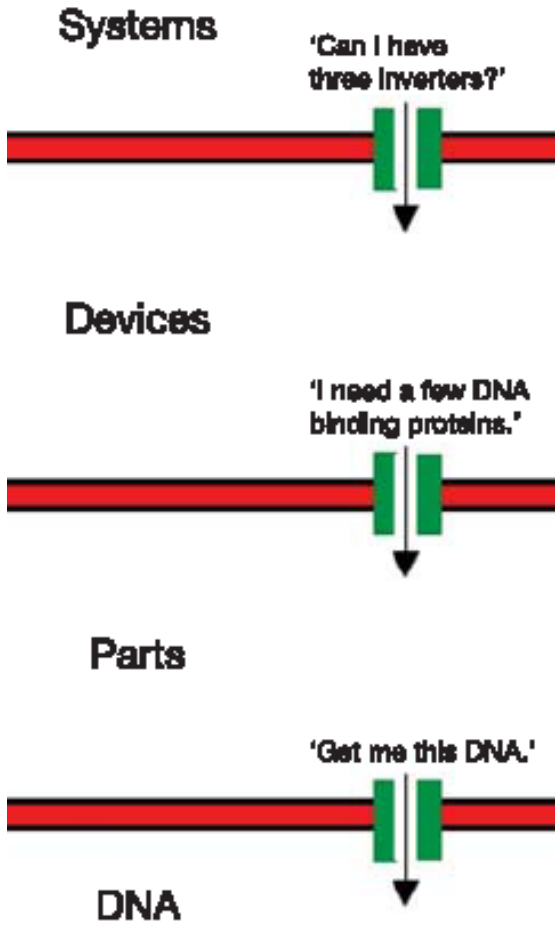
Standards in Scientific Communities II; Cell Viability

Module 3, Lecture 4

20.109 Spring 2011

Lecture 3 review

- What can you learn from a confidence interval? A t-test?
- What are three general engineering principles that might help make biology more “engineerable”?



From D. Endy, *Nature* **438**:449

Topics for Lecture 4

- Standards in tissue engineering
  - introduction
  - writing exercise
  - discussion
- Cell viability
  - your data
  - relation to diffusion

How valued are TE standards?

- 2007 strategic plan for TE clinical success by 2021
  - 24 int'l leaders in TE listed high-priority areas
  - 1/3 named standards
- Analysis
  - concept dominance
  - progress so far
  - standards 7th of 14

P.C. Johnson et al., *Tissue Eng* **13:**2827 (2007)

TABLE 6. NORMALIZED CONCEPT DOMINANCE (I.E., TAKING PRESENT PROGRESS INTO CONSIDERATION)

	O/P
Angiogenic control	3.3
Stem cell science	3.2
Clinical understanding/interaction	2.2
Immunologic understanding and control	2.0
Manufacturing/scale-up	1.1
Regulatory transparency	1.1
Multidisciplinary understanding/cooperation	0.8
Expectation management/communication	0.4
Pharmacoeconomic/commercial pathway	0.3
Multilevel funding	0.0

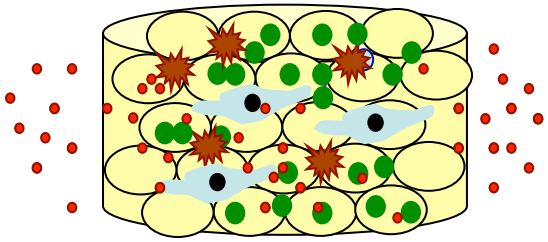
4. Cell sourcing/characterization.

7 (tie). Standardized models.

- 2007 US govt. strategic plan
  - standards listed as part of "implementation strategy"

How useful are TE standards?

- See 2005 editorial by A. Russell
  - proposes need for standards
  - in data collection and sharing
- Choose and respond to a student excerpt (~10')
- Pros/cons/etc… ?



Can we standardize this TE construct?

Module progress: week 2

- Day 3: viability/cytotoxicity testing
- Groups generally found
  - mostly live
  - mostly round
  - not much clustering
- How can we improve the assay?
- What conditions killed cells?
- Other interesting findings?
- How do we explain the results?

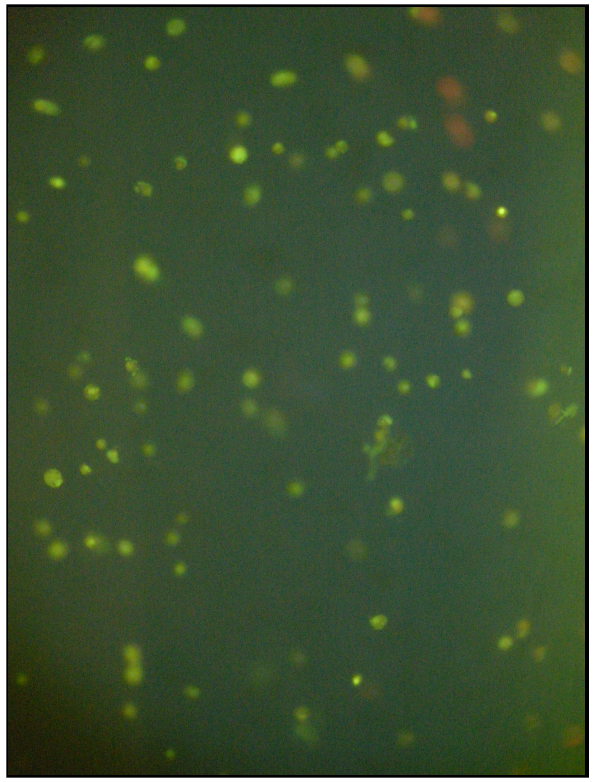
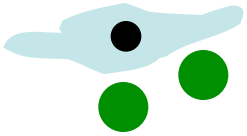
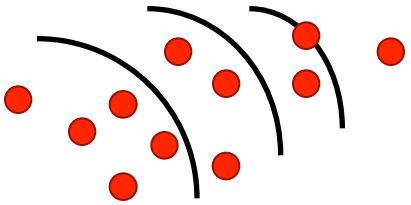


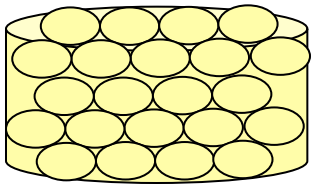
Image from W/F Orange

Factors affecting cell viability

- Cell-related
  - density
  - interactions
- Cytokine-related
  - proliferative
  - apoptotic
- Materials-related
  - bulk permeability
  - macro-porosity
  - toxicity

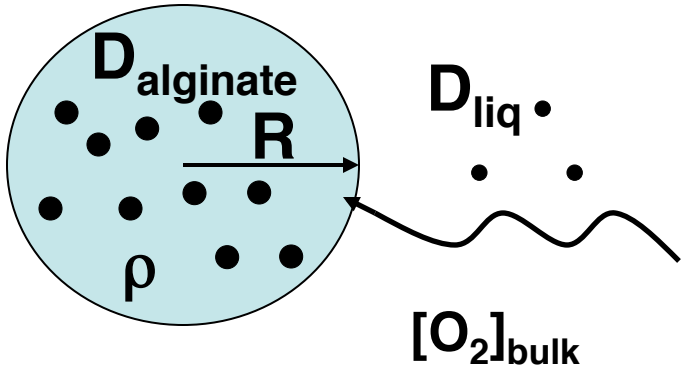


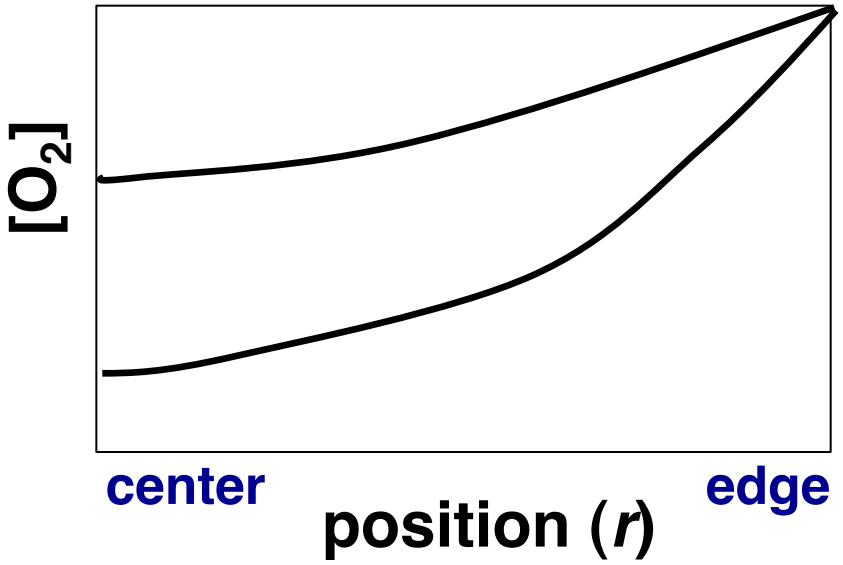




Diffusion in 3D constructs

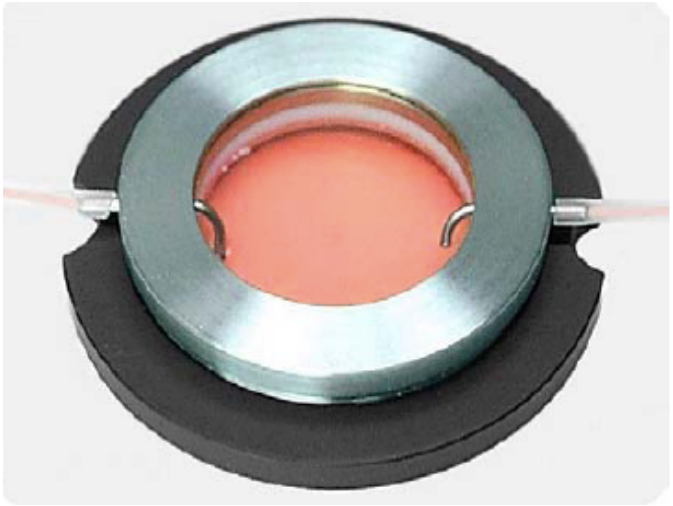
- Nutrients, O_2
- Affected by
  - construct size R
  - cell density ρ
  - diffusivity D
  - conc. in medium $[O_2]_{bulk}$
- Concentration profile
  - can be solved (DE)
  - [O2] ↓ toward center
  - steepness = f(D, ρ, ...)





Significance of diffusion in TE

- Characteristic limit ~100 μm
- Diffusion and viability profiles correlated
- How can we make thick tissues?
  - *in vitro*: dynamic/perfusion culture
  - *in vivo*: promote rapid angiogenesis

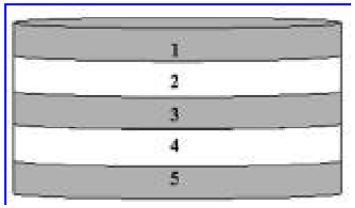


perfusion system
zeiss.com.sg

Modeling cell viability in TE constructs

- Porous PLGA scaffolds
- Seeded cells as in (A) or (B)
- Observed after 10 days
- Model includes
  - Diffusion
  - O_2 use
  - Cell growth
- Model assumes
  - $[O_2]_{bulk}$ is constant
  - Quasi-steady state

A Cells in odd layers

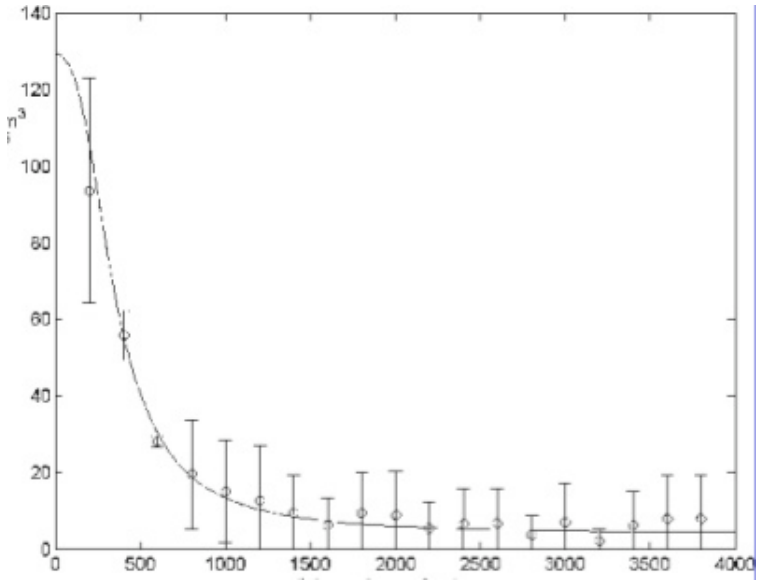


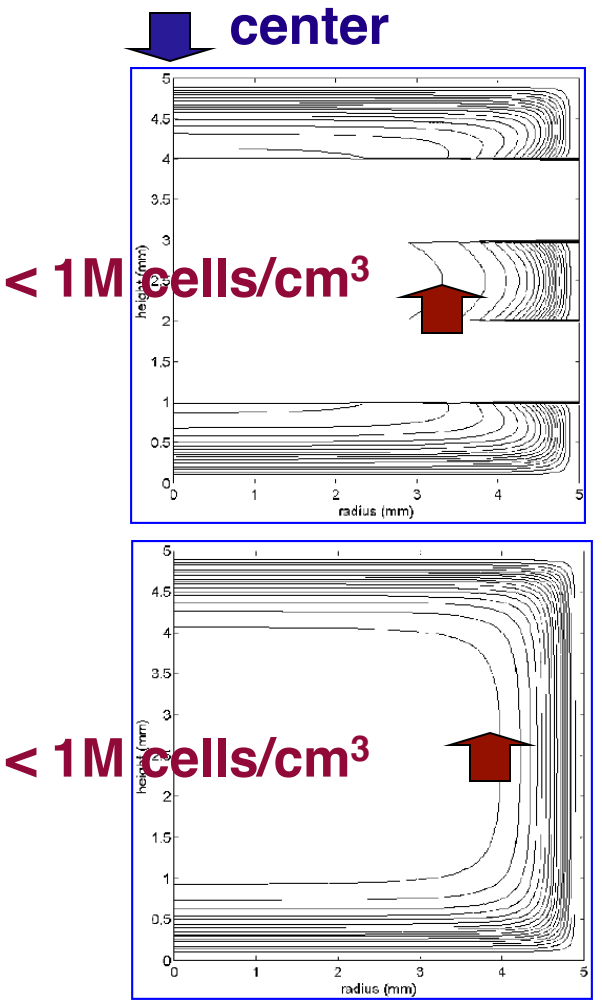
B Cells in all layers

Dunn, et al. *Tissue Eng* 12:705 (2006)

Dunn et al. results for cell viability

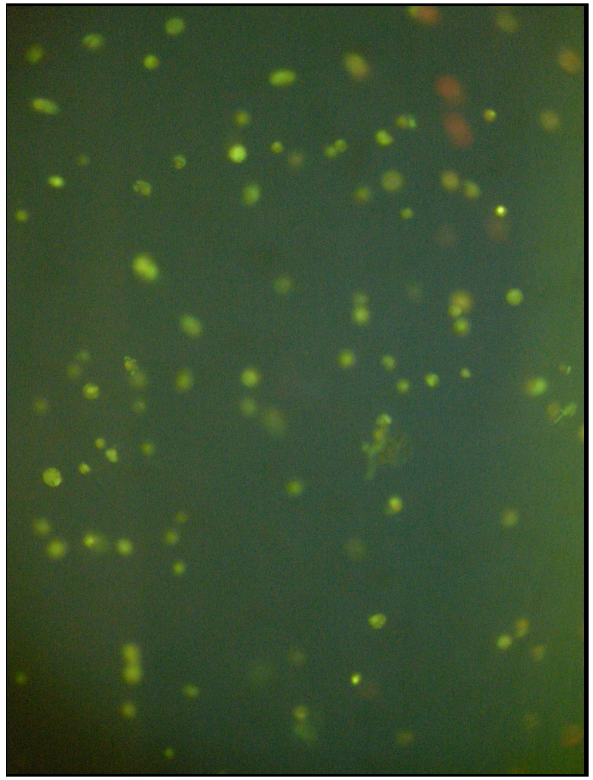
- A more uniform than B
- Cell growth matches O_2 tension
- Claim of predictive capability





Lecture 4: conclusions

- Strategies besides standardization may take precedence in some BE fields.
- Cell viability in TE constructs is affected by cell, material, and soluble factors.
- Modeling can elucidate nutrient diffusion and cell viability profiles.



Next time: transcript and protein assays, imaging.