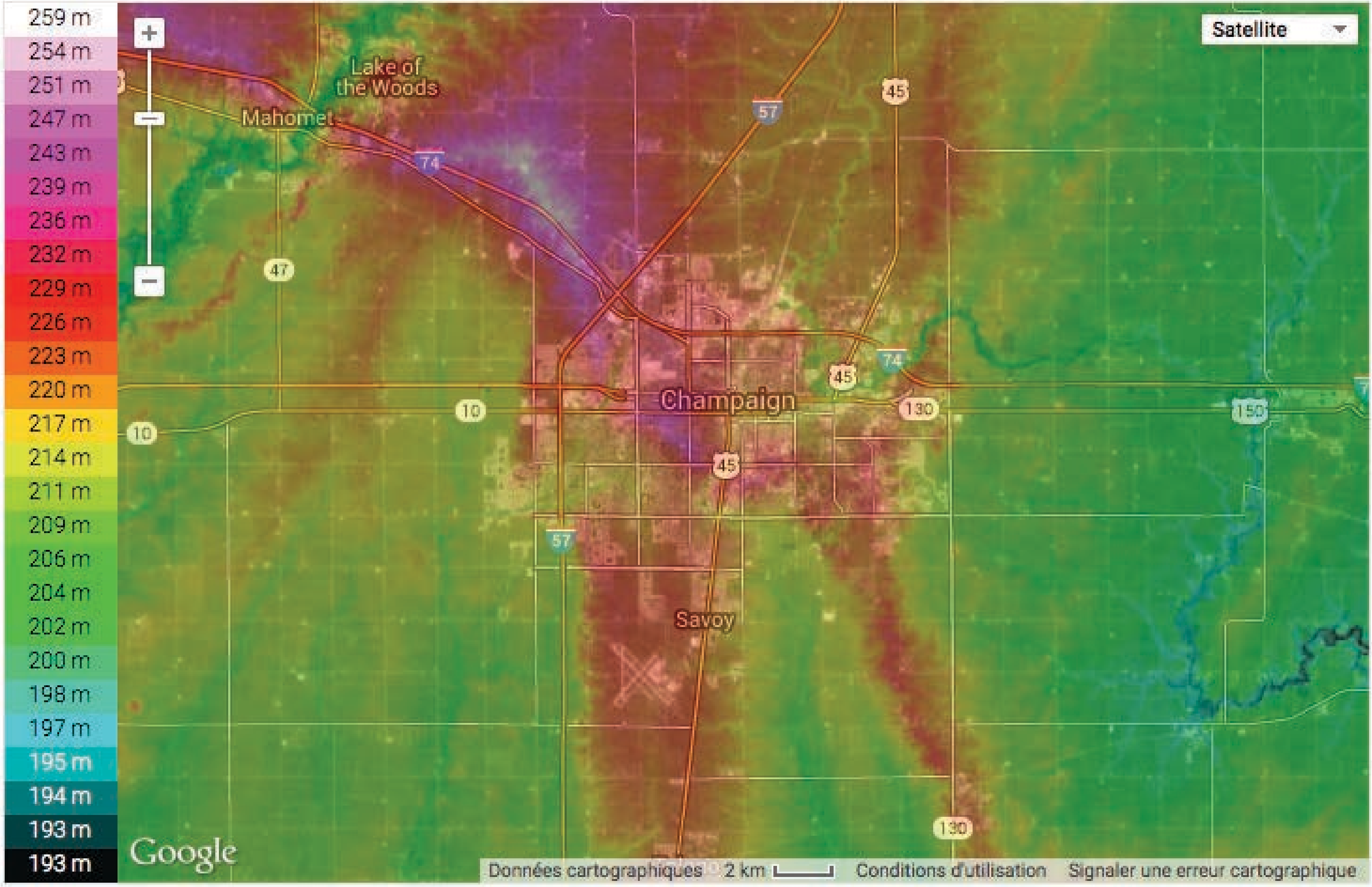
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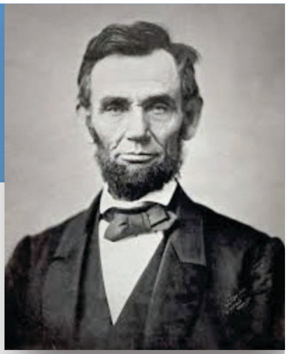

## History

The University of Illinois at Urbana-Champaign is one of the original 37 public land-grant institutions created after President Abraham Lincoln signed the Morrill Act in 1862.

*emphasis on engineering, agriculture, military science*

| 1867 | 1868 | 1885 |
|---|---|---|
| ILLINOIS INDUSTRIAL UNIVERSITY FOUNDED | ILLINOIS INDUSTRIAL UNIVERSITY OPENED | RENAMED THE UNIVERSITY OF ILLINOIS |

*illinois.edu/about/facts.html*

# Some notable scientific achievements of faculty

tissue engineering and bone

Scaffold and material system

in vivo observations

in vitro test hypothesis

in vivo verify hypothesis

9 Nobel laureates

**Quantum-well laser and LED** Nick Holonyak, first graduate student under two-time Nobel Prize winner John Bardeen, also from U Illinois, has accomplishments that have changed the world. He introduced the quantum-well laser and invented the first practical light-emitting-diode. Today, all L-E-Ds and lasers use Holonyak's quantum well lasers.

**Magnetic Resonance Imaging (MRI)** Paul C. Lauterbur received the 2003 Nobel Prize in physiology or medicine for his development of MRI, which has become invaluable to the medical field.

**Discovery of 3rd Branch of the 'Tree of Life' Archaea** Carl Woese revolutionized molecular biology when he announced that life came in three forms, not two (bacteria and all else). Woese discovered the third branch, Archaea.

*illinois.edu/about/awards.html*

# Some scientific & technological achievements of alumni

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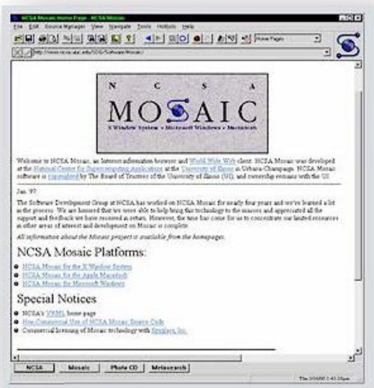
10 Nobel laureates




**First Graphical Browser** Students Marc Andreessen and Eric Bina created the prototype for Mosaic, the first browser in 1993. Mosaic was credited with enabling the Web to gain widespread popularity. He was co-founder of Netscape.

**Development of Radioimmunoassay** Rosalyn Sussman Yalow shared 1977 Nobel Prize in medicine and physiology for the discovery and development of radioimmunoassay, a technique that employs radioactive isotopes to detect and measure the levels of insulin and hormones. Yalow was the 2nd woman to win the Nobel Prize in medicine.

**Inventor of pH meter.** Arnold O. Beckman

**Co-founder of YouTube** Steve Chen

**Creator of Eudora** Steve Dorner

**Co-founder of PayPal** Max Levchin

*illinois.edu/about/awards.html*

# What is tissue engineering?

tissue engineering and bone

Scaffold and material system

in vivo observations

in vitro test hypothesis

in vivo verify hypothesis

*"…an interdisciplinary field that applies the principles of engineering and life sciences toward the development of biological substitutes that restore, maintain, or improve tissue function or a whole organ".*

~ Prof. Bob Langer and Dr. Joseph Vacanti, MD.

Langer R; Vacanti JP (May 1993). "Tissue engineering". *Science* **260** (5110): 920–6.

| Indication | Procedures or patients per year |
|---|---|
| Skin | |
| Burns* | 2,150,000 |
| Pressure sores | 1,500,000 |
| Venous stasis ulcers | 500,000 |
| Diabetic ulcers | 600,000 |
| Neuromuscular disorders | 200,000 |
| Spinal cord and nerves | 40,000 |
| Bone | |
| Joint replacement | 558,200 |
| Bone graft | 275,000 |
| Internal fixation | 480,000 |
| Facial reconstruction | 30,000 |
| Cartilage | |
| Patella resurfacing | 216,000 |
| Chondromalacia patellae | 103,400 |
| Meniscal repair | 250,000 |
| Arthritis (knee) | 149,900 |
| Arthritis (hip) | 219,300 |
| Fingers and small joints | 179,000 |
| Osteochondritis dissecans | 14,500 |
| Tendon repair | 33,000 |
| Ligament repair | 90,000 |
| Blood vessels | |
| Heart | 754,000 |
| Large and small vessels | 606,000 |
| Liver | |
| Metabolic disorders | 5,000 |
| Liver cirrhosis | 175,000 |
| Liver cancer | 25,000 |
| Pancreas (diabetes) | 728,000 |
| Intestine | 100,000 |
| Kidney | 600,000 |
| Bladder | 57,200 |
| Ureter | 30,000 |
| Urethra | 51,900 |
| Hernia | 290,000 |
| Breast | 261,000 |
| Blood transfusions | 18,000,000 |
| Dental | 10,000,000 |

*Approximately 150,000 of these individuals are hospitalized and 10,000 die annually.

# Engineered tissues and components

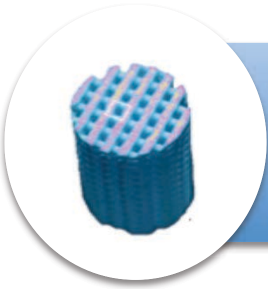
tissue engineering and bone

Scaffold and material system

in vivo observations

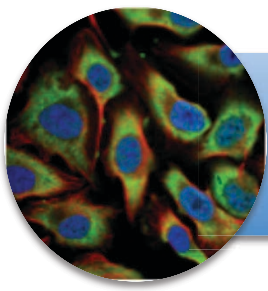
in vitro test hypothesis

in vivo verify hypothesis



"*scaffold*" or support

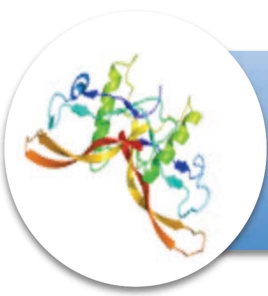
(porous metal, ceramic, polymer)



abdserotec.com

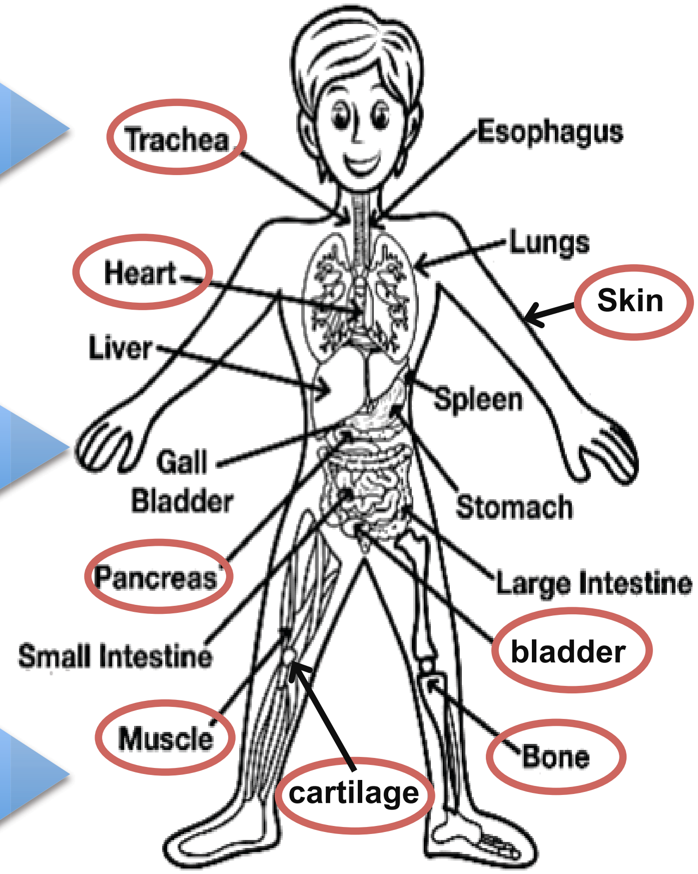
*cells*

(allo/auto graft; in/ex vivo)



*biologics*

(growth factors, peptides, antibiotics...)



# Why *bone* tissue engineering? (statistics)



- Bone and joint disease (www.boneandjointburden.org)
  - leading cause of disability in US
  - > 1 in 4 Americans
  - $849 billion/year – 7.7% of GDP

- Increasing numbers due to aging population
  - Number over 65 will double in next 25 years

(US Census Bureau, 2010)

# Why *bone* tissue engineering? – *aging/disease*

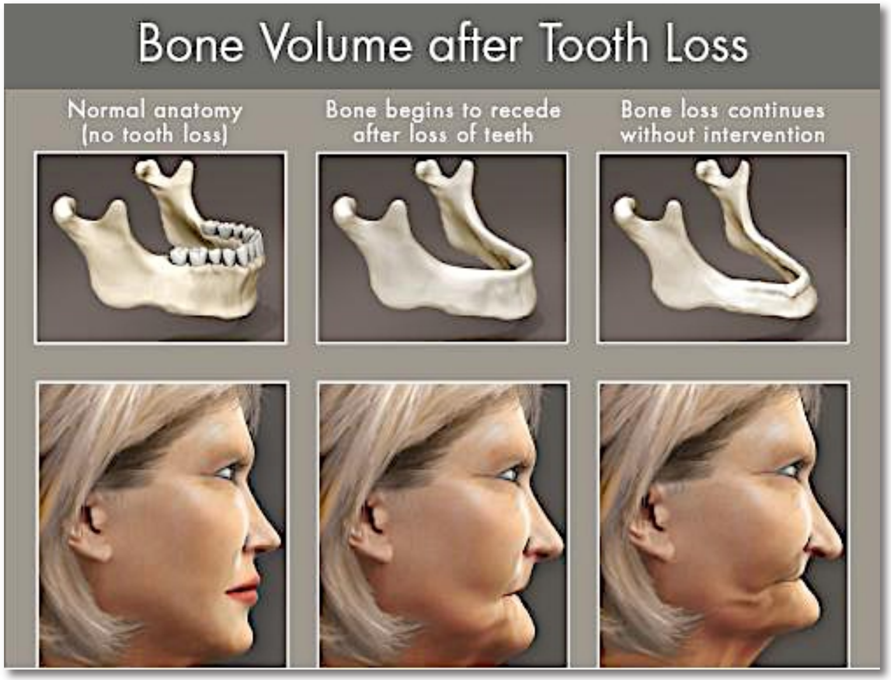
tissue engineering and bone

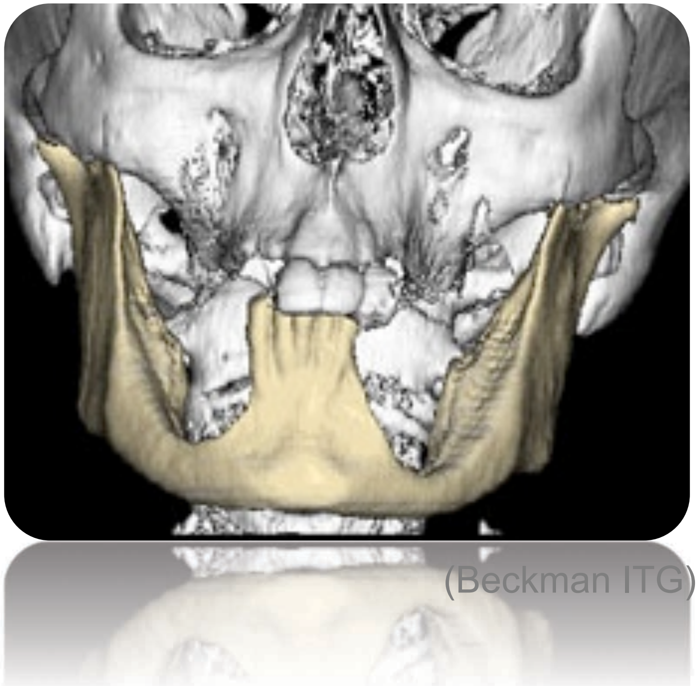
Scaffold and material system

in vivo observations

in vitro test hypothesis

in vivo verify hypothesis



(Beckman ITG)

# Why *bone* tissue engineering? - *cancer*

tissue engineering and bone

Scaffold and material system

in vivo observations

in vitro test hypothesis

in vivo verify hypothesis



## Roger Ebert

Film critic

Roger Joseph Ebert was an American film critic, journalist, and screenwriter. He was a film critic for the Chicago Sun-Times from 1967 until his death in 2013. In 1975, Ebert was the first film critic to win the Pulitzer Prize for Criticism. Wikipedia

**Born:** June 18, 1942, Urbana, Illinois, United States

**Died:** April 4, 2013, Chicago, Illinois, United States

also trauma, congenital defects…

# Current "gold standard" for bone defect repair

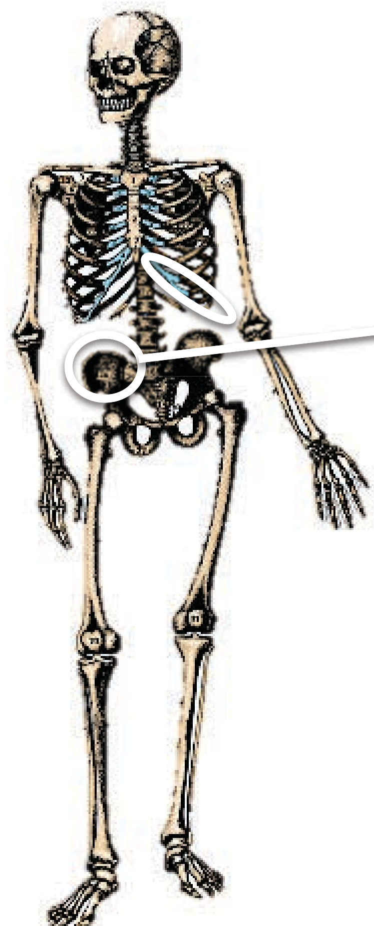
tissue engineering and bone

Scaffold and material system

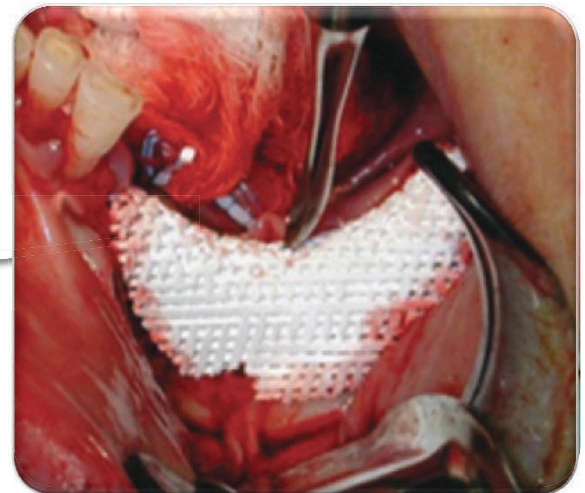
in vivo observations

in vitro test hypothesis

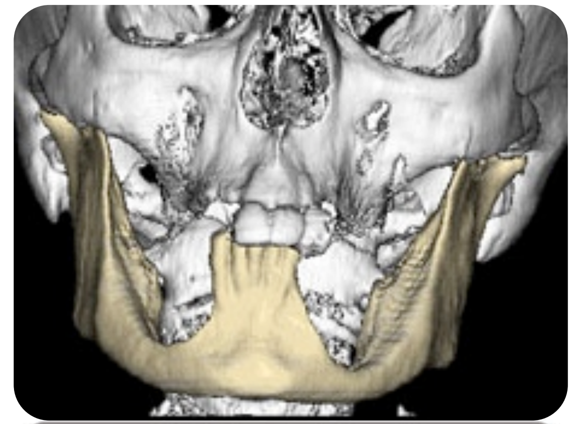
in vivo verify hypothesis



merriam-webster.com



(Cesarano, 2005)



(Beckman ITG)

## Autograft (self)

- Limited supply
- Donor site complications
  - o Nerve injury
  - o Infection
  - o Chronic pain
  - o others

8.5 – 20% of operations

(Giannoudis, 2005)

## Allograft (donor)

- Limited supply
- Disease transmission (e.g HIV)
- Property degradation

# Ultimate goal:  the site specific implant

- tissue engineering and bone
- Scaffold and material system
- in vivo observations
- in vitro test hypothesis
- in vivo verify hypothesis

Optimize for specific size, shape, mechanics, etc.

Mandible reconstruction project:
www.itg.uiuc.edu/technology/reconstruction/

# Bone has a complex hierarchical structure

tissue engineering and bone

Scaffold and material system

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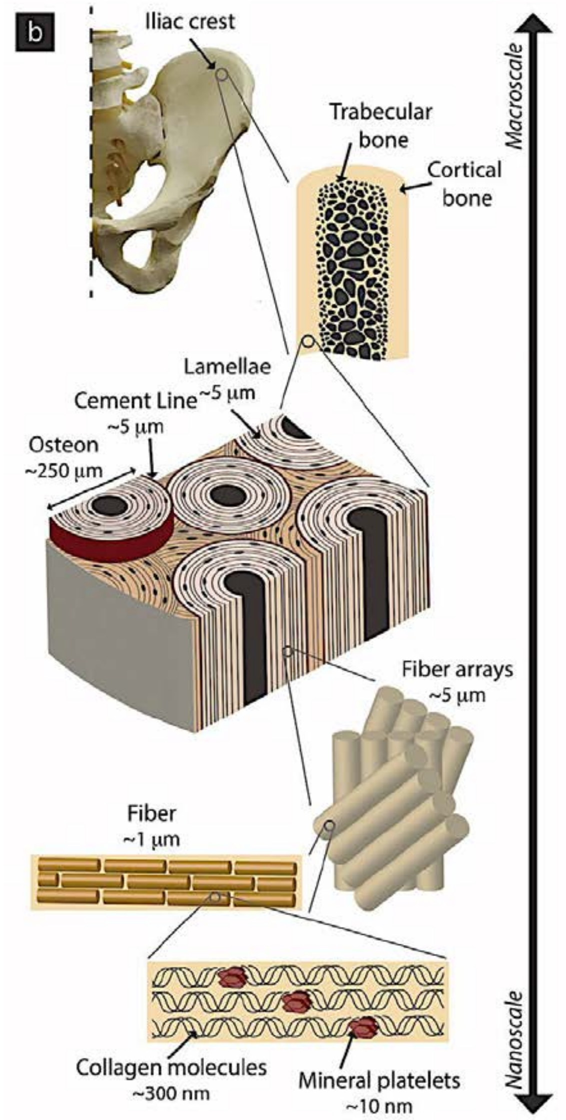
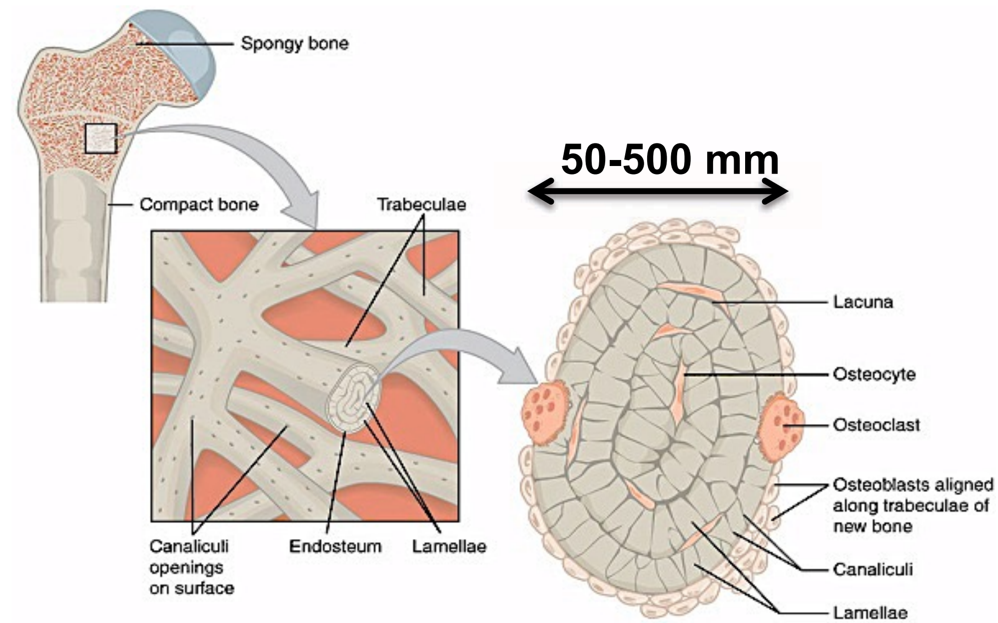
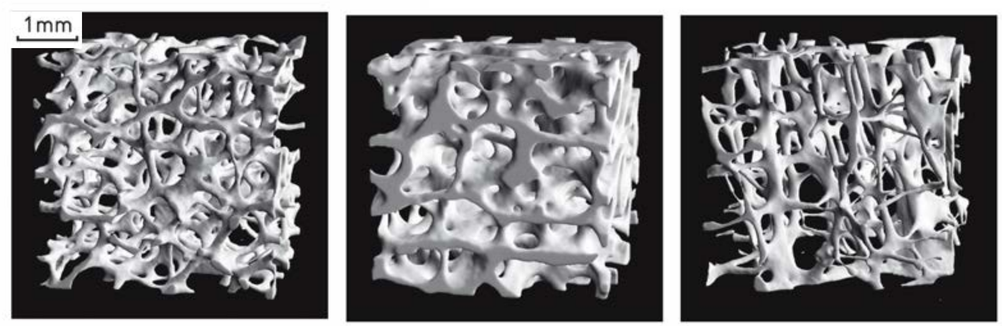
in vivo verify hypothesis




Zimmerman et al, JBMR, 2014



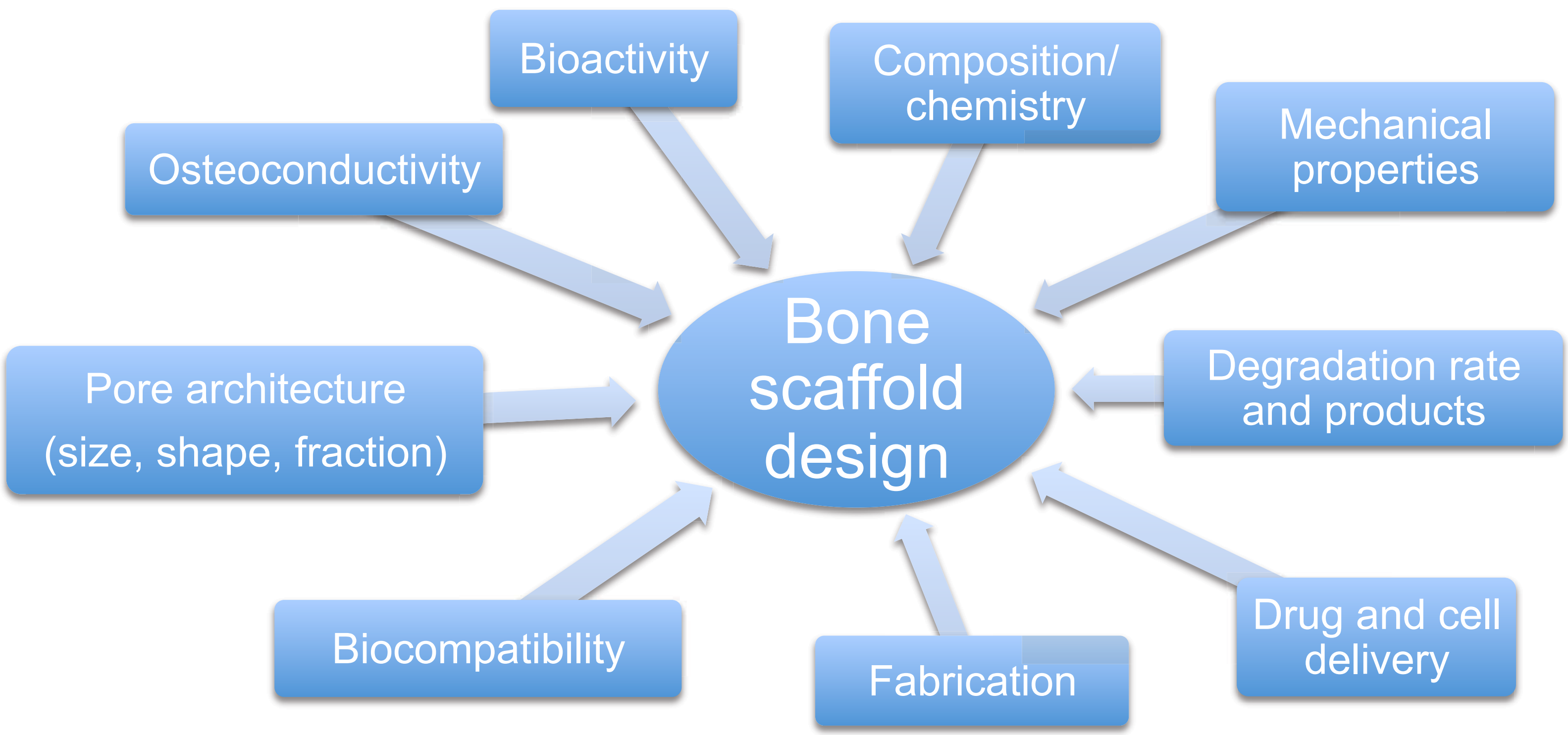




Gibson, Ashby, Harley, 2010

# A long list of considerations in scaffold design



**Biggest challenge: complex, large, load bearing defects**



# "…pores must be > 100 μm for bone ingrowth…"

tissue engineering and bone

Scaffold and material system

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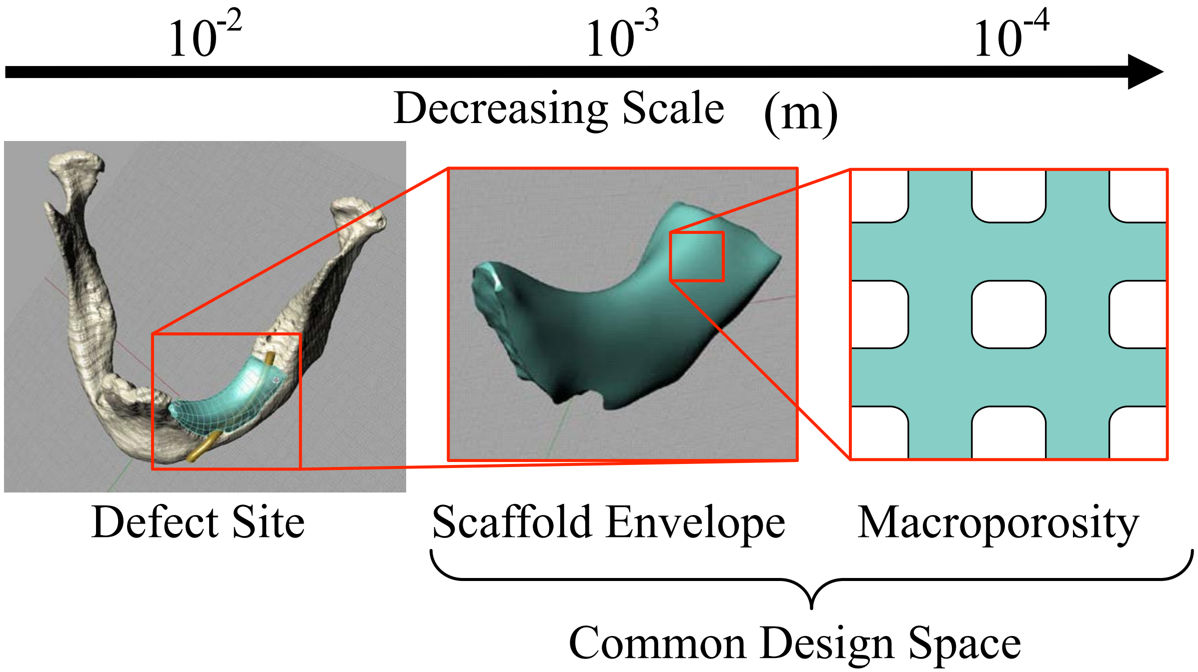


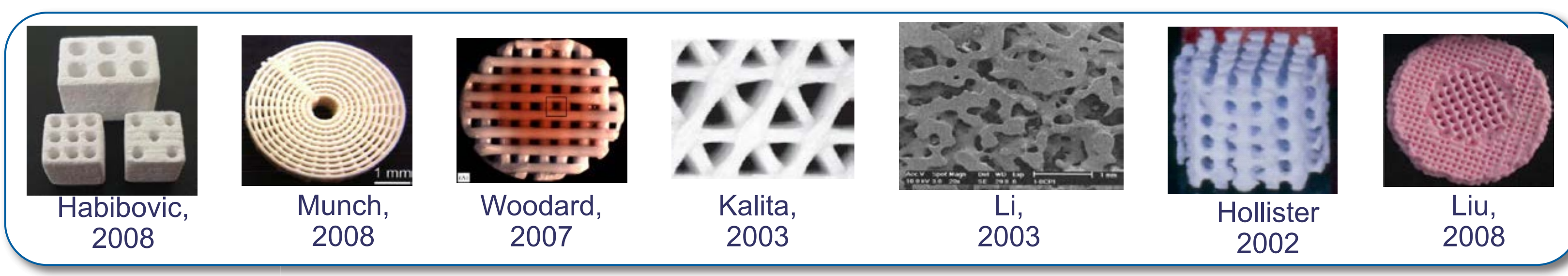


ITG UIUC (mandible), D. Hoelzle (figure)

# "…pores must be > 100 μm for bone ingrowth…"

- tissue engineering and bone
- Scaffold and material system
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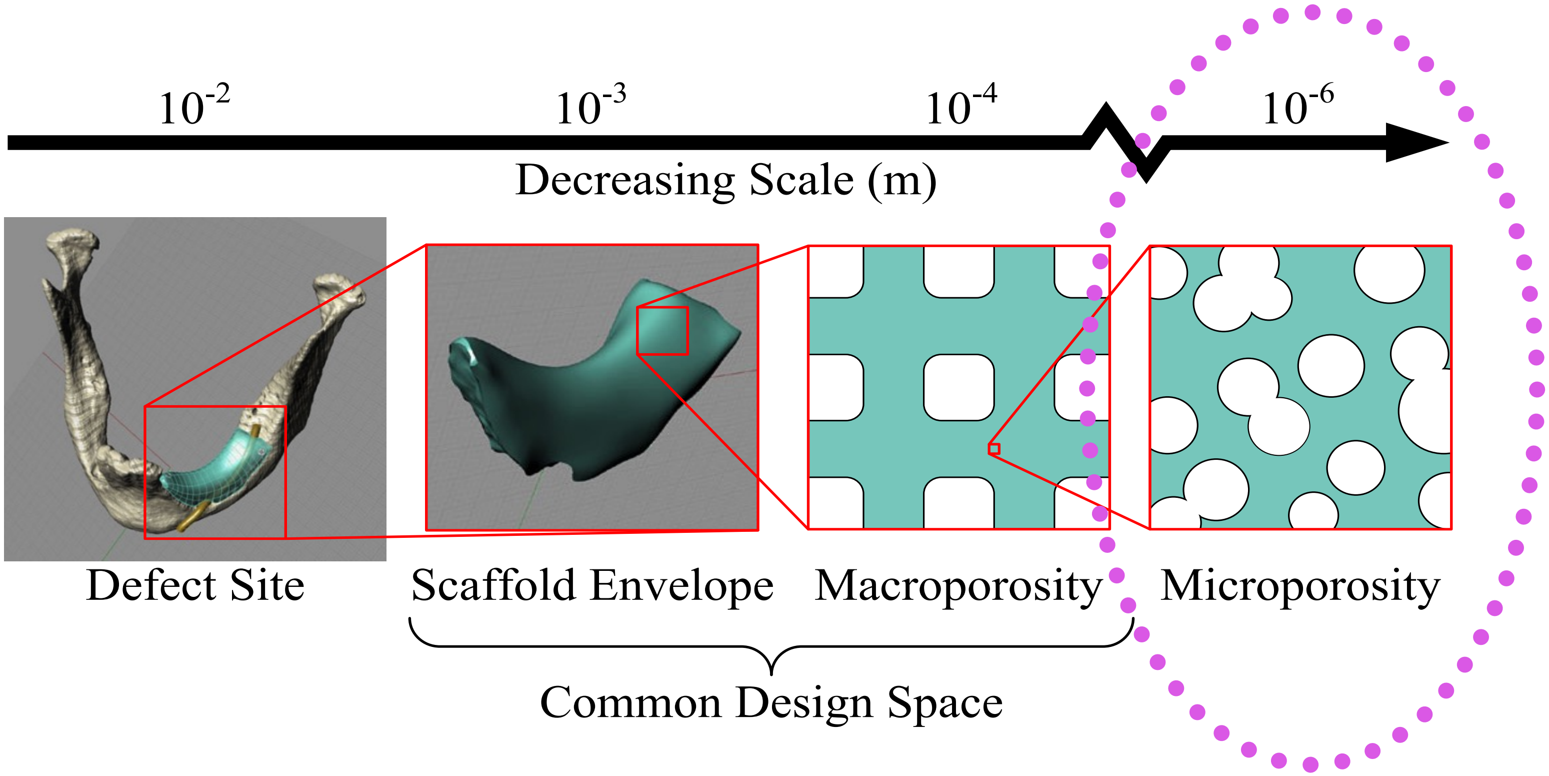
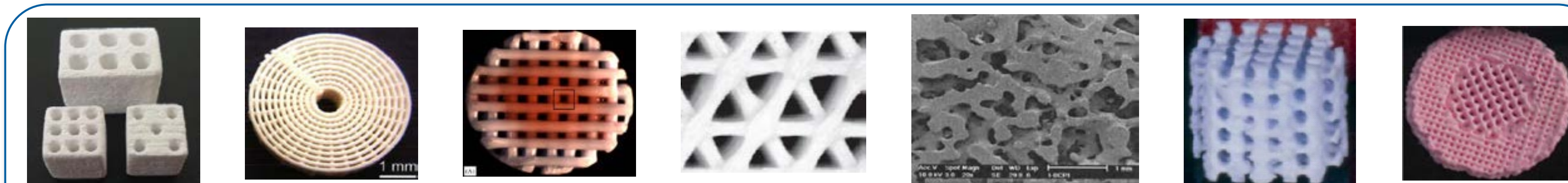


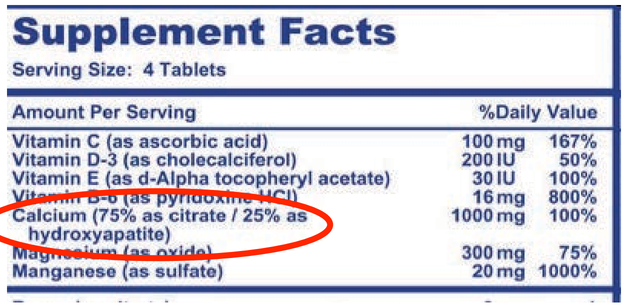

Habibovic, 2008 · Munch, 2008 · Woodard, 2007 · Kalita, 2003 · Li, 2003 · Hollister 2002 · Liu, 2008

ITG UIUC (mandible), D. Hoelzle (figure)

# Our material system – biphasic calcium phosphate (BCP)



## CaPs are everywhere…

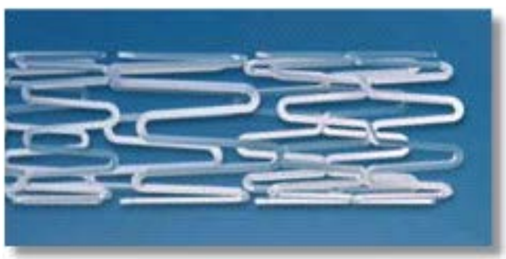


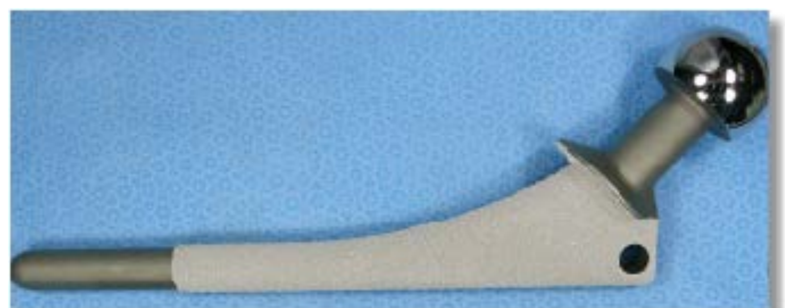
**Supplement Facts**

Serving Size: 4 Tablets

| Amount Per Serving | | %Daily Value |
|---|---|---|
| Vitamin C (as ascorbic acid) | 100 mg | 167% |
| Vitamin D-3 (as cholecalciferol) | 200 IU | 50% |
| Vitamin E (as d-Alpha tocopheryl acetate) | 30 IU | 100% |
| Vitamin B-6 (as pyridoxine HCl) | 16 mg | 800% |
| Calcium (75% as citrate / 25% as hydroxyapatite) | 1000 mg | 100% |
| Magnesium (as oxide) | 300 mg | 75% |
| Manganese (as sulfate) | 20 mg | 1000% |





# Scaffold fabrication and characteristics

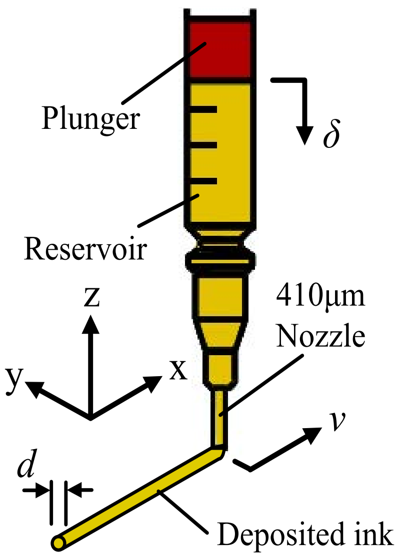
tissue engineering and bone

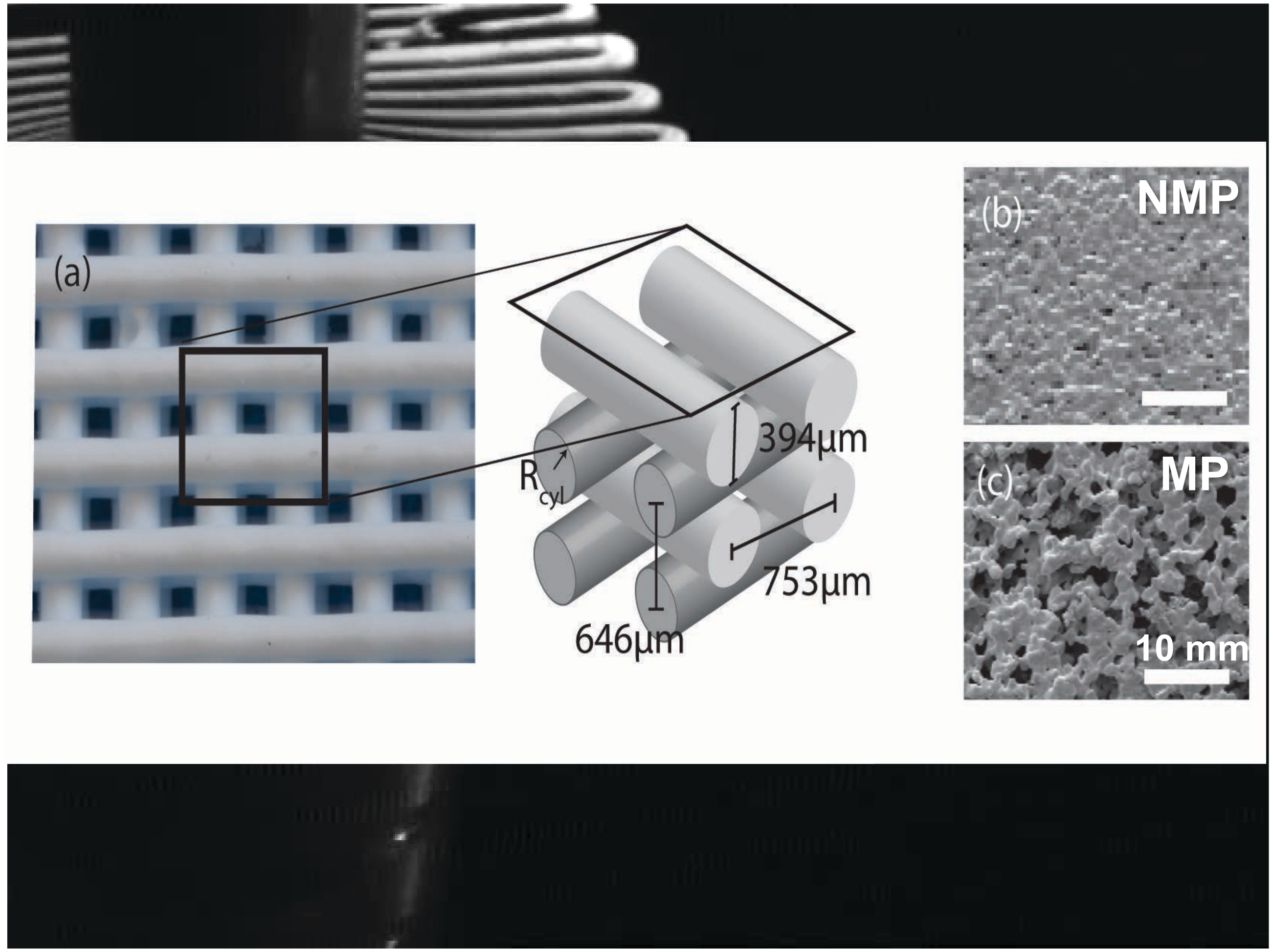
Scaffold and material system

in vivo observations

in vitro test hypothesis

in vivo verify hypothesis




Polak, 2010; Hoelzle, et al 2008, 2011

# *Micropores introduced via sacrificial polymer beads*

tissue engineering and bone

Scaffold and material system

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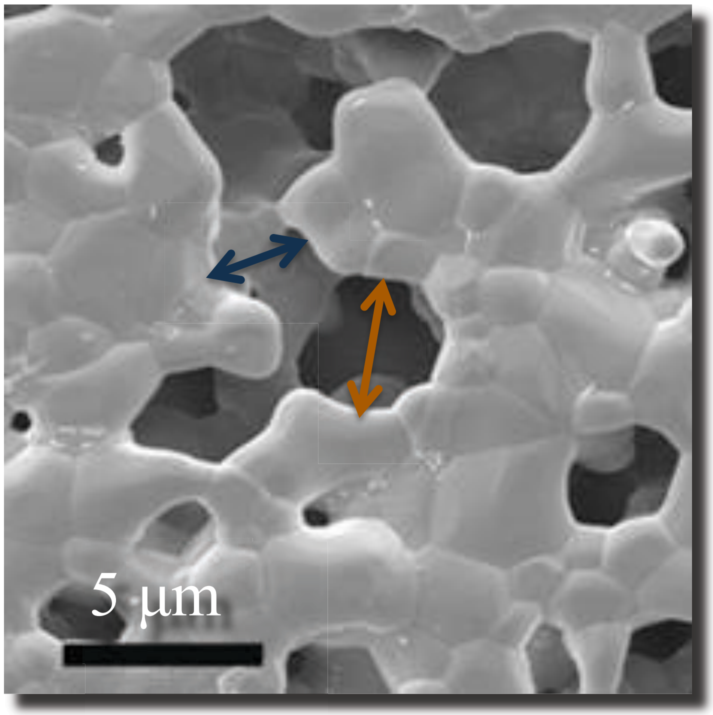
in vitro test hypothesis

in vivo verify hypothesis

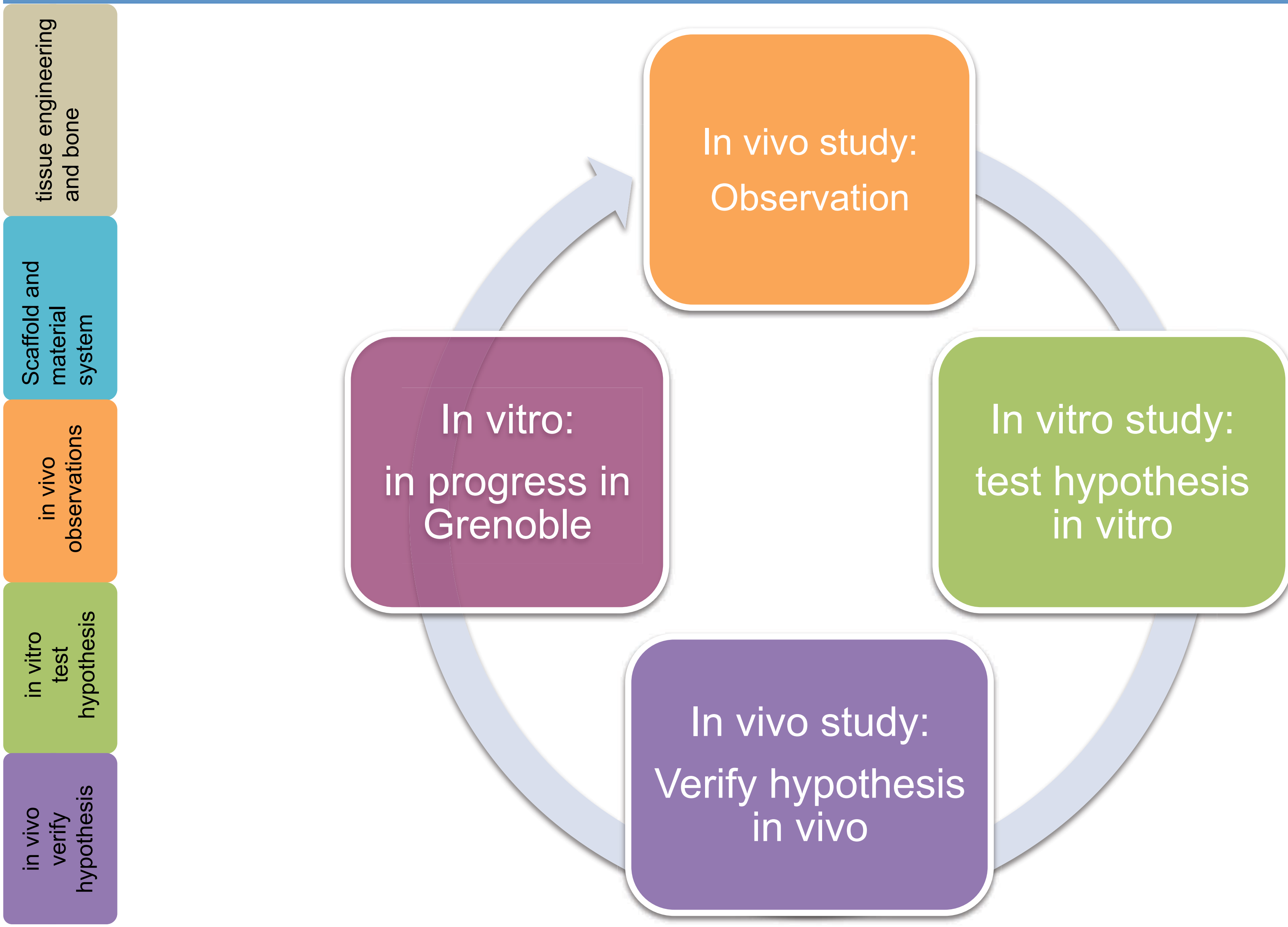



*micro porosity in scaffold rods*

- Sacrificial porogen
  - PMMA beads
  - Burn out - sintering 1300C, 2hrs
- ~46% microporous
- ***4.86 ± 3.62 µm diameter pores***
  - ***Line intercept method***
- ***2.15 µm interconnections***
  - ***Mercury intrusion porosymmetry (MIP)***

Woodard et al Biomater, 2007; Lan Levengood et al Biomater, 2010; Lan Levengood et al Acta Biomater, 2010; Polak et al Acta Biomater 2011

# Our series of studies…



# Our series of studies…

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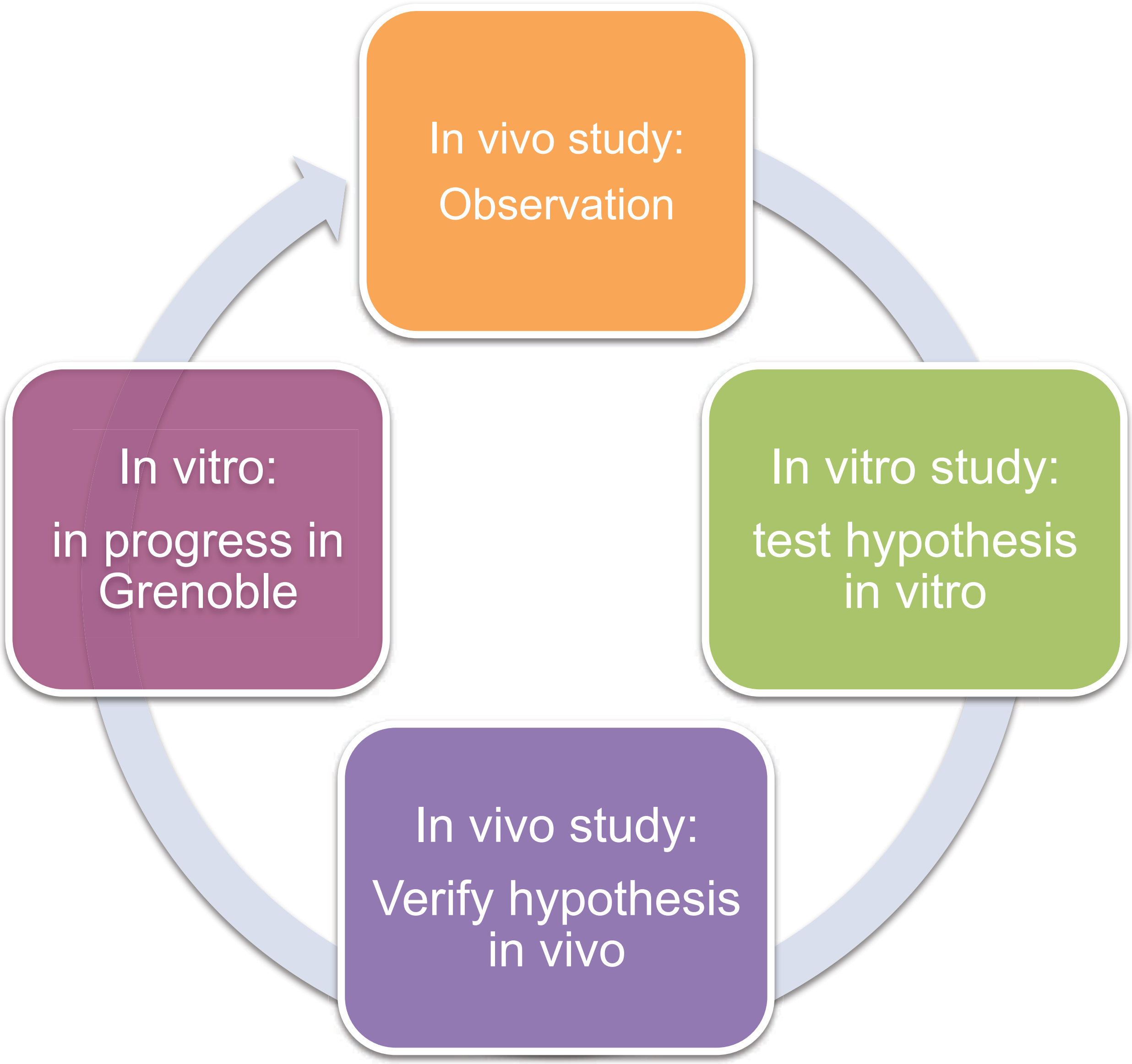


# Microporous scaffolds: *more bone, more uniform bone*

tissue engineering and bone

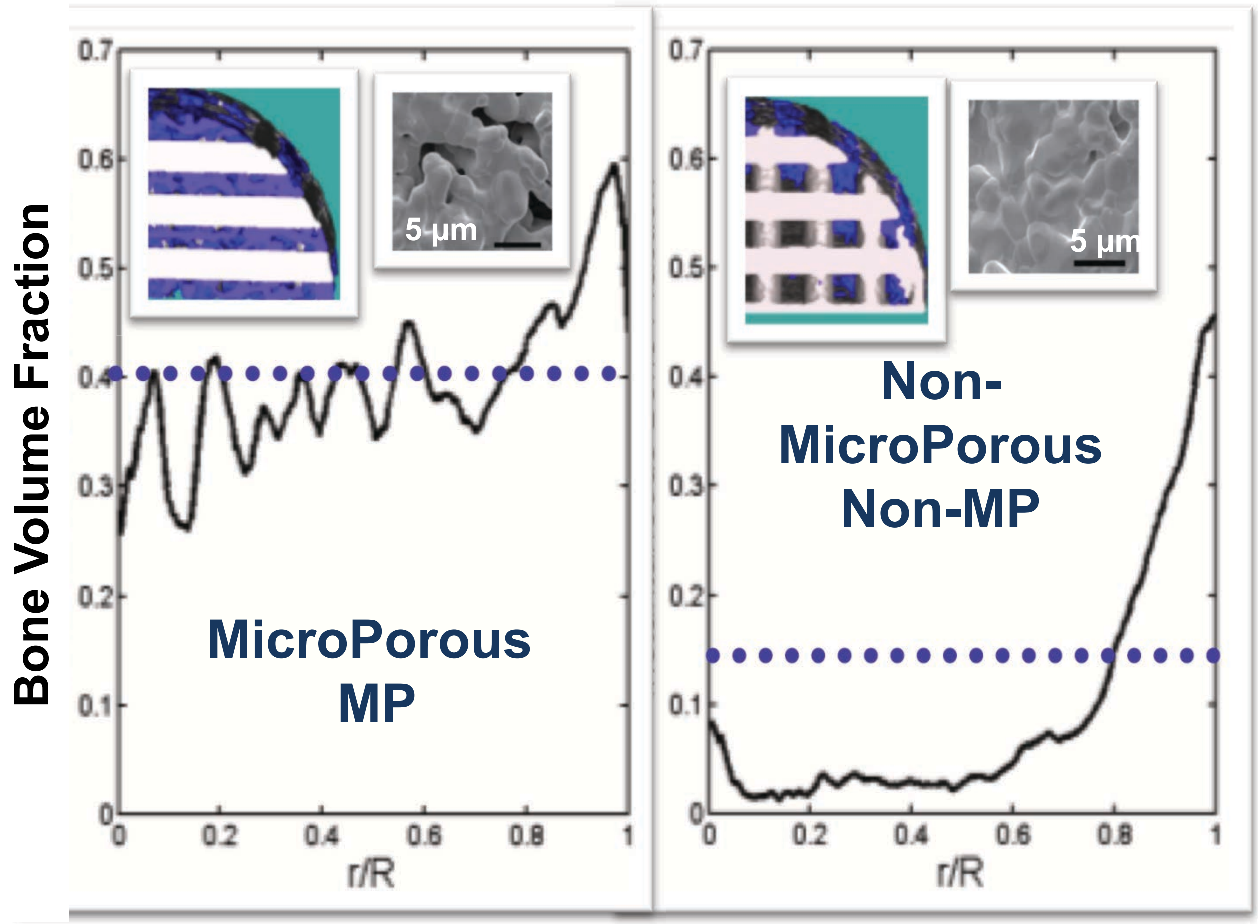
Scaffold and material system

in vivo observations

in vitro test hypothesis

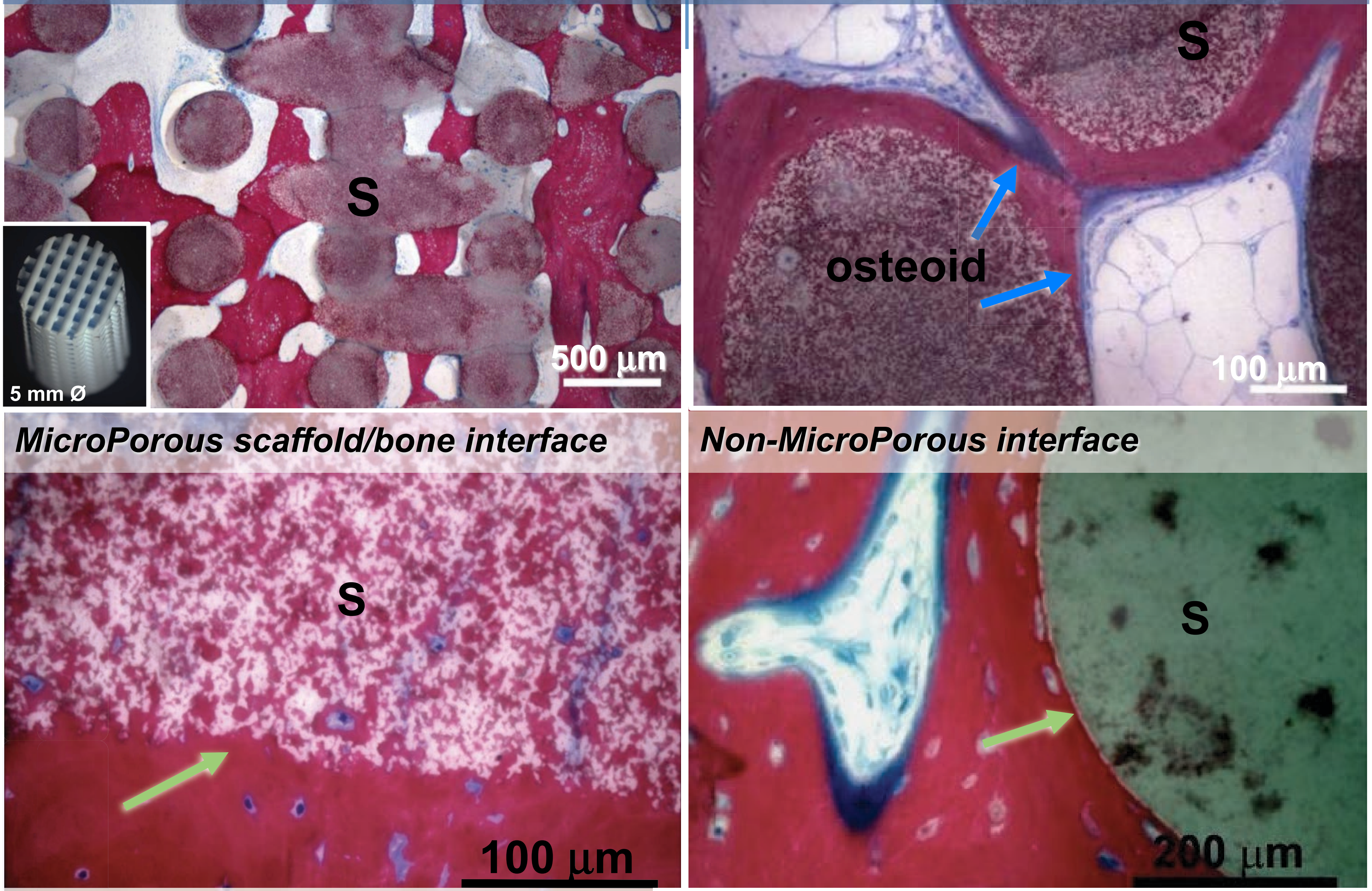
in vivo verify hypothesis


**Results based on 3D micro-ct data analysis**



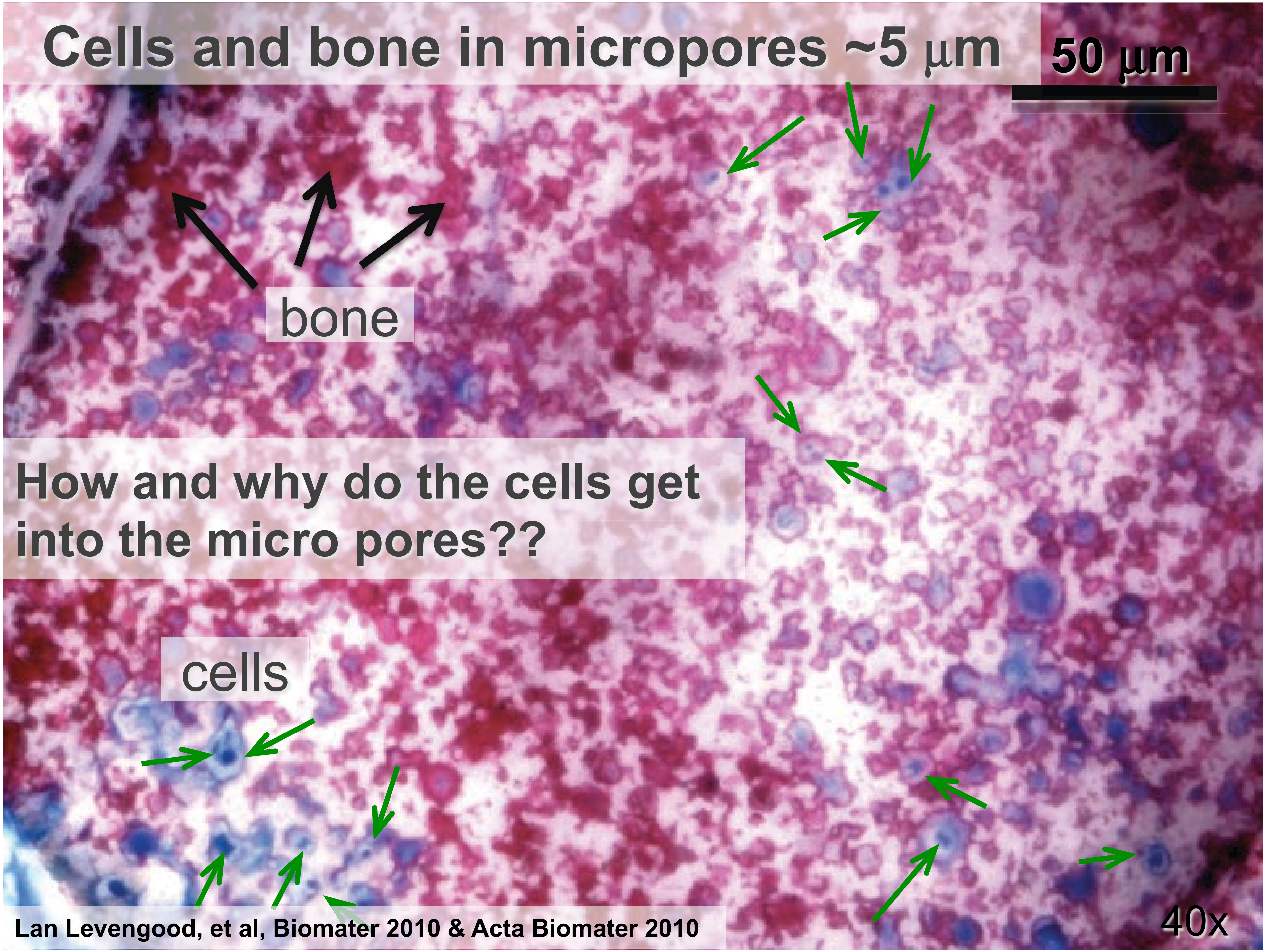

Polak et al, Acta Biomater 2010; Polak et al. Comp. Med Imag Graphics, 2011

# Microporous scaffolds: multiscale osteointegration




**[plastic embedded, sanderson's rapid bone stain & acid fuchsin counterstain]**

Lan Levengood et al, Biomater. 2010 & Acta Biomater 2010, Polak et al, Acta Biomater 2010.


Cells and bone in micropores ~5 μm
50 μm
bone
How and why do the cells get into the micro pores??
cells
Lan Levengood, et al, Biomater 2010 & Acta Biomater 2010
40x

# Our series of studies…

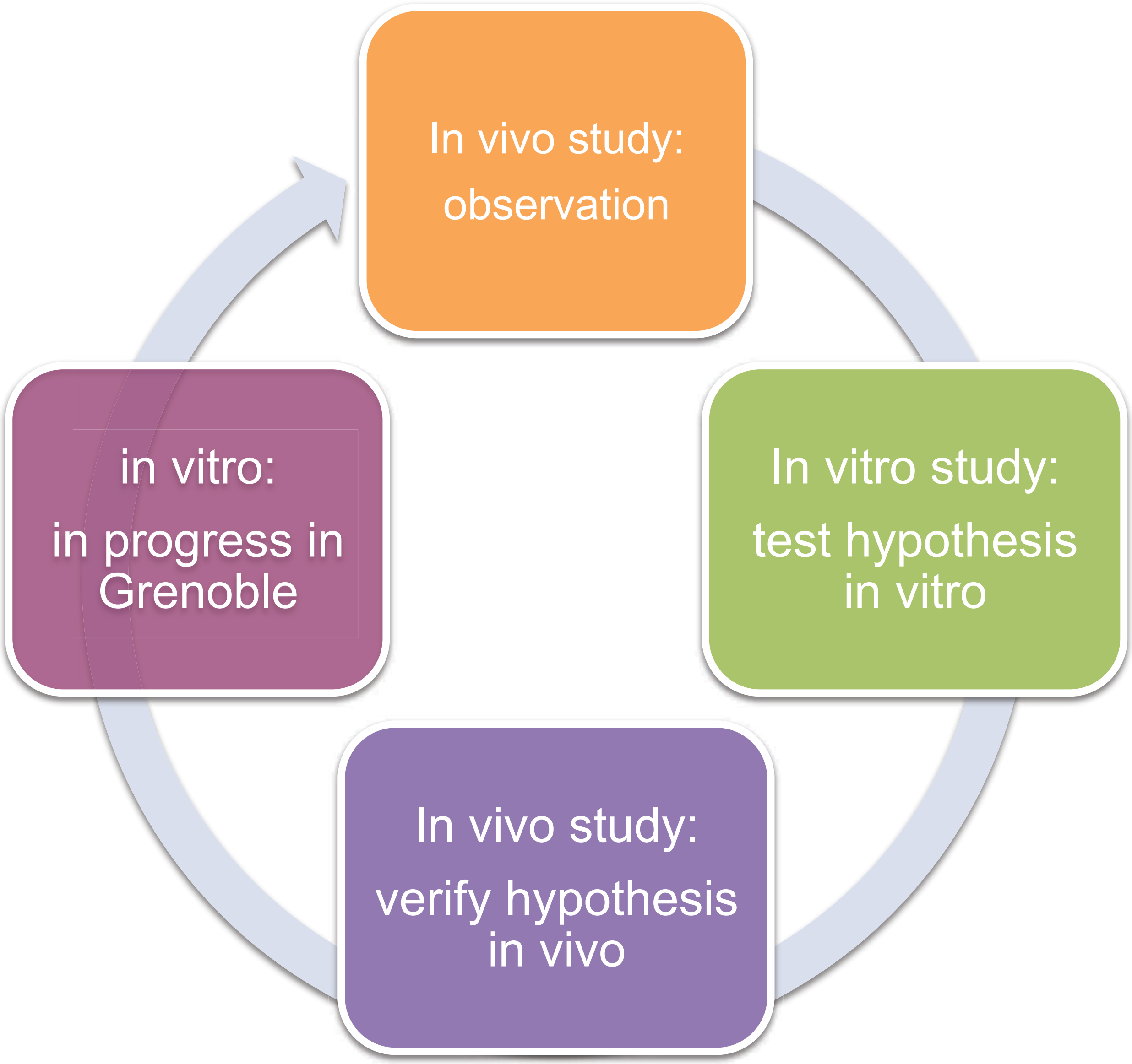
tissue engineering and bone

Scaffold and material system

in vivo observations

in vitro test hypothesis

in vivo verify hypothesis



# Can cells be drawn in via capillary forces?

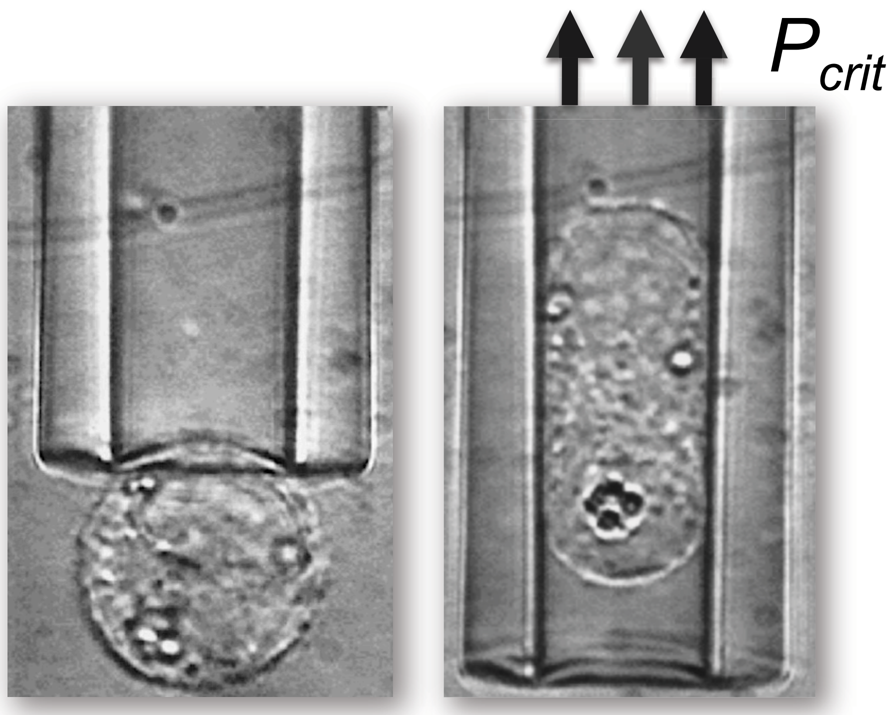
tissue engineering and bone

Scaffold and material system

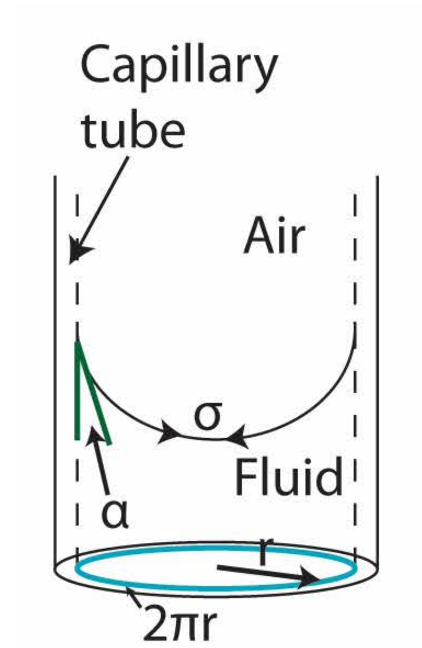
in vivo observations

in vitro test hypothesis

in vivo verify hypothesis




Cells deform to enter pipette




$$F_c = 2\pi r \sigma \cos(\alpha)$$

$$P_{crit} = 2\gamma_{ten}\left(\frac{1}{R_p} - \frac{1}{R_c}\right)$$

$\gamma_{ten}$: cortical tension of cell (stiffness)
$R_p$: pore radius
$R_c$: cell radius

Hochmuth, J Biomech, 2000 (image)

# Critical pressure for cell to enter pore

tissue engineering and bone

Scaffold and material system

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in vitro test hypothesis

in vivo verify hypothesis

| Cell | $\gamma\ 10^{-6}$ ($kg/s^2$) | Rc (mm) | $P_{crit}$ (Pa) |
|---|---|---|---|
| Neutrophil | 24 | 4.2 | 7.77 |
| Osteoblast (OB) | 520 | 7.5 | 277 |
| MSC | 520 | 11.5 | 326 |
| Chondrocyte | 2200 | 4.5 | 1131 |
| D1 (pre-OB) | N/A | 7.5 | N/A |
| E1 (OB) | 520 | 6.9 | 265 |

$$P_{crit} = 2\gamma_{ten}\left(\frac{1}{R_p} - \frac{1}{R_c}\right)$$

$\gamma_{ten}$: cortical tension of cell

***$R_p$: pore radius (~2.5 $\mu m$)***

$R_c$: cell radius

*Polak et al 2013*

# Capillary rise experiments

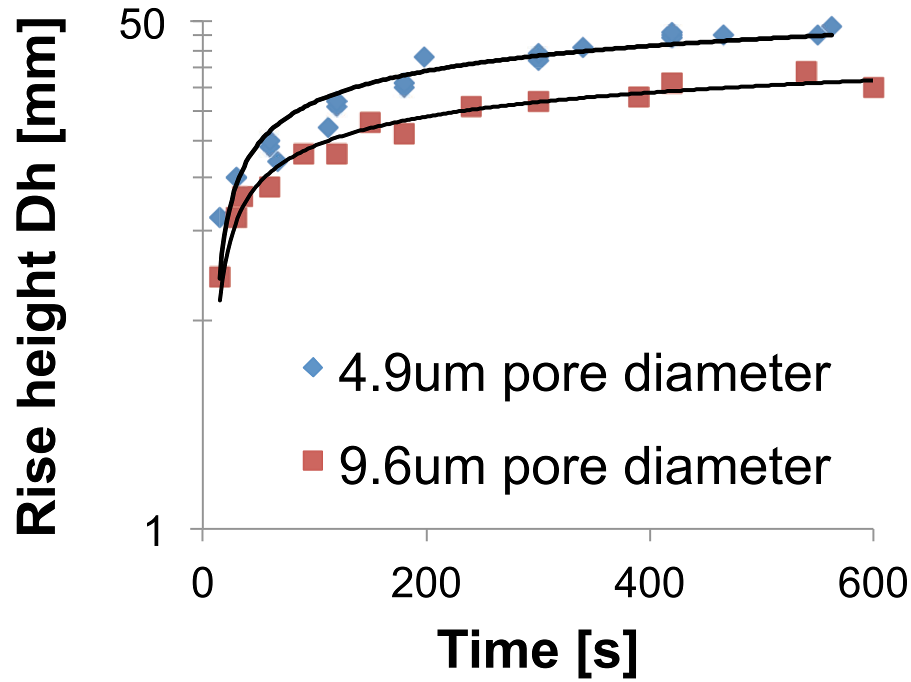
tissue engineering and bone

Scaffold and material system

in vivo observations

in vitro test hypothesis

in vivo verify hypothesis


$$\Delta P = \rho g \Delta h$$

ΔP = 588 Pa (5 μm)

ΔP = 412 Pa (10 μm)

Δh = 60 mm, (5 μm)
Δh = 42 mm, (10 μm)

# Critical pressure for cell to enter pore

tissue engineering and bone

Scaffold and material system

in vivo observations

in vitro test hypothesis

in vivo verify hypothesis

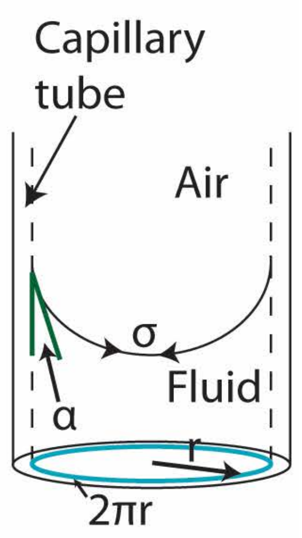
*Pressure generated in 4.9 μm dia. pore substrate: 588 Pa*

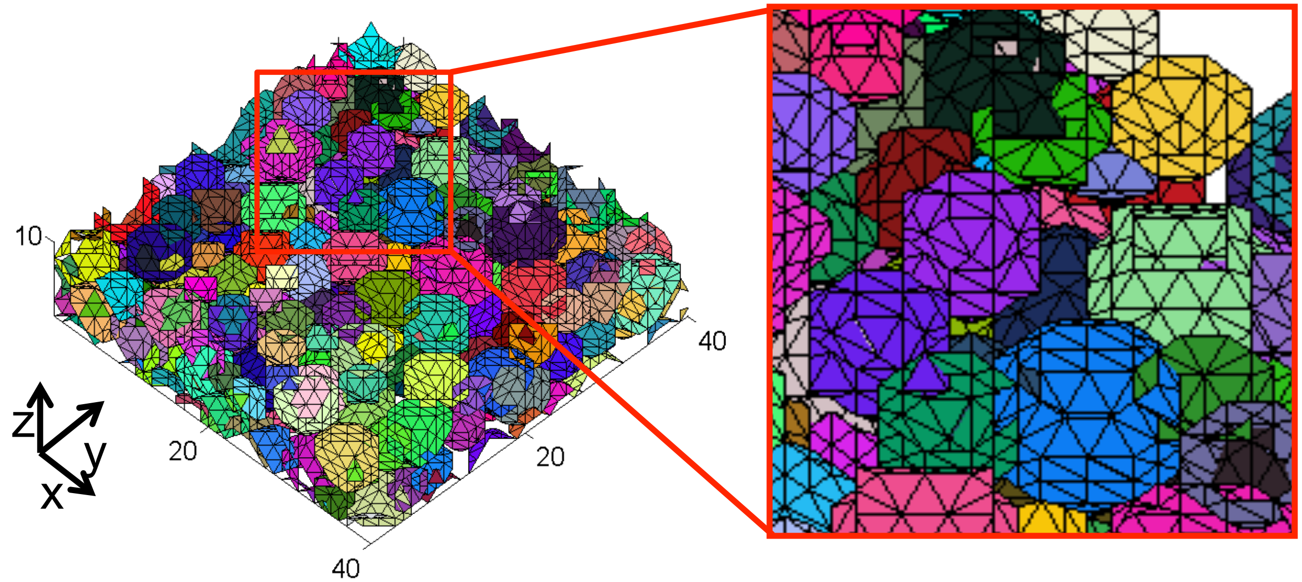
| Cell | $\gamma\ 10^{-6}$ (kg/s$^2$) | Rc (mm) | $P_{crit}$ (Pa) |
|---|---|---|---|
| Neutrophil | 24 | 4.2 | 7.77 |
| Osteoblast (OB) | 520 | 7.5 | 277 |
| MSC | 520 | 11.5 | 326 |
| Chondrocyte | 2200 | 4.5 | 1131 |
| D1 (pre-OB) | N/A | 7.5 | N/A |
| E1 (OB) | 520 | 6.9 | 265 |

*Polak et al 2013*

# Microstructural model to predict capillary forces

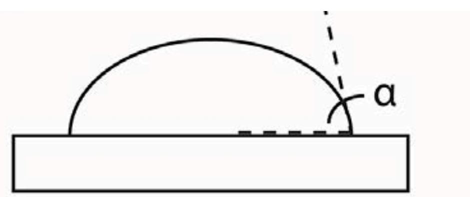





$$F_c = \boxed{2\pi r}\sigma\cos(\alpha)$$

Measured α = 89.8±5.0



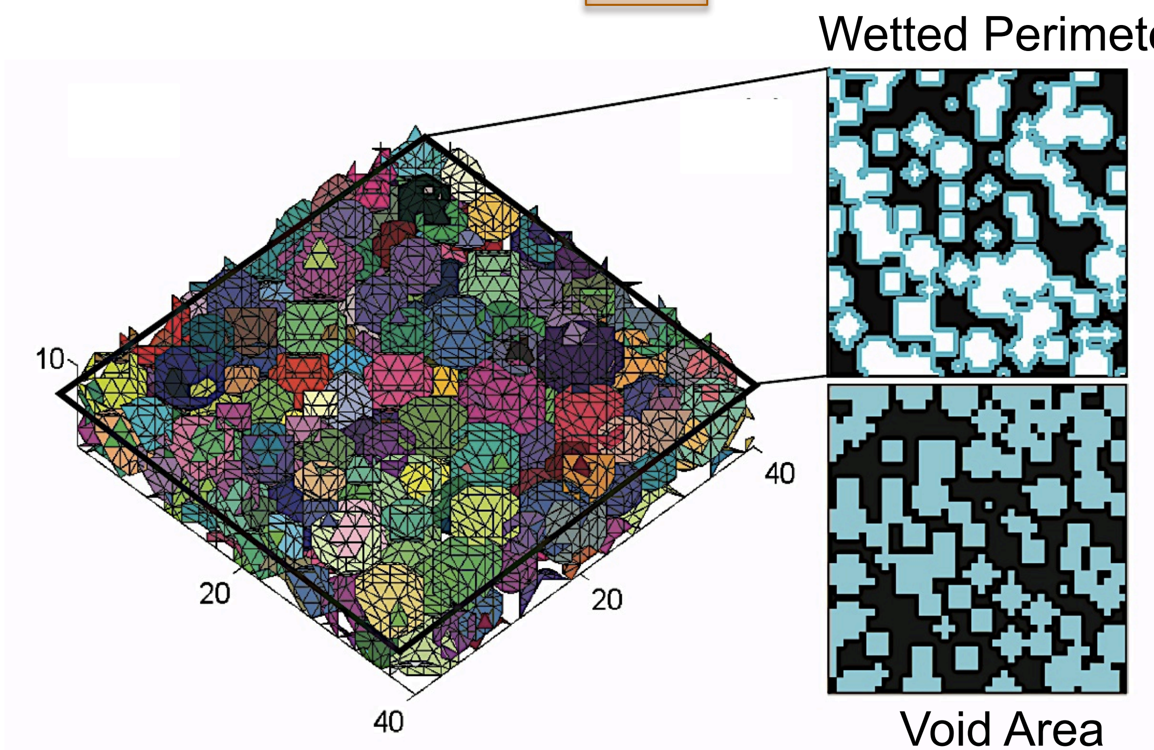

*Non-overlapping spheres*

*4.9 ± 3.6 µm diameter pores*

# Wetted perimeter from model to predict capillary forces



Wetted perimeter $F_c = \boxed{2\pi r}\sigma\cos(\alpha)$




Model predicts: 584 Pa *4.9 ± 3.6 μm diameter pores*

345 Pa *9.6 ± 6.7 μm diameter pores*

# Experiments validate model

tissue engineering and bone

Scaffold and material system

in vivo observations

in vitro test hypothesis

in vivo verify hypothesis

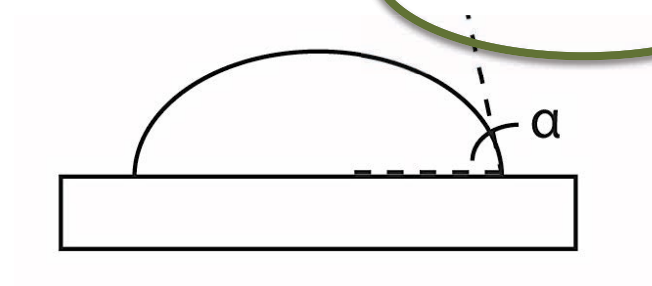

| Pore φ (μm) | P (Pa) measured | α (°) calculated |
|---|---|---|
| 4.9 | 588 | 89.3 |
| 9.6 | 412 | 89.2 |

$$\Delta P = \rho g \Delta h$$

Δh = 60 mm, 4.9 μm
Δh = 42 mm, 9.6 μm

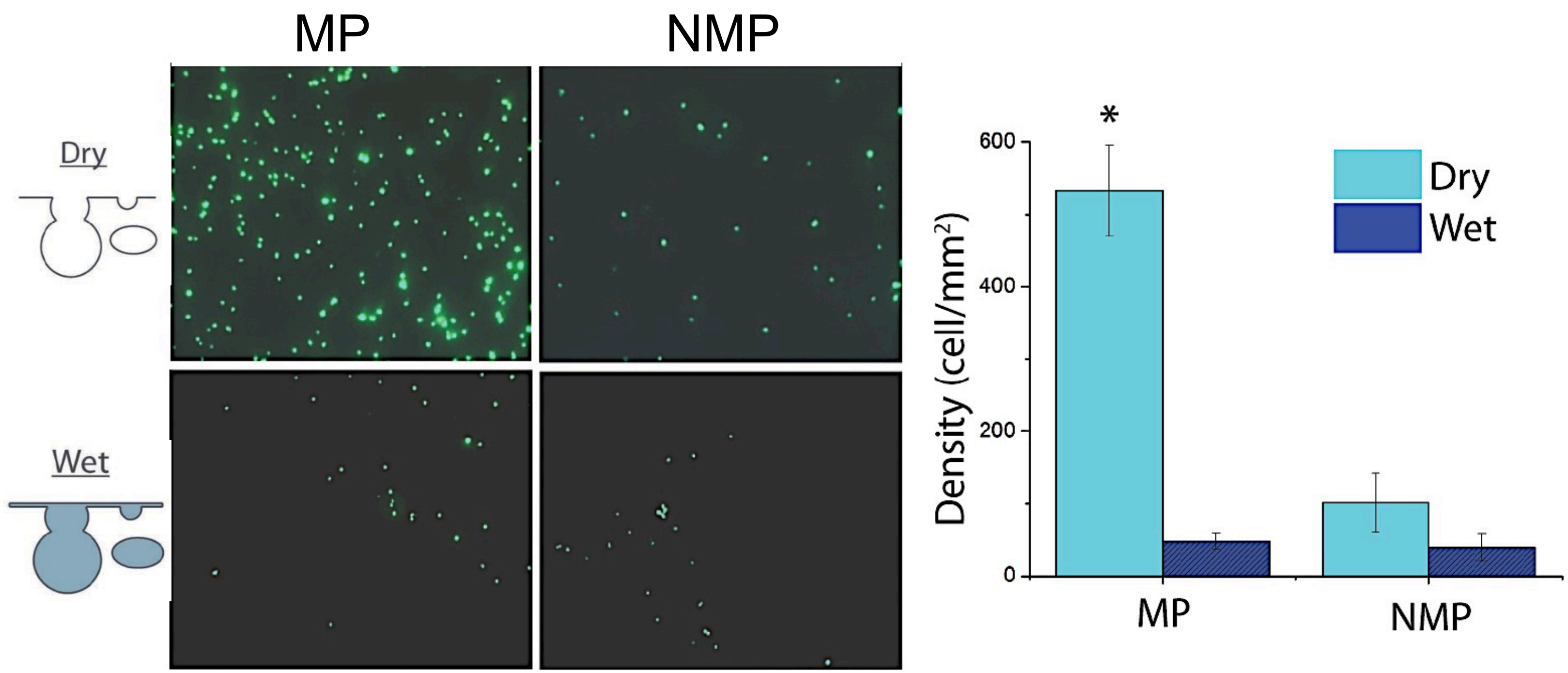
$$F_c = 2\pi r\sigma\cos(\alpha)$$

Measured α = 89.8±5.0



# Capillary forces localize cells to surface






D1 cells stained with cell tracker green

***Capillary forces, and not other surface characteristics (roughness, surface area), dominate the localization.***

# Cells penetrate micropores, depth cell-type dependent

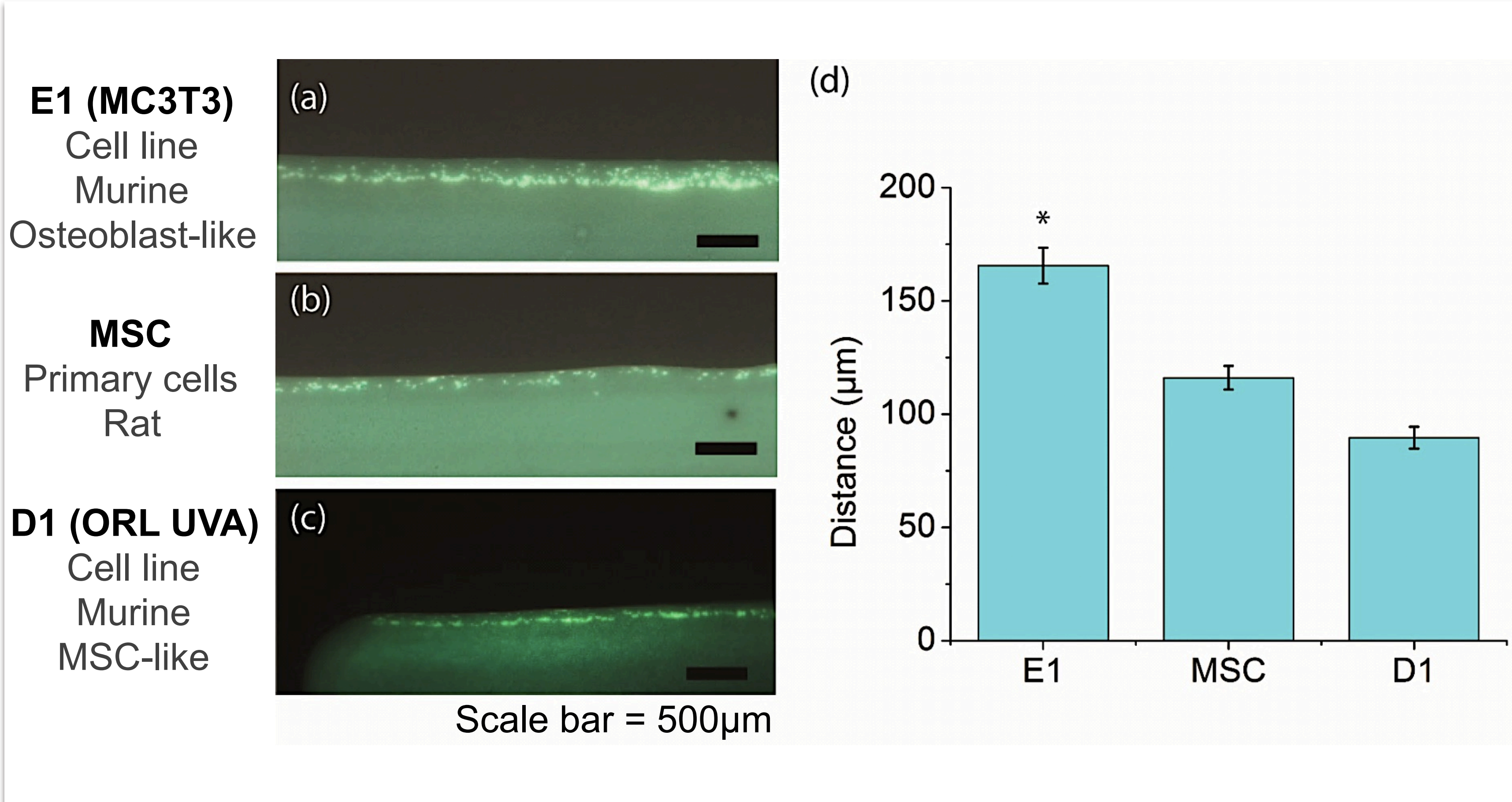
tissue engineering and bone

Scaffold and material system

in vivo observations

in vitro test hypothesis

in vivo verify hypothesis



# Penetration distance consistent with critical pressure

tissue engineering and bone

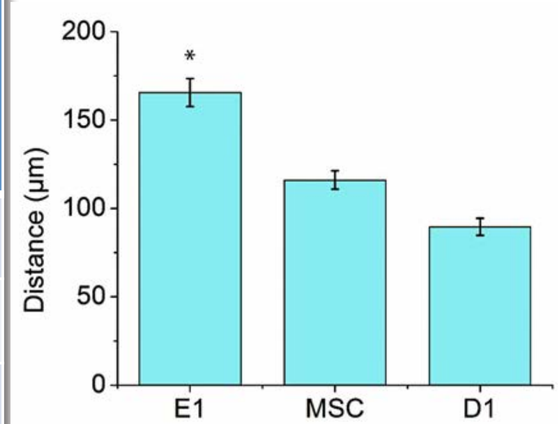
Scaffold and material system

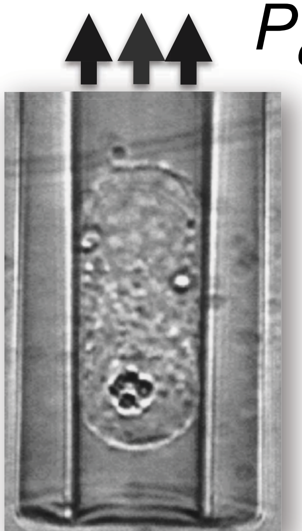
in vivo observations

in vitro test hypothesis

in vivo verify hypothesis

| Cell | $\gamma$ $10^{-6}$ (kg/s$^2$) | Rc (µm) | $P_{crit}$ calculated (Pa) | Distance measured (µm) |
|---|---|---|---|---|
| E1 (OB) | 520 | 6.9 | 265 | 165 |
| MSC | 520 | 11.5 | 326 | 116 |
| D1 (pre-OB) | N/A | 7.5 | >MSC | 89.6 |




$$P_{crit} = 2\gamma_{ten}\left(\frac{1}{R_p} - \frac{1}{R_c}\right)$$

*Pressure generated: 588Pa*

# Our series of studies…

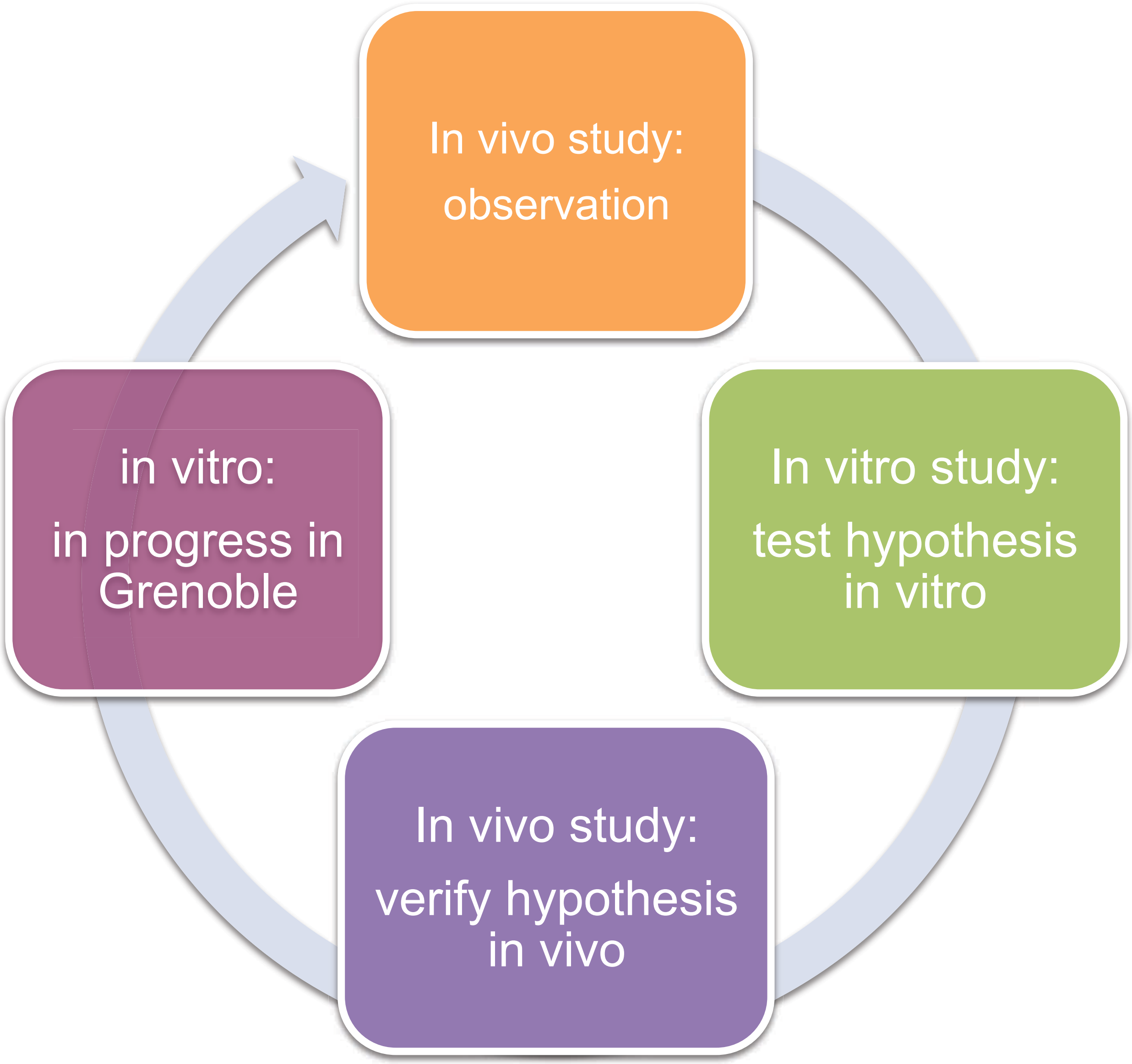
tissue engineering and bone

Scaffold and material system

in vivo observations

in vitro test hypothesis

in vivo verify hypothesis



# What role do capillary forces play in vivo?

tissue engineering and bone

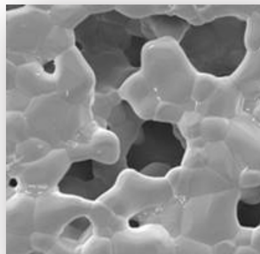
Scaffold and material system

in vivo observations

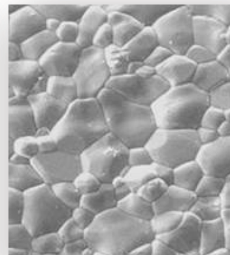
in vitro test hypothesis

in vivo verify hypothesis

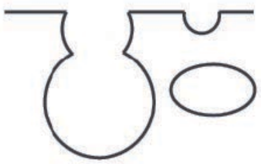
**MP**



**NMP**



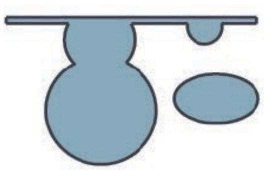
Dry



capillary forces

NO capillary forces

Wet



*suppressed* capillary forces

**8mm diameter**

Treatments
- Dry - MP (capillary forces)
- Wet - MP (suppressed)
- NMP (no capillary forces)

In defect:
- 15-30 minutes (no NMP)
- 3 weeks

# Cells penetrate DRY micropores *at implantation*

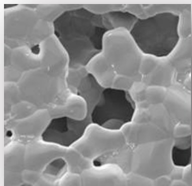
tissue engineering and bone

Scaffold and material system

in vivo observations

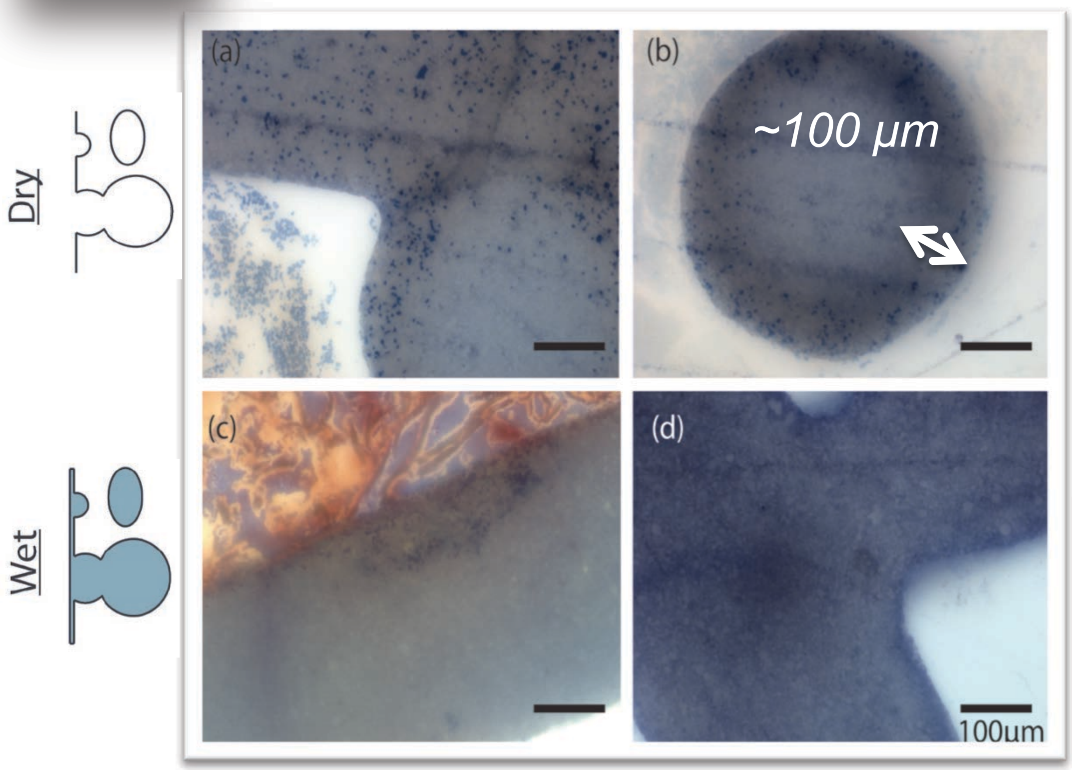
in vitro test hypothesis

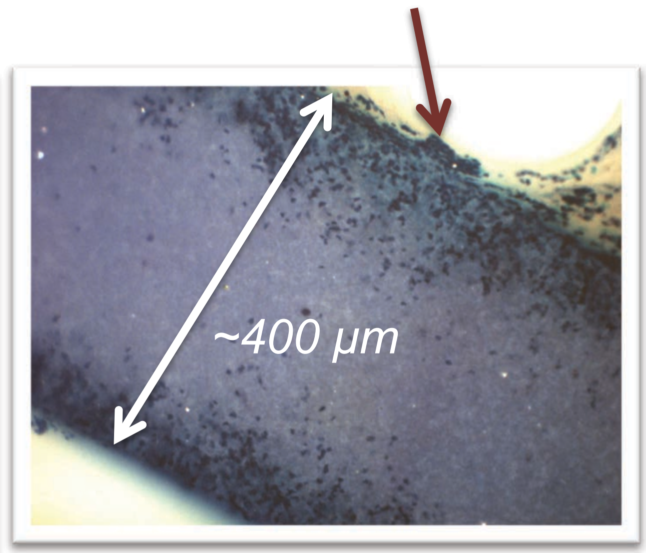
in vivo verify hypothesis



***MP***

*cell localization*




*15-30 min in defect, hard plastic embedding*

# Bone volume fraction and distribution (3 weeks)

tissue engineering and bone

Scaffold and material system

in vivo observations

in vitro test hypothesis

in vivo verify hypothesis

Unpublished data suppressed

# Quantification of radial bone distribution

tissue engineering and bone

Scaffold and material system

in vivo observations

in vitro test hypothesis

in vivo verify hypothesis

Unpublished data suppressed

# Capillary forces and bone growth

tissue engineering and bone

Scaffold and material system

in vivo observations

in vitro test hypothesis

in vivo verify hypothesis

Unpublished data suppressed

# Use MP and capillary forces to instruct bone formation

tissue engineering and bone

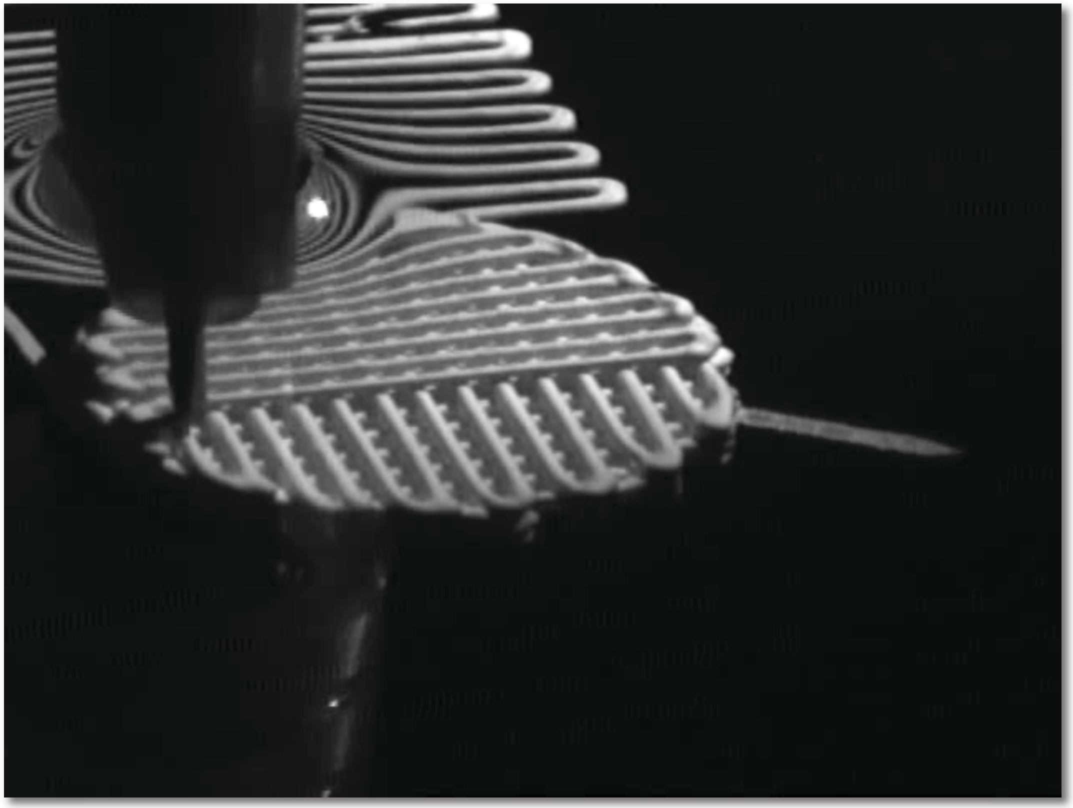
Scaffold and material system

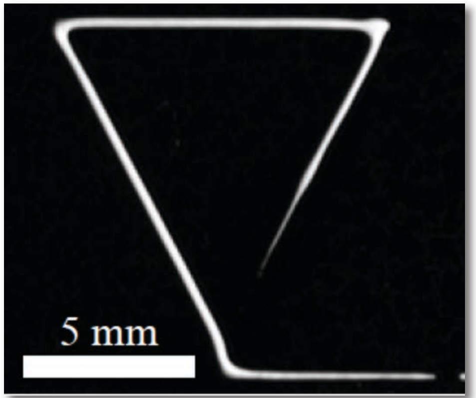
in vivo observations

in vitro test hypothesis

in vivo verify hypothesis

- Not possible with standard printing approach






Hoelzle et al, 2011

# Complex fabrication to instruct/direct bone formation

tissue engineering and bone

Scaffold and material system

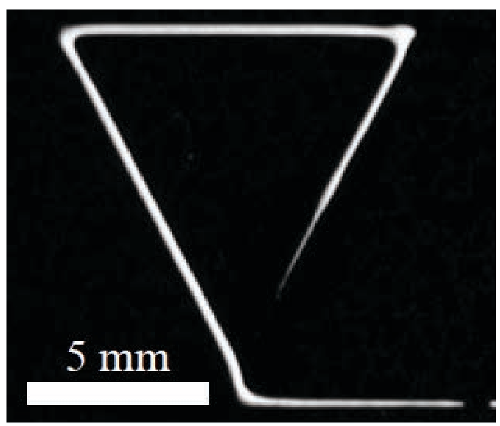
in vivo observations

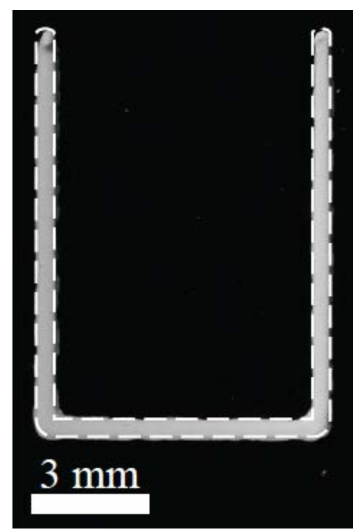
in vitro test hypothesis

in vivo verify hypothesis

- Vision-based, iterative learning control for multiple materials

1




Hoelzle et al, 2011




53

# Complex fabrication to instruct/direct bone formation

tissue engineering and bone

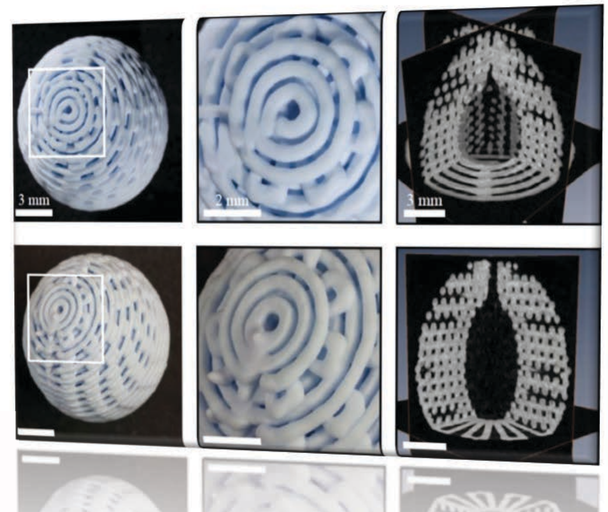
Scaffold and material system

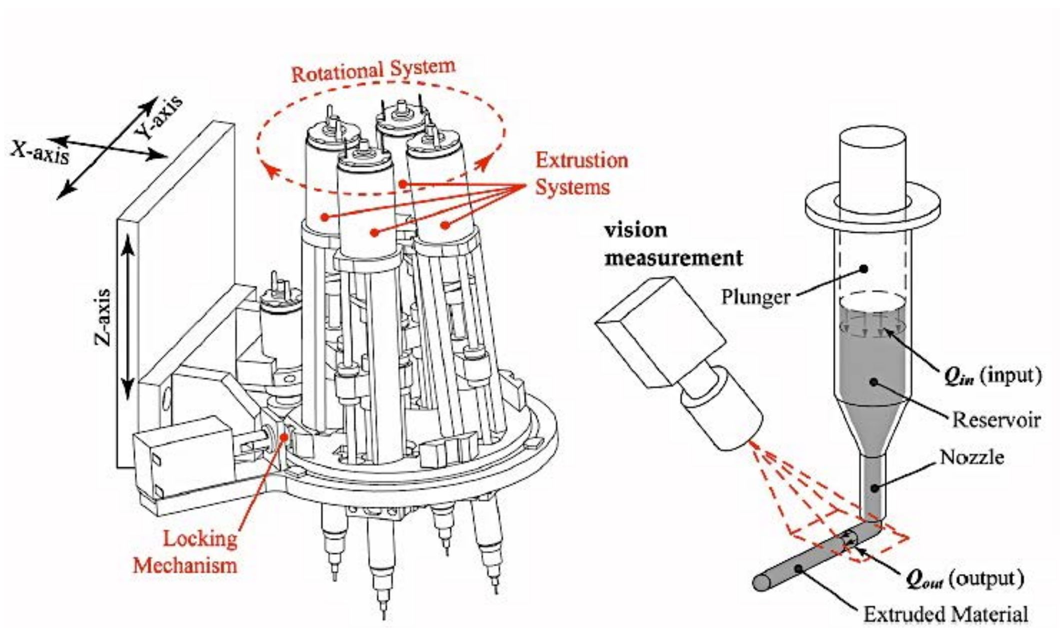
in vivo observations

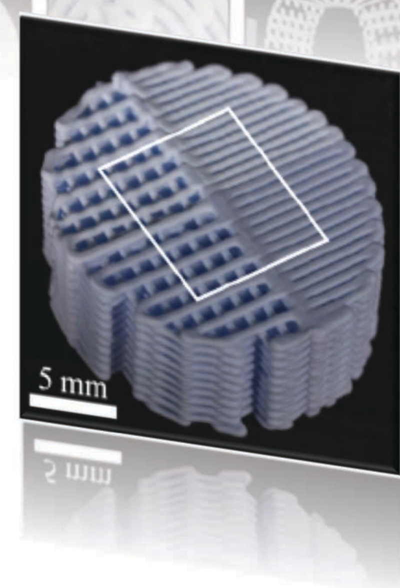
in vitro test hypothesis

in vivo verify hypothesis

- Now can make complex, multi-material structures
- Use patterns to instruct bone growth
- Yield heterogeneous characteristics (like bone)




Hoelzle et al, 2011

# Microporosity and capillarity – to instruct bone growth in MP domains vs Non-MP domains

tissue engineering and bone

Scaffold and material system

in vivo observations

in vitro test hypothesis

in vivo verify hypothesis

Unpublished data suppressed

# In summary

tissue engineering and bone

Scaffold and material system

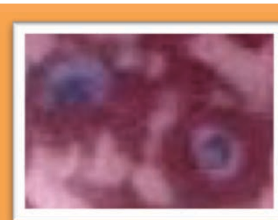
in vivo observations

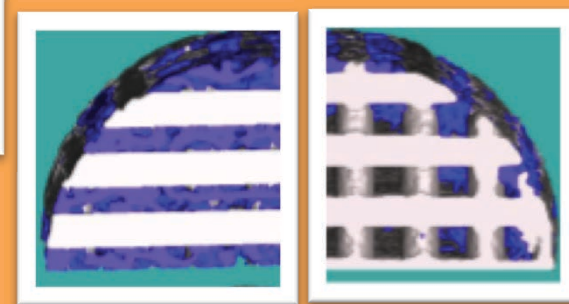
in vitro test hypothesis

in vivo verify hypothesis

**In vivo observations:**

* Bone and cells in micropores
* Bone growth enhanced w/ micropores
* Multiscale osteointegration





***How do cells get in?***

in vitro:

in progress in Grenoble

In vitro study:

test hypothesis in vitro

In vivo study:

verify hypothesis in vivo

# In summary

tissue engineering and bone

Scaffold and material system

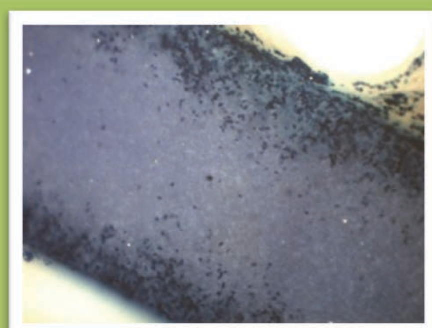
in vivo observations

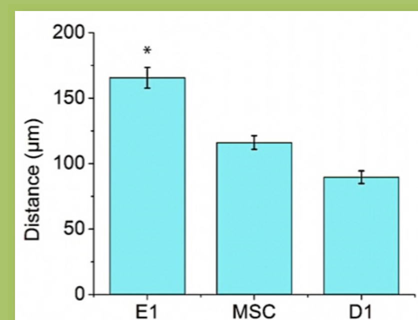
in vitro test hypothesis

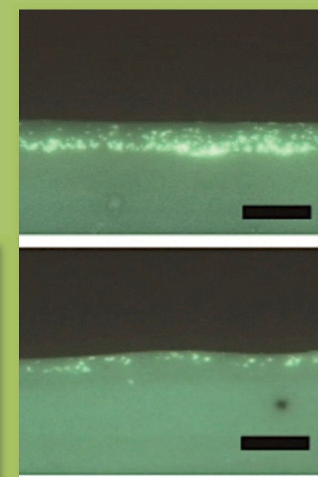
in vivo verify hypothesis

In vivo study: observation

In vitro
* Capillary forces pull in cells
* Physical model explains
* Penetration depth is cell type specific, consistent with critical pressure





in vitro:

in progress in Grenoble

In vivo study:

test hypothesis in vivo

***Does it influence growth?***
***Can they be used to pattern bone?***

# In summary

tissue engineering and bone

Scaffold and material system

in vivo observations

in vitro test hypothesis

in vivo verify hypothesis

in vitro: in progress in Grenoble

In vivo study: observation

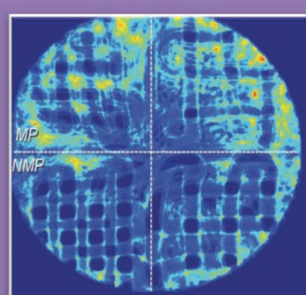
In vitro study: test hypothesis in vitro

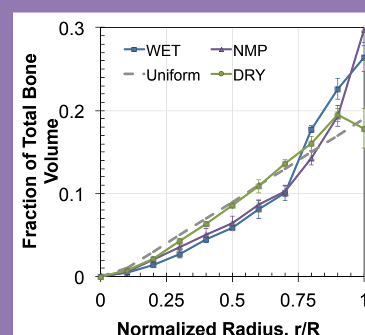
***Does it influence growth?***
***Can they be used to pattern bone?***

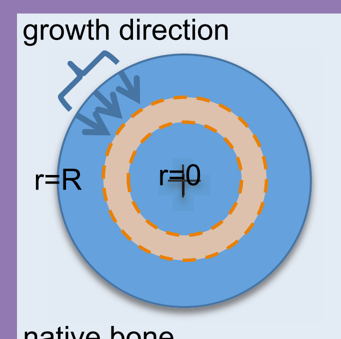
***In vivo***

* Scaffolds with active capillarity have better bone distribution and more complete growth

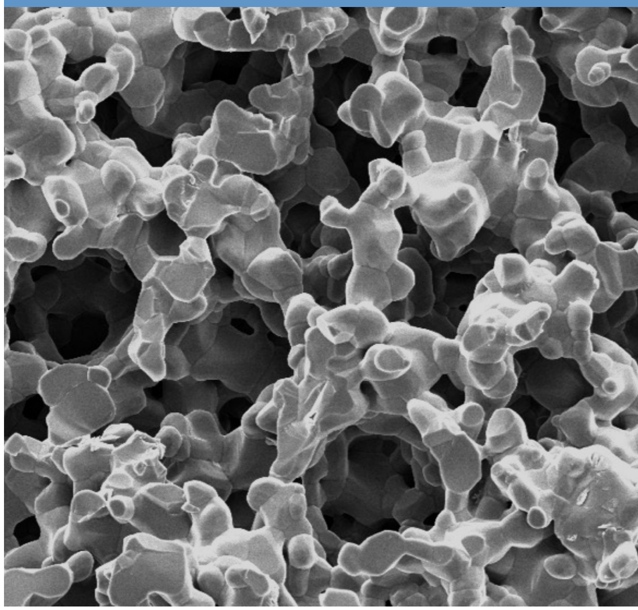
* This mechanism can be used to pattern growth in complex scaffolds

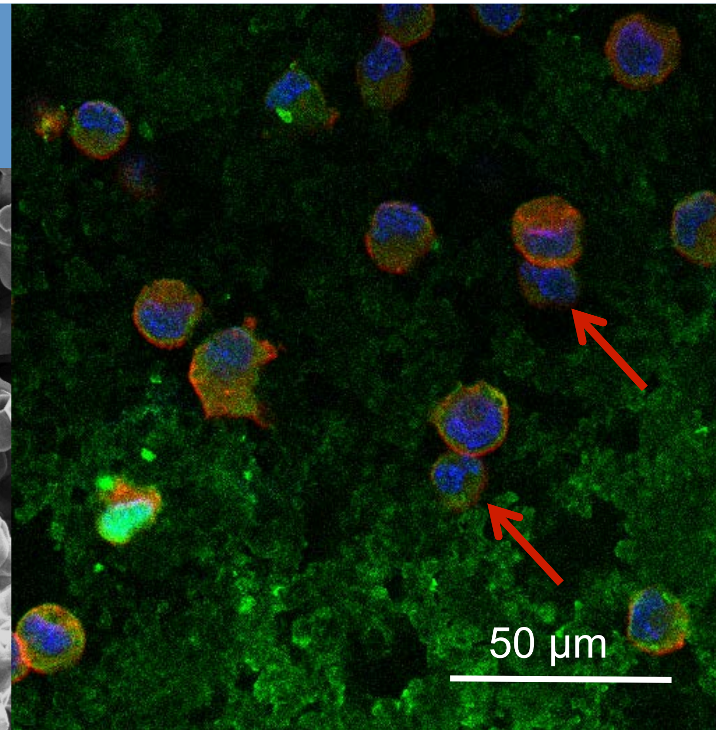


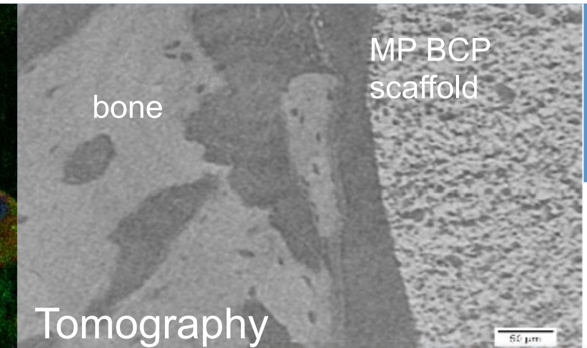



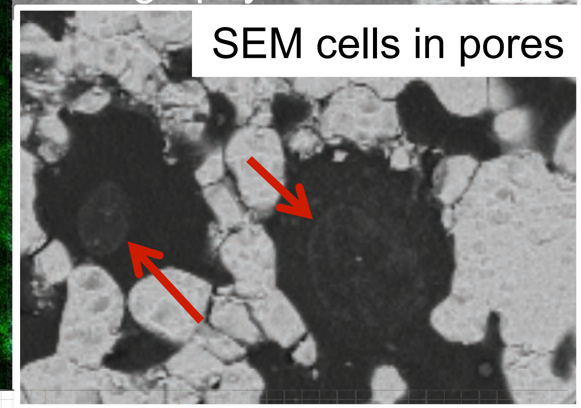



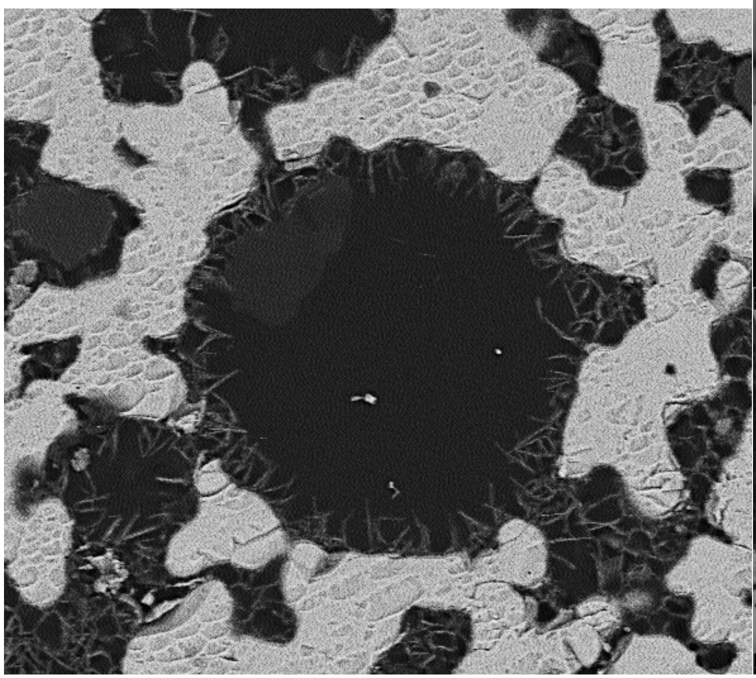
# In Grenoble…

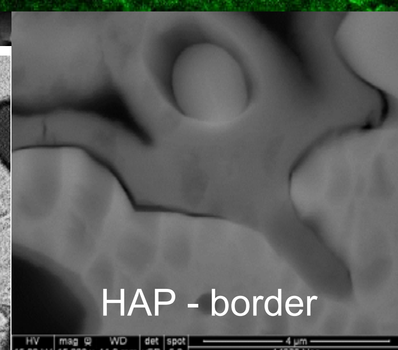


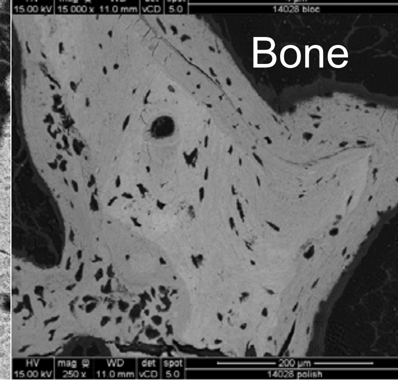


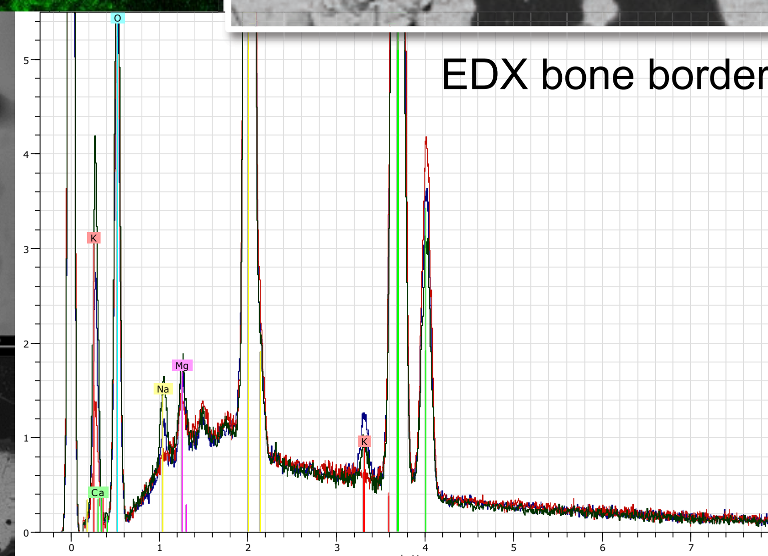






**Ca/P Ratios:**

- HAP : 1.37 $\pm$ 0.03 (N=6 measures)
- Border: 1.32 $\pm$ 0.06 (N=10 measures)
- Bone : 1.25 $\pm$ 0.02 (N=8 measures)

# I hope you learned something new about…

tissue engineering and bone

Scaffold and material system

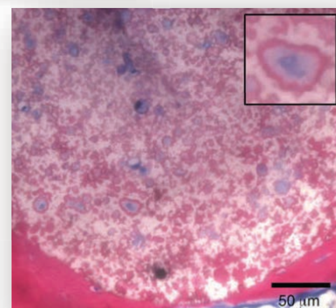
in vivo observations

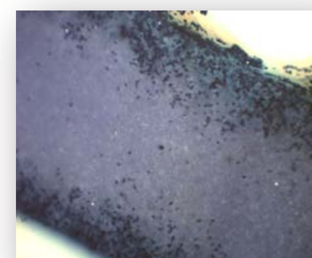
in vitro test hypothesis

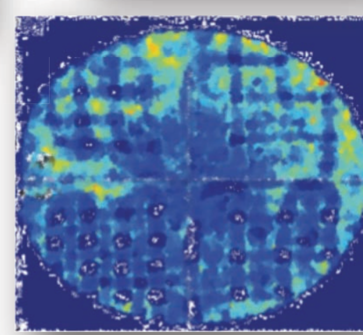
in vivo verify hypothesis

- Bone tissue engineering
  - Why we care
  - Challenges
  - Current solutions


- Our unique approach
  - Multi-scale osteointegration
  - Use of capillary forces
  - Use of microporosity and manufacturing technology to pattern bone





# Acknowledgements

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**Sheeny Lan Levengood, PhD**

***<u>Students (current or former)</u>***
***Samantha Polak***, Aaron Maki, Michael Poellmann,
**Laurie Rustom** (Bioengineering, UIUC)
***Sheeny Lan Levengood***, *PhD*
(Washington University)
***Dave Hoelzle***, *PhD*
(Assist Prof, Mechanical Engineering, Notre Dame)

***<u>Faculty</u>***
**Guy Genin, PhD (Mechanical Engineering, Wash U)**
**Mike Talcott, DMV, (Wash U Medical School)**
**Andrew Alleyne, PhD (Mechanical Science and Engineering, UIUC)**
Mathew Wheeler, PhD (Animal Sciences, UIUC)
Michael Goldwasser, MD (Carle Foundation Hospital)
Sherrie Clark-Deener, PhD (Vet. Medicine, Va Tech)
Bill Murphy, PhD (Bioengineering, UW Wisconsin)

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# Questions?