Processing Considerations for Degradable Materials: The Many Profiles of 'Polylactide'

Karen J.L. Burg, Ph.D.
Hunter Endowed Chair, Bioengineering
Director, Institute for Biological Interfaces of Engineering
Clemson University
Clemson, South Carolina

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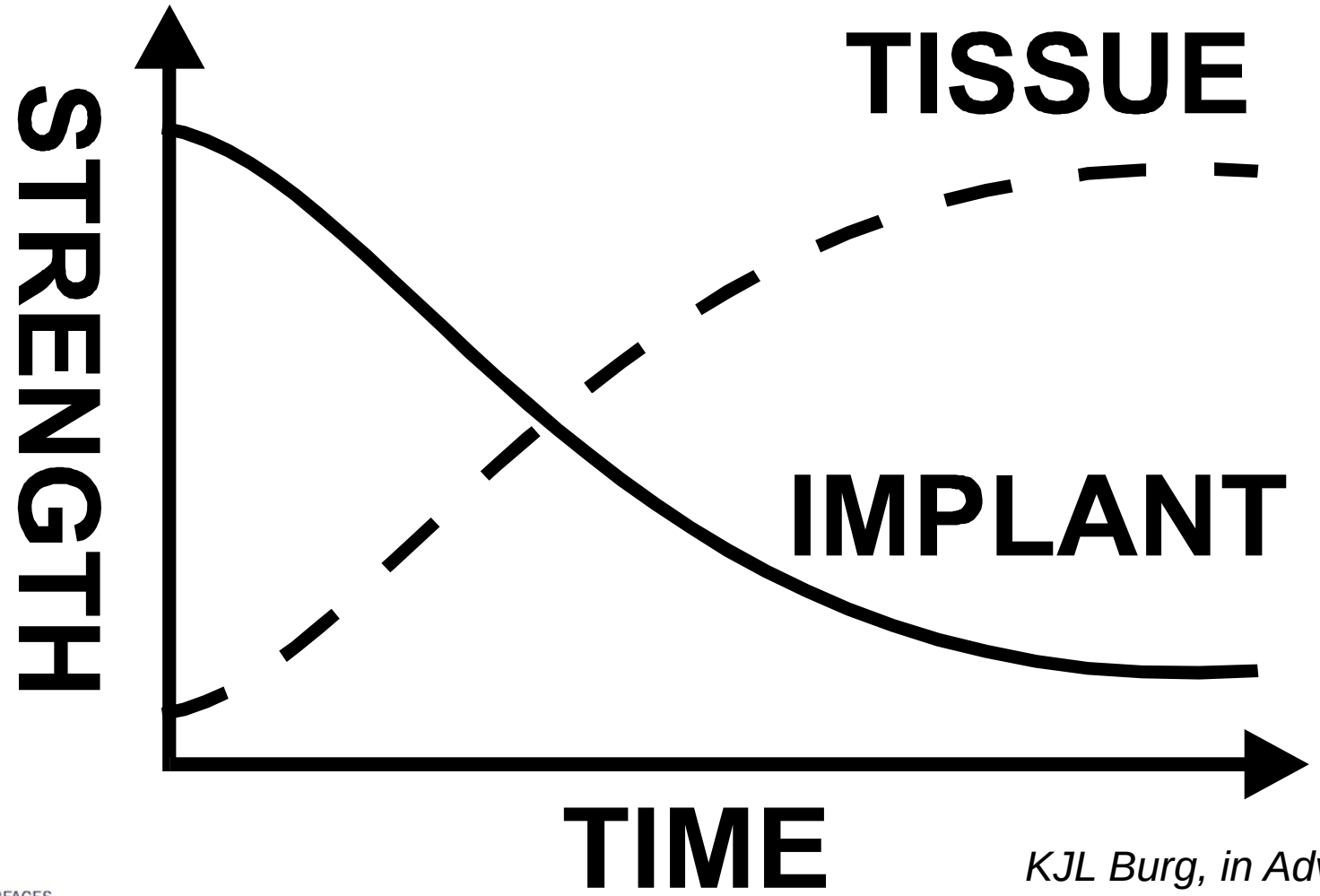
The IBIOE mission is to develop, study, and translate tissue test systems to understand, treat, and prevent the disease process.

Test System Functions

- Diagnose disease state
- Study disease patterns
- Study normal tissue
- Develop therapies
- Develop preventatives
- Test new device

Complexity will vary based on use (basic science, commercial, clinical)

“Polylactide Was Used in the Study”



KJL Burg, in Adv Polym Mater, CRC Press: 2003

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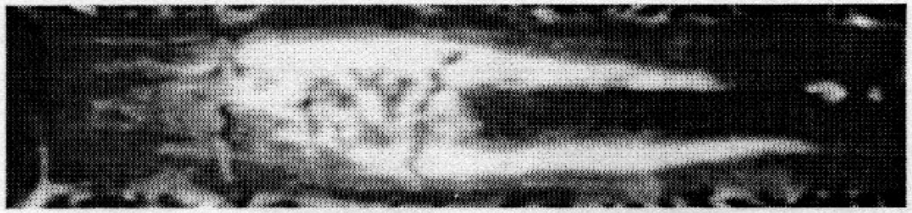
Define Polylactide (PL)?

- Example: surface erosion versus bulk erosion

Nonoriented PL film (As received: 268,000 Da); 58,000, 2 months



Oriented PL film (As received: 268,000 Da); 58,000 Da, 8 months

Surface-center differential and resulting release of acidic by-products affects cell-material "handshake"

KJL Burg et al., Cells Mater, 9(2):127-134. 1999.

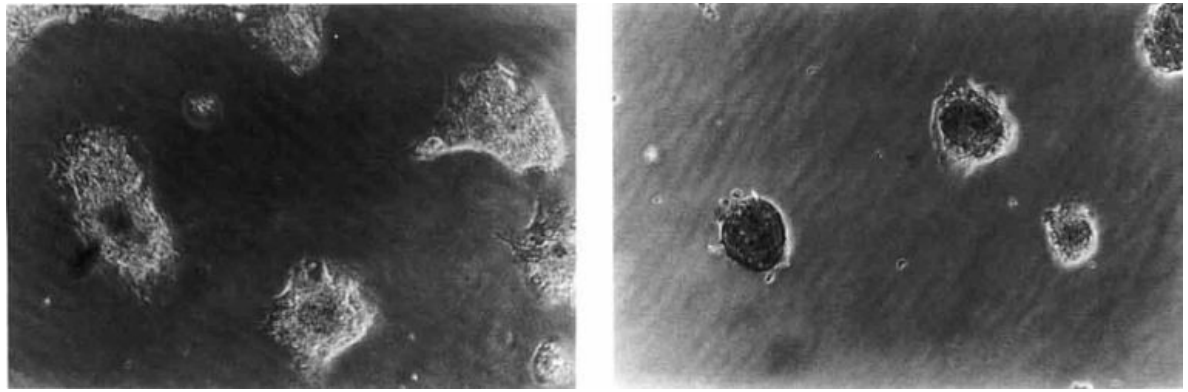
Material is Only a "Tool" Perspective

- "Gel permeation chromatography and differential scanning calorimetry were performed on the polylactide for no apparent reason. This paper is focused on the biology of the adipocytes, and the data does not tie in to anything else in the paper"

Anonymous reviewer, 2011

Biomaterial is a Proactive Collaborator

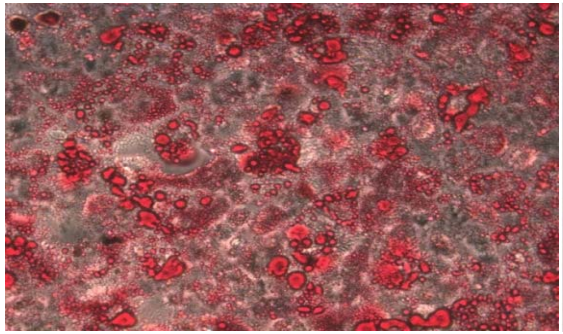
- Park & Griffith, Journal of Biomedical Materials Research, 1996
  - Hepatocyte spheroid formation faster on crystalline polylactide substrates
  - Growth rate of 3T3 fibroblasts lower on crystalline substrates
  - 45,000Da, PD 1.9

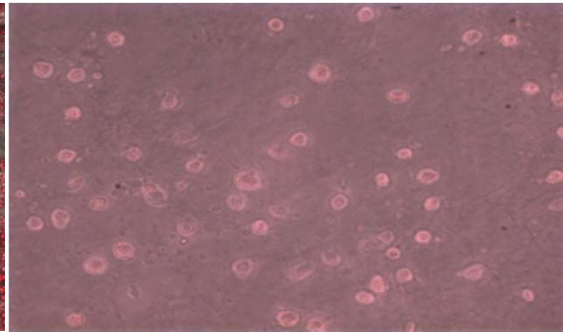


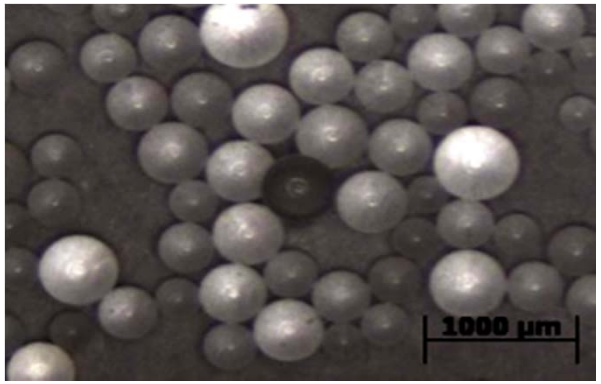
120 hr, 100X; amorphous (L), crystalline (R)

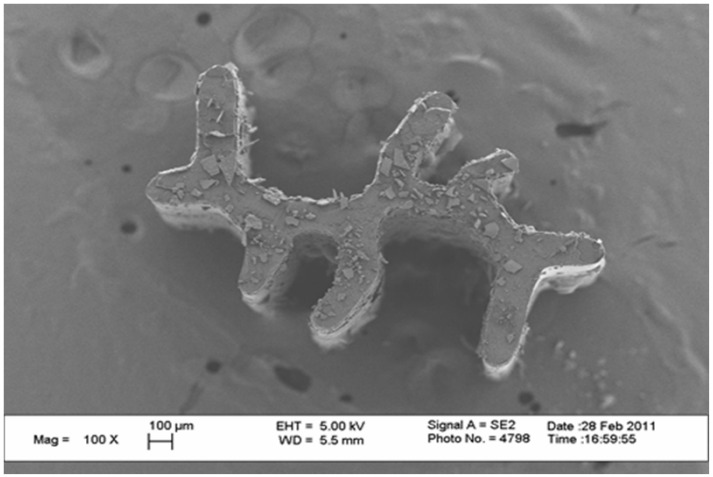
Biomaterial and Process Matters!

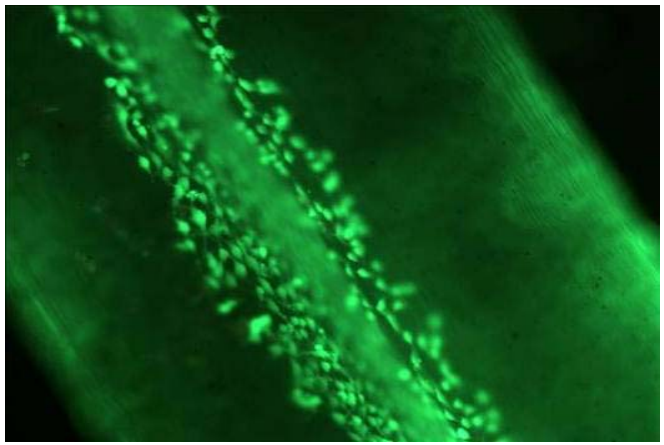
- Chemistry, charge, form, crystallinity topography, stiffness, molecular weight











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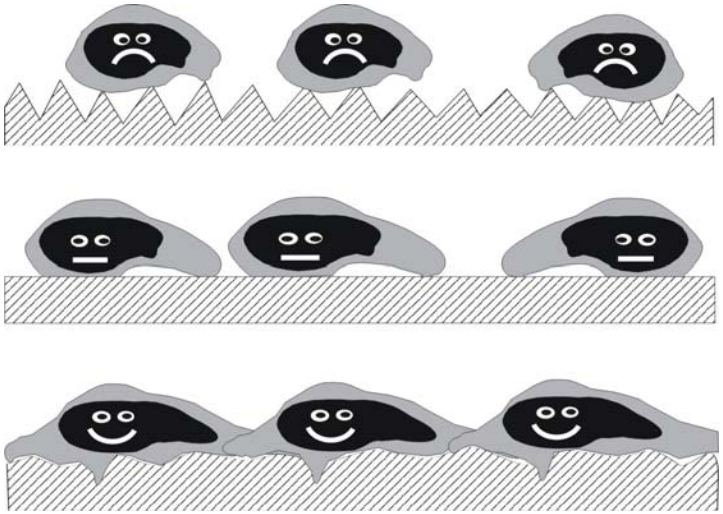
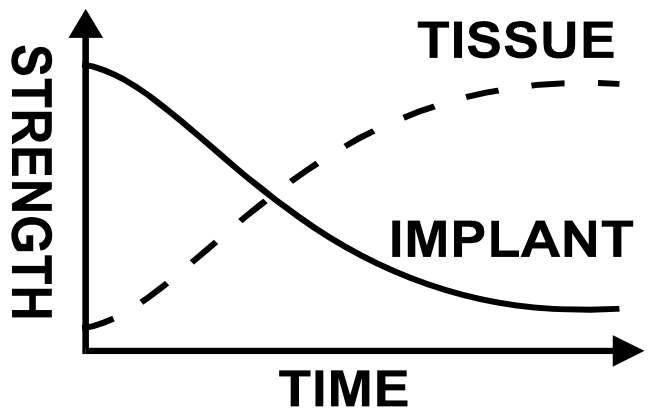
Factors Affecting Cellular Attachment

- Modulus
- Molecular weight
- Crystallinity
- Cross linking density
- Charge
- Chemistry
- Topography



Dynamic Interaction



KJL Burg, in Adv Polym Mater, CRC Press: 2003; Chaubey & Burg, in Encycl Biomater Biomed Eng, Taylor & Francis. 2008.

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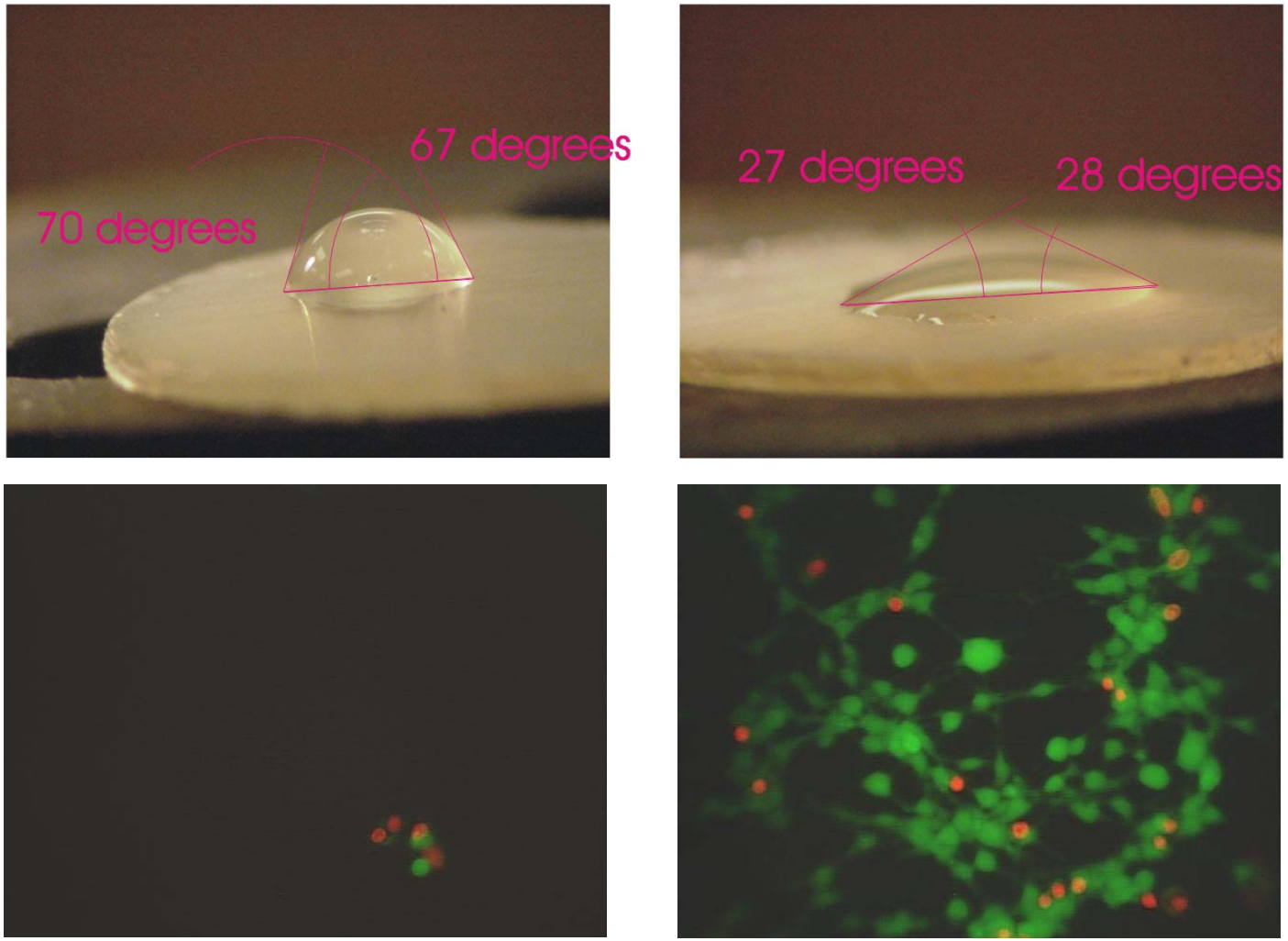
Cell-Material Interaction is Dynamic



Renshaw & Burg, Trans 28th Ann Meeting Soc Biomater, 5/2002.

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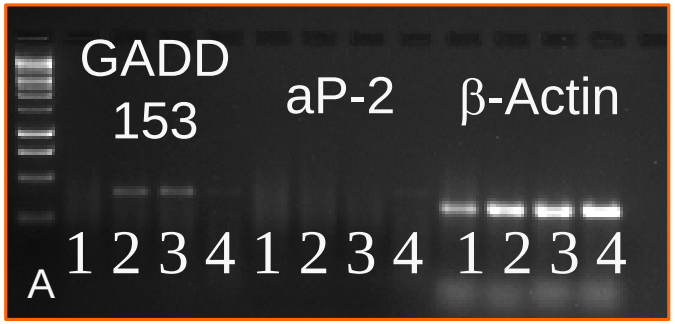
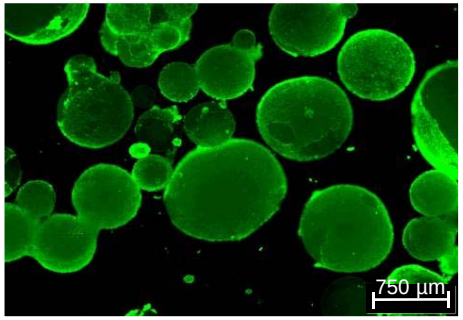
270,000 Da, amorphous (L), semi-crystalline (R), 3T3M cells, 5 days

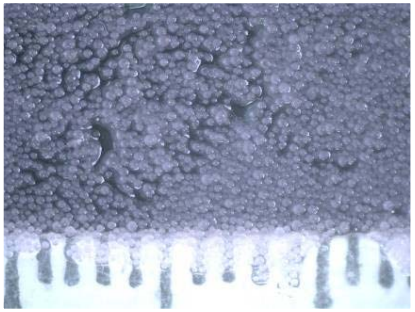
Biomaterial can Influence Gene Expression

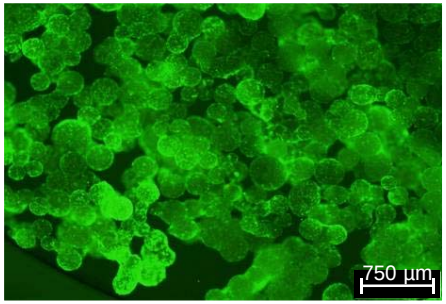


Polylactide beads, 10 days, no adipogenic inducer

Gelatin beads, 10 days, no adipogenic inducer







3T3-L1

GADD (early marker)
PPAR (mid to late marker)
aP-2 (late marker)

Burg et al., in Adipose Stem Cells & Regen Med. Springer: 2011.

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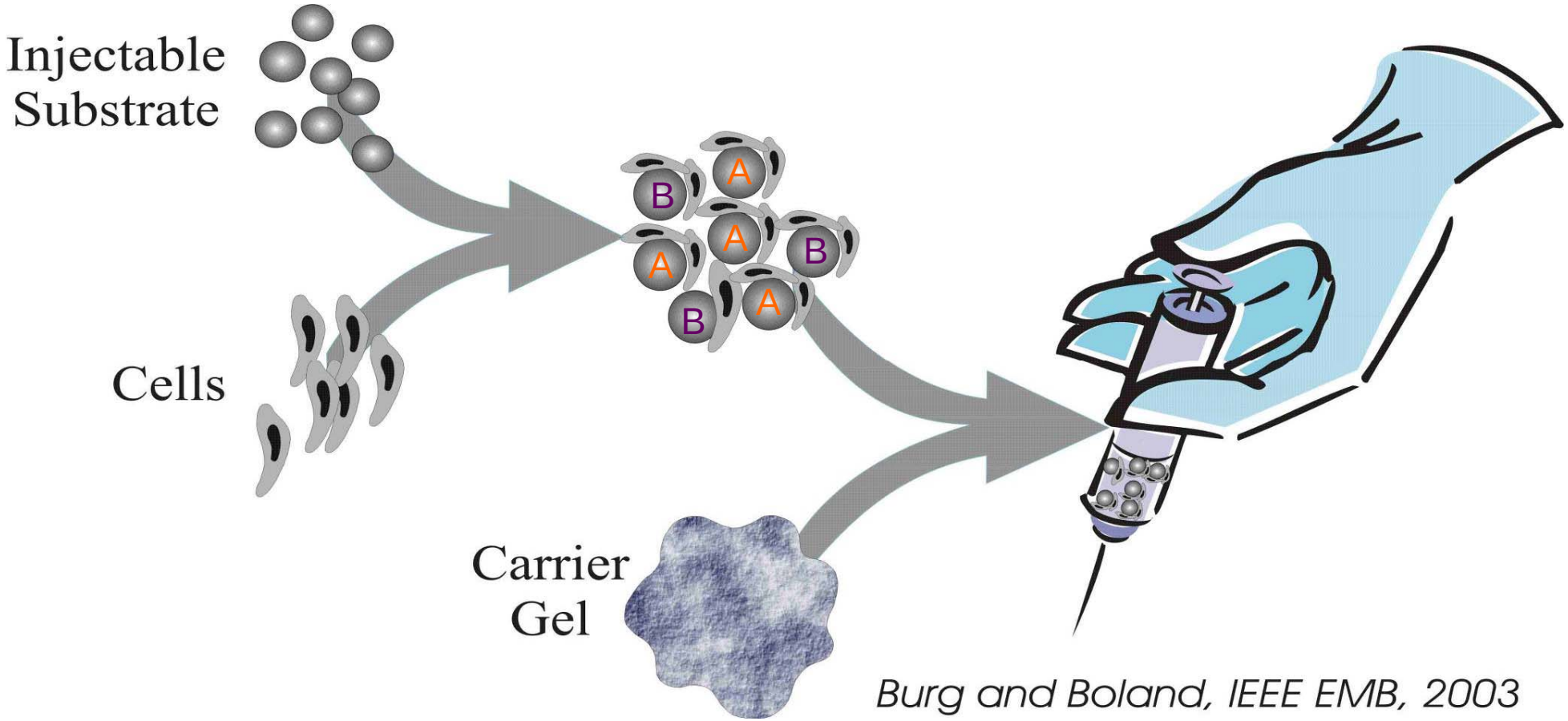
Injectable Engineered Tissue Systems



Burg and Boland, IEEE EMB, 2003

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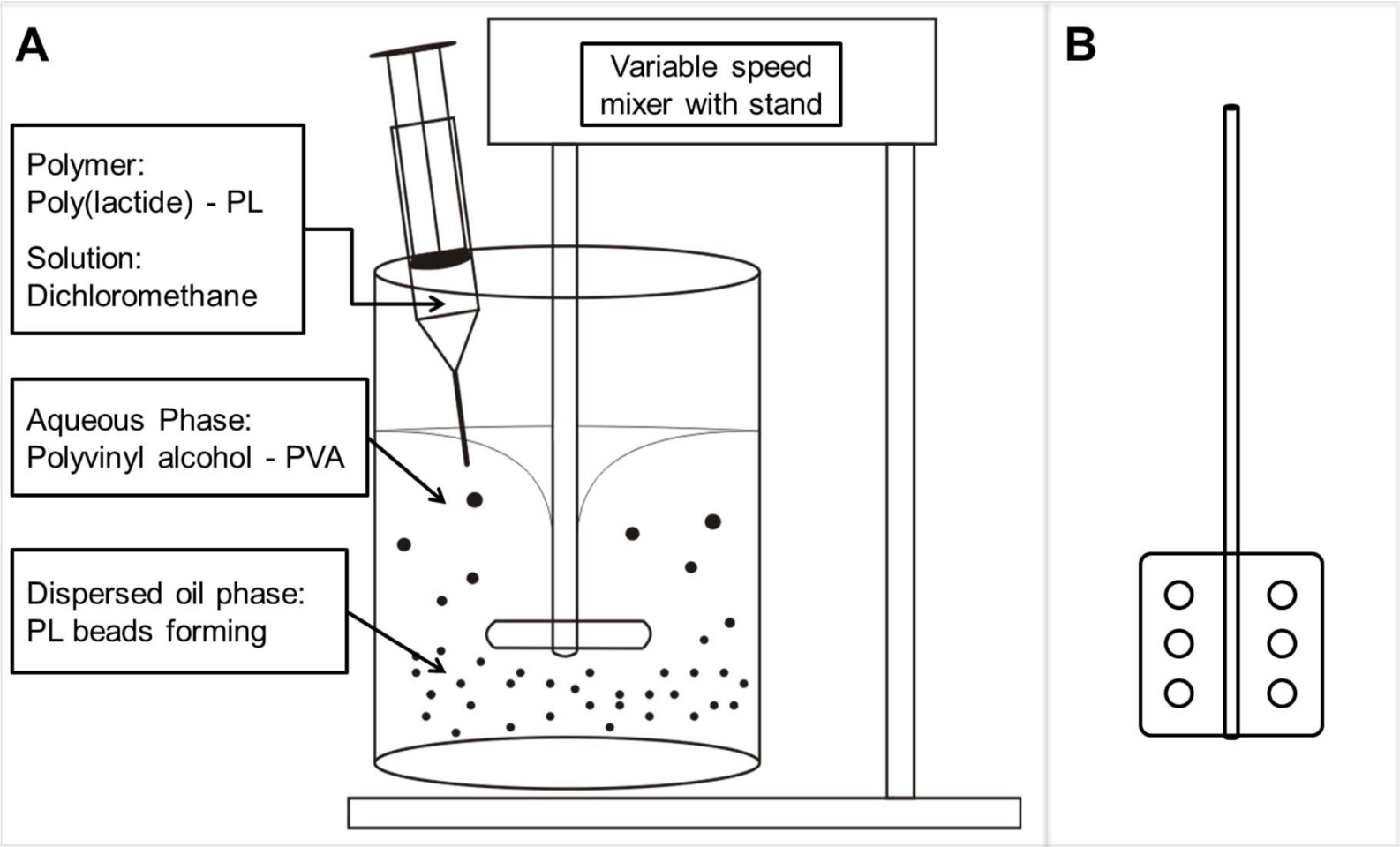
Common, Not Standard, Bead Processing Method



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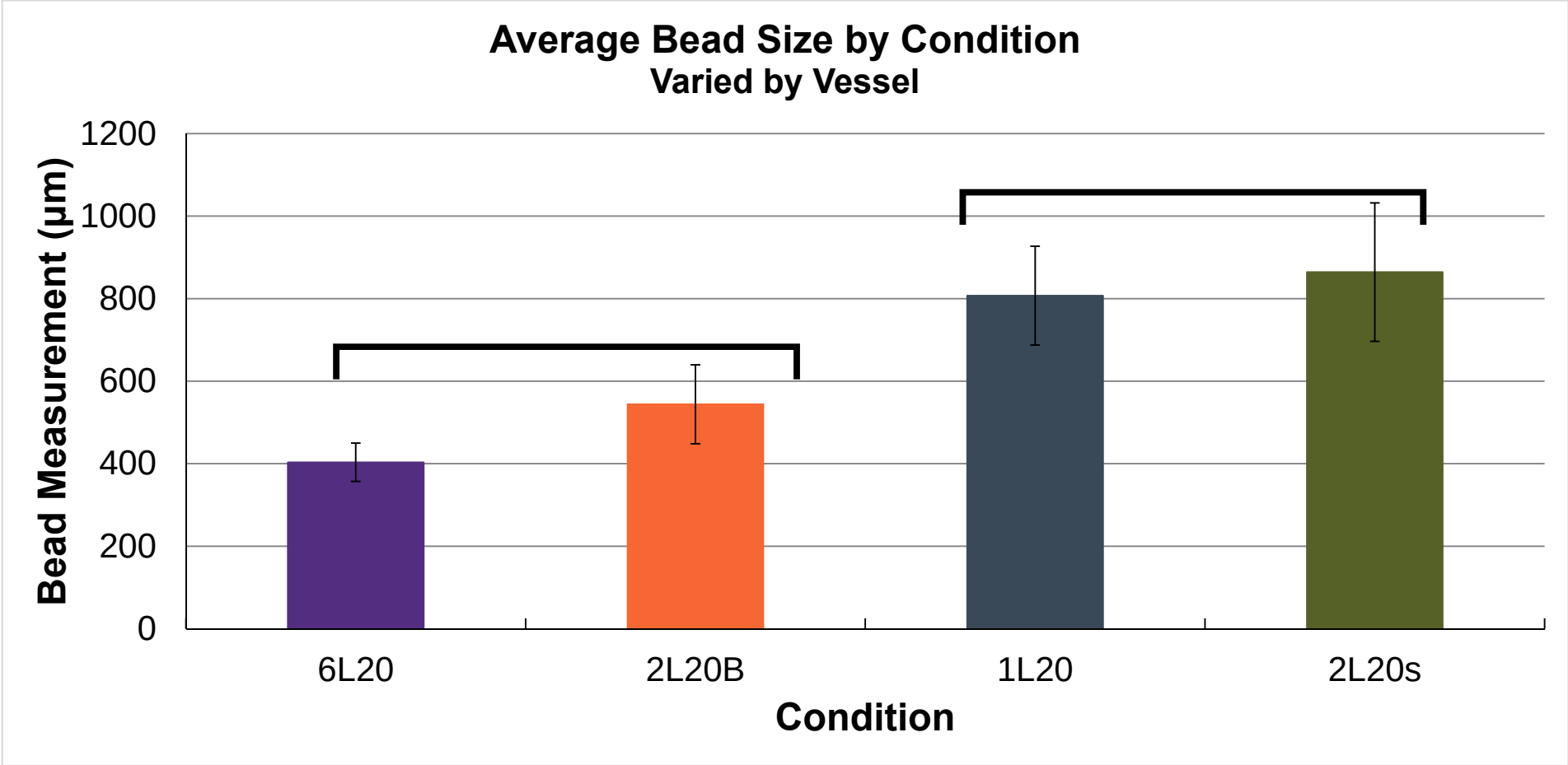
McCave et al., J Biomat Sci: Polym Ed, in review.

Processing Vessel Size Influences Bead Size



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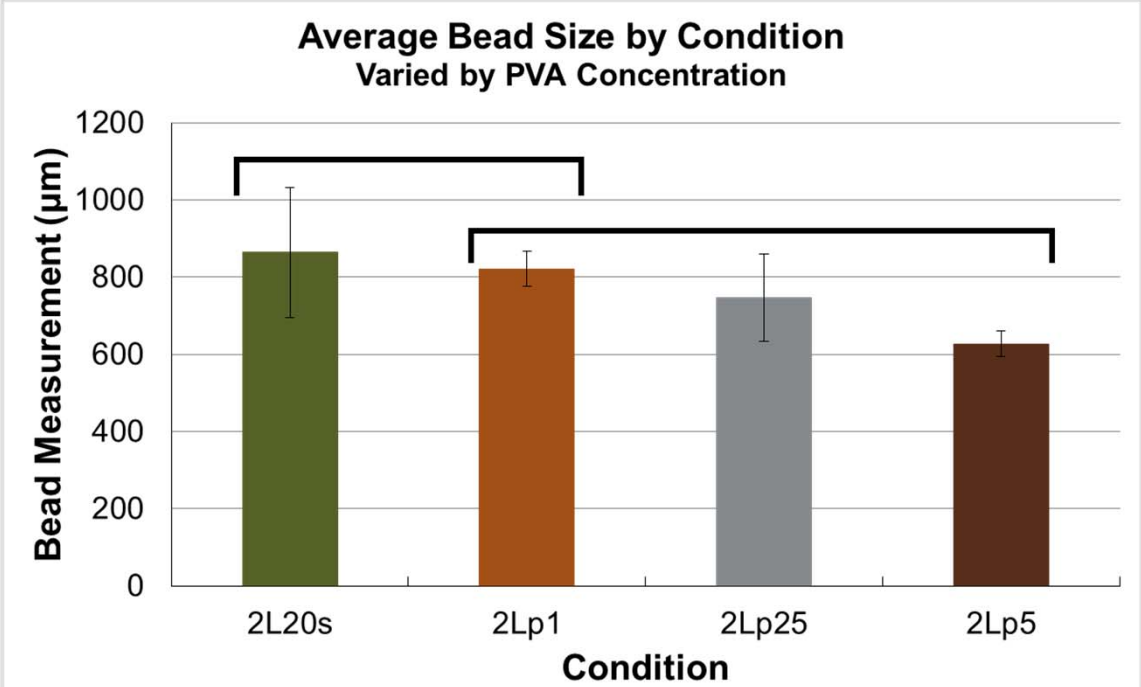
McCave et al., J Biomat Sci: Polym Ed, in review.

Processing Components Affect Bead Shape, Size



McCave et al., J Biomat Sci: Polym Ed, in review.

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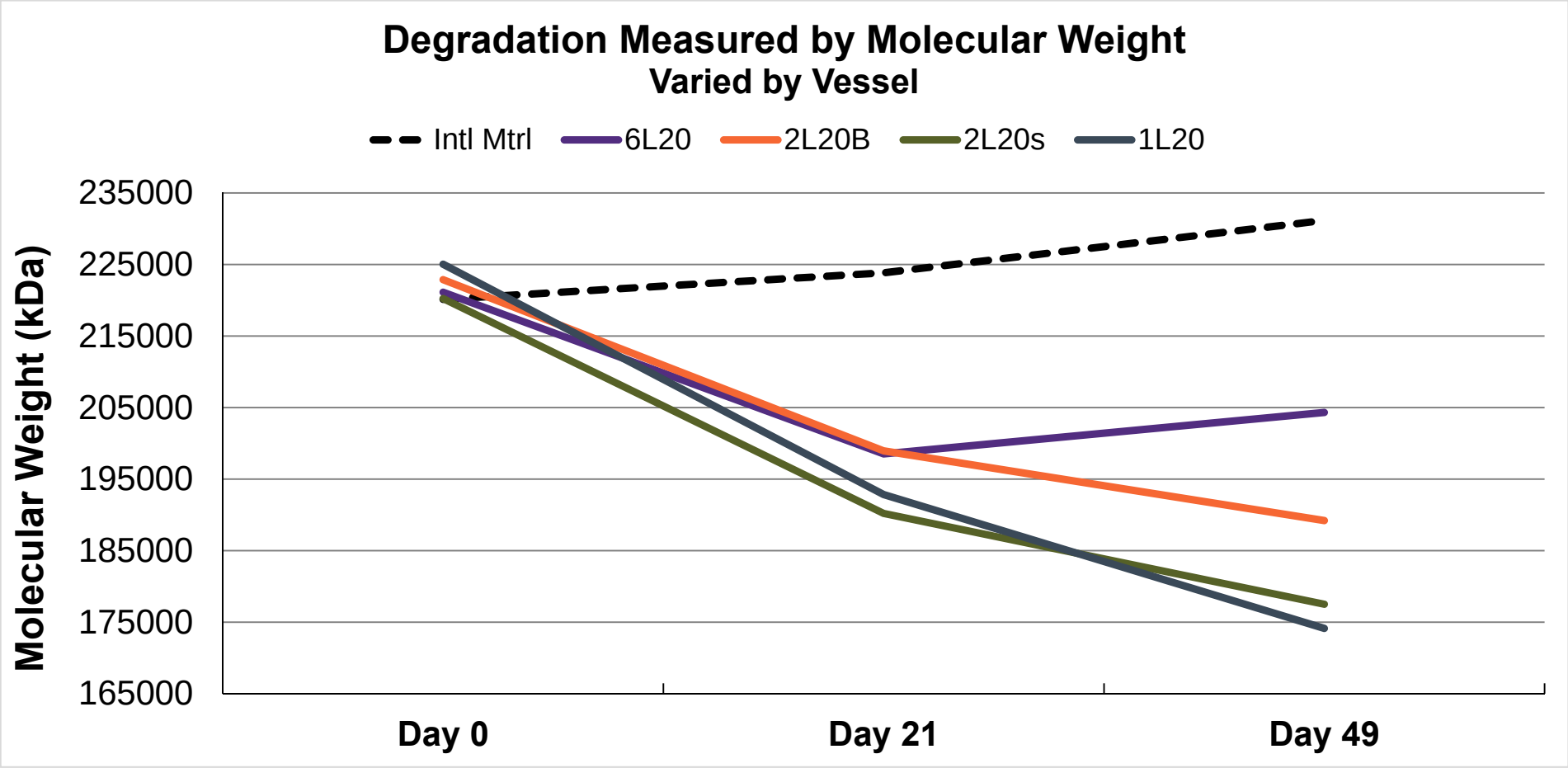
Processing Conditions Affect Bead Degradation



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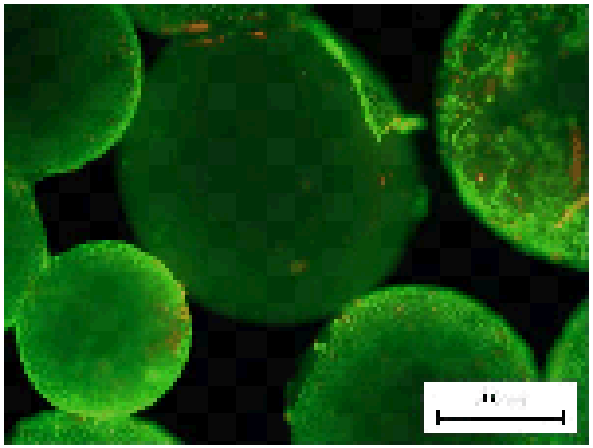
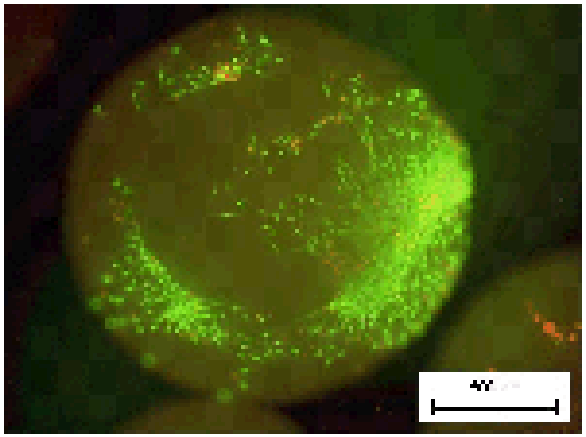
McCave et al., J Biomat Sci: Polym Ed, in review.

Cell and Biomaterial Influence

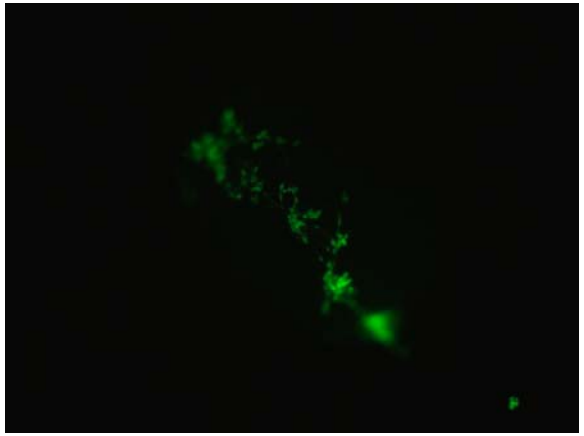


D1 on PDLL
195,000 Da
Day 4, 50X



MC3T3 on PDLL
195,000 Da
Day 4, Amorphous
50x

D1 on PL
Day 2, Semi-crystalline
50X



Thomas et al., J Biomater Sci: Polym Ed, 22:589-610, 2011; McCave et al., J Biomat Sci: Polym Ed, in review.

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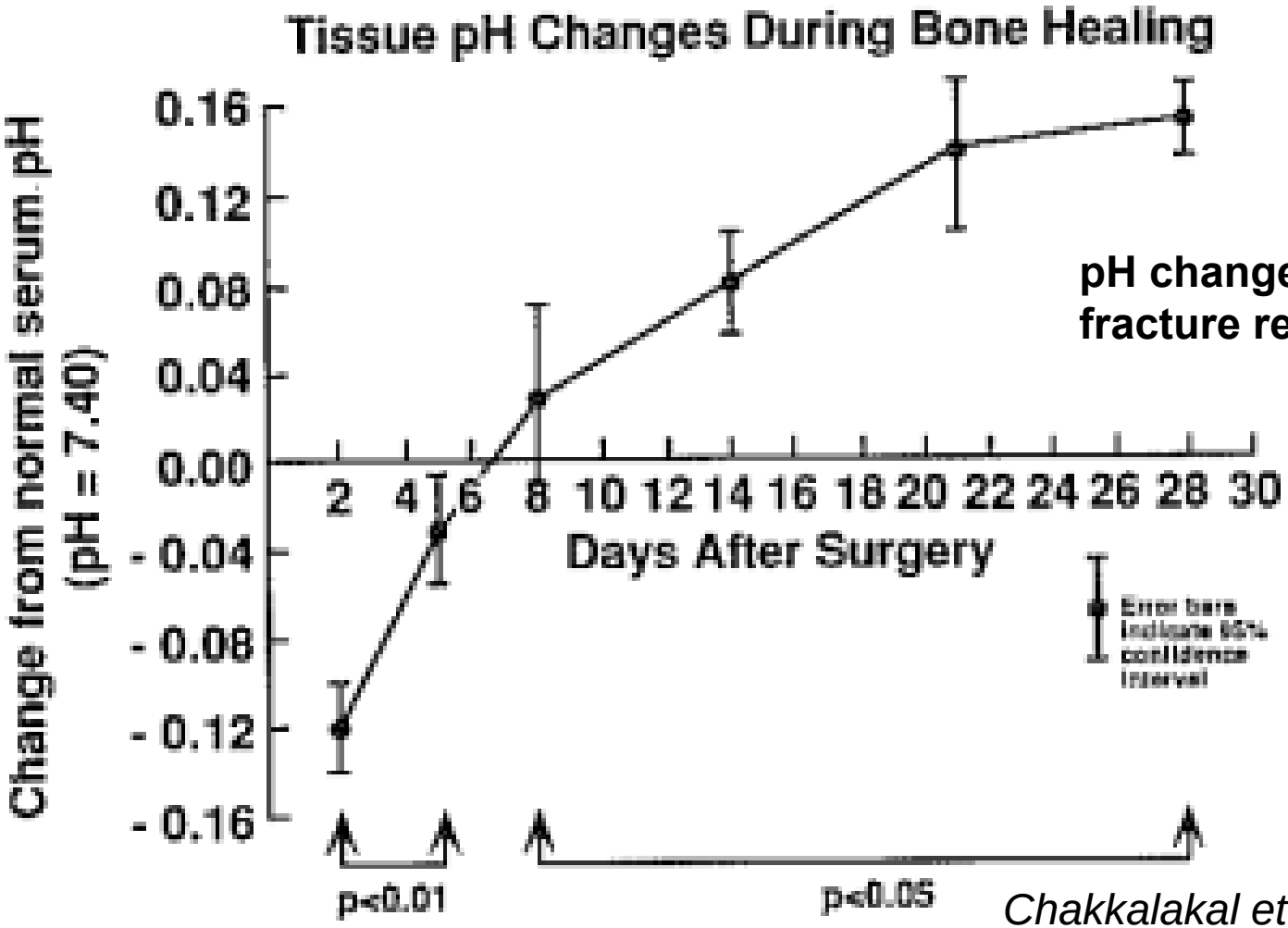
Biomaterials by Design



pH changes in a murine fracture repair model

Chakkalakal et al., JBMR, 1994

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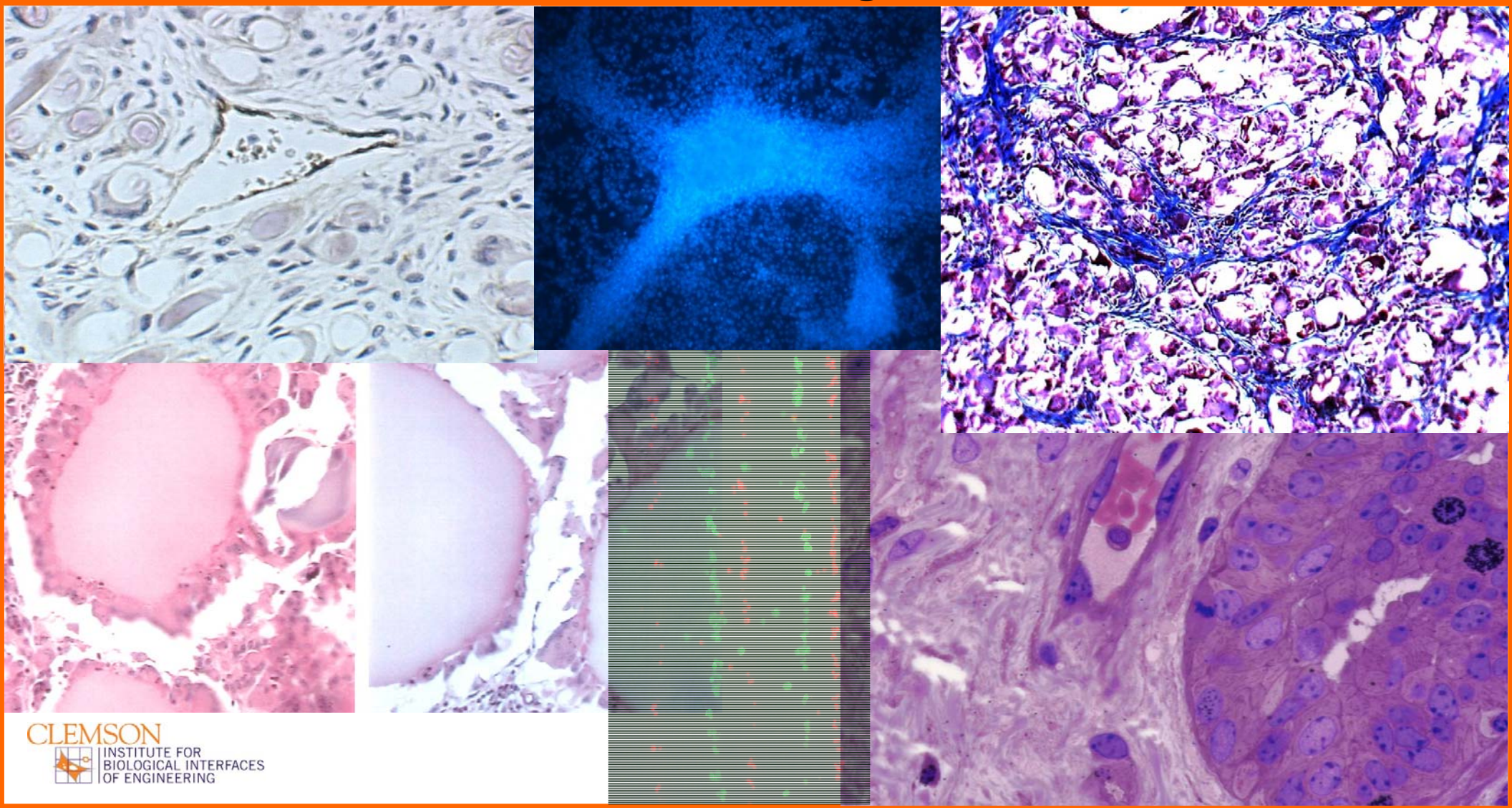
Preliminary Conclusions

- Processing methods may be purposefully modulated to tune polymeric substrates for specific tissue engineering applications
- Slight variations in method can have a significant impact on substrate characteristics and cell behavior
- Processing specifications (e.g. tank size, paddle size, press temperature) affect characteristics of PL product
- “Handshake” between PL and cells changes with culture time

Engineering Tissue for *Ex Vivo* Tissue Test Systems



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Innovation Lies at the Intersection of Disciplines

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