Standards in Scientific Communities II; Cell Viability

Module 3, Lecture 4

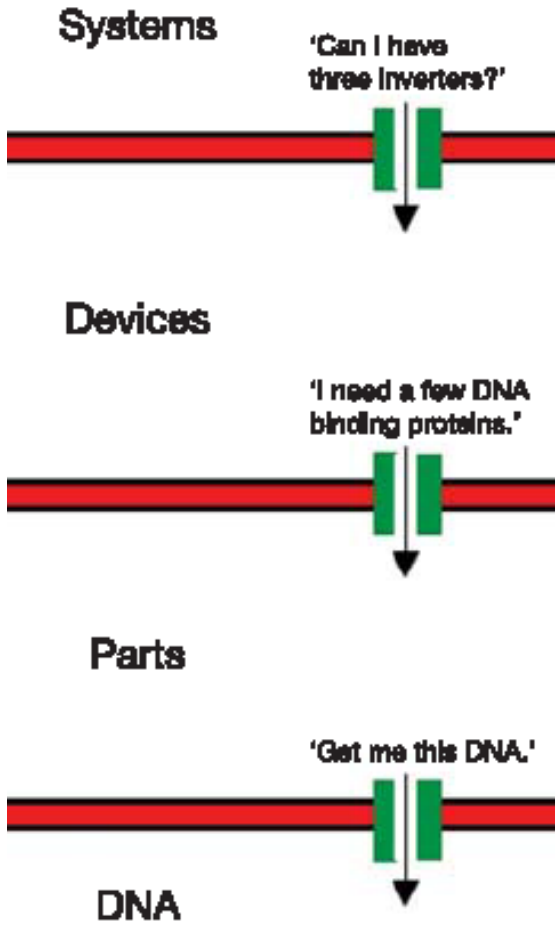
20.109 Spring 2012

Topics for Lecture 4

- Standards in tissue engineering(+)
  - review and introduction
  - writing exercise
  - discussion
- Cell viability
  - your data
  - relation to diffusion

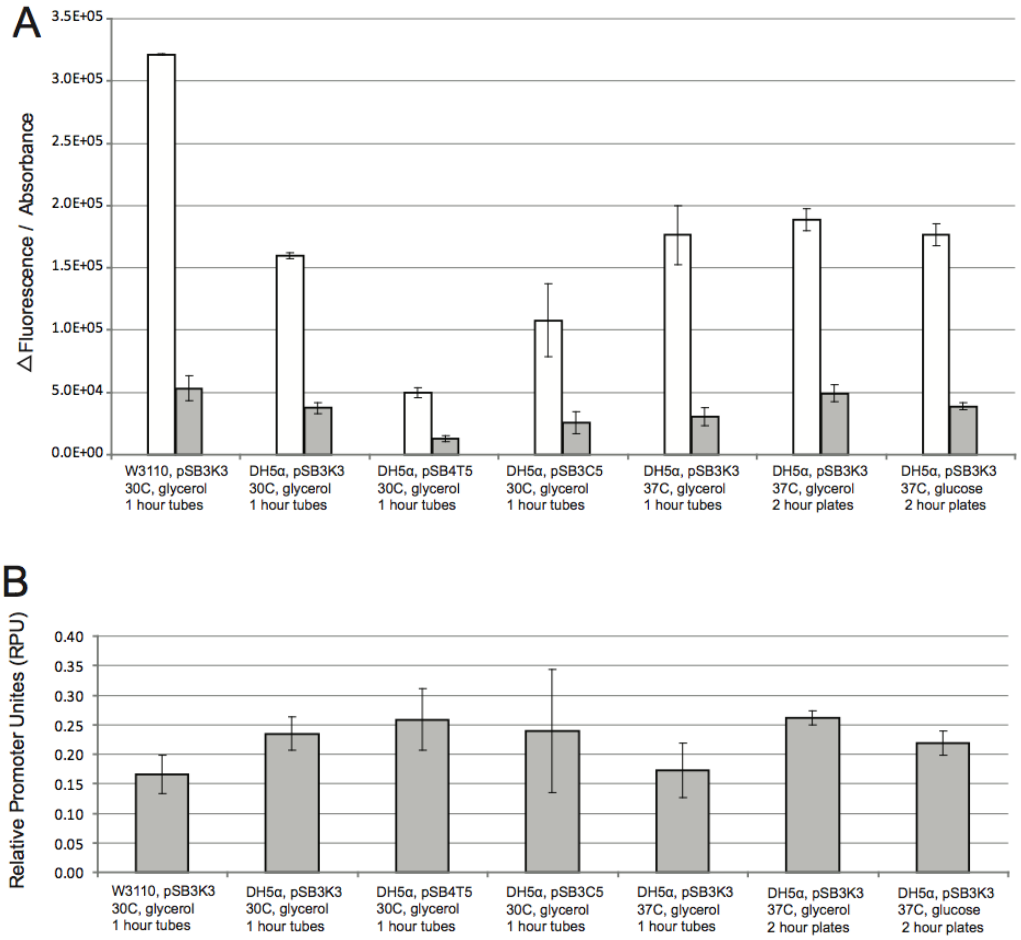
Lecture 3 review

- 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

Functional standard for promoters



Absolute promoter strength

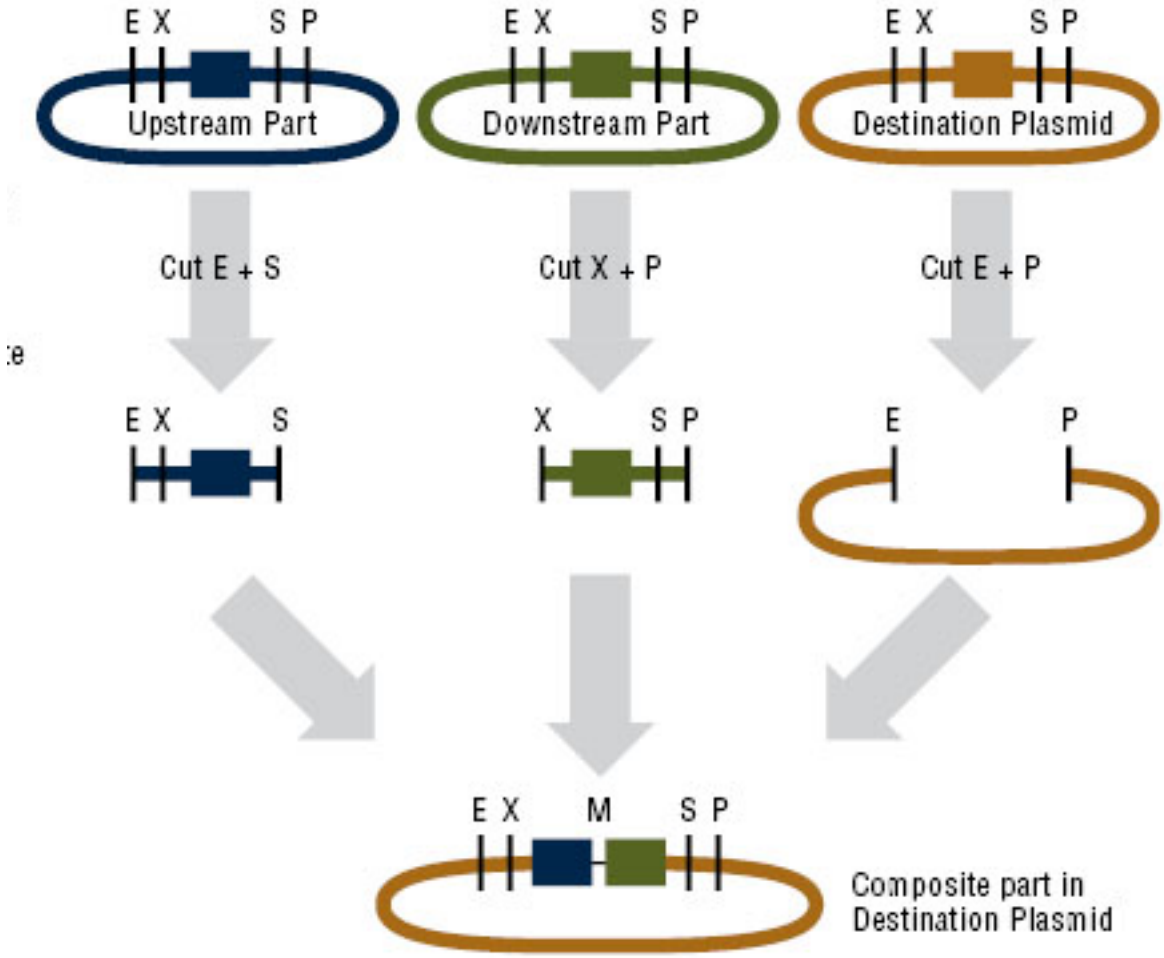
Measurement varies widely (cell line, equipment, etc.)

Relative promoter strength

Measurement less varied

J.R Kelly et al., *J Biol Eng* **3**:4 (2009)

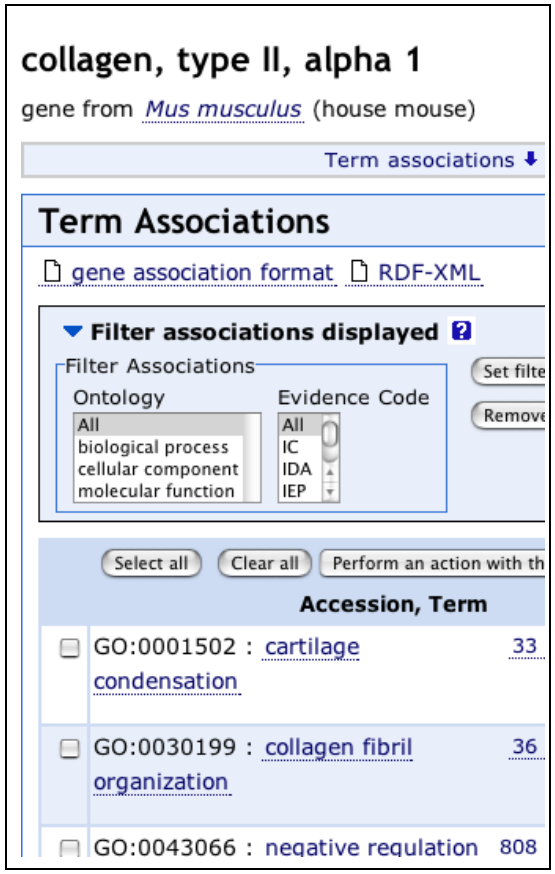
Assembly standard for plasmids



Development: T.F. Knight, R.P. Shetty, D. Endy; Image: neb.com

Data standards: what and why?

- Brooksbank & Quackenbush, *OMICS*, **10**:94 (2006)
- High-throughput methods are data-rich
- Standards for **collection** and/or **sharing**
- Reasons
  - shared language (human and computer)
  - compare experiments across labs
  - integration of information across levels
  - avoid reinventing the wheel (save t, $)
- Examples
  - MIAME for microarrays
  - Gene Ontology (protein functions)
- Who drives standards?
  - scientists, funding agencies, journals, industry



www.geneontology.org

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
[illegible]	[illegible]
Immunologic understanding and control	2.0
Manufacturing/scale-up	1.1
[illegible]	[illegible]
Multidisciplinary understanding/cooperation	0.8
Expectation management/communication	0.4
Pharmacoeconomic/commercial pathway	0.3
Multilevel funding	0.0

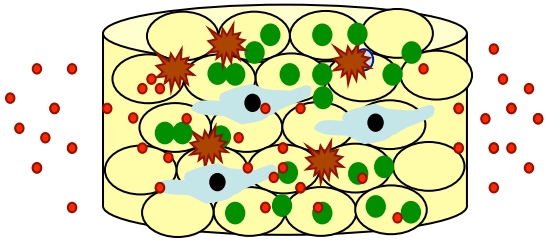
4. Cell sourcing/characterization.

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?

Beyond TE standards: targeted support and improving communication

- P.C. Johnson et al., *Tissue Eng A* **17:**5 (2011)
- Survey of all interested parties in a TE society, from academia to early and established companies
- What are greatest hurdles to TE commercialization?

Academics

Obtaining sufficient funds for research
Orienting research to market needs

Startup companies

Obtaining adequate operating capital
Recruiting experienced management
Working with technology transfer offices

Development-stage companies

Generating sufficient revenue while staying financed
Maintaining focus on the evolving market

Established companies

Managing growth

Growing the intellectual property base
Working with the FDA

Module progress: week 2

- Day 3: viability/cytotoxicity testing
- Groups generally found
  - mostly live CDR
  - many dead MSC
  - mostly round
  - not much clustering
- What conditions killed cells?
- Other interesting findings?
- How to explain the results?
- How to improve the assay?

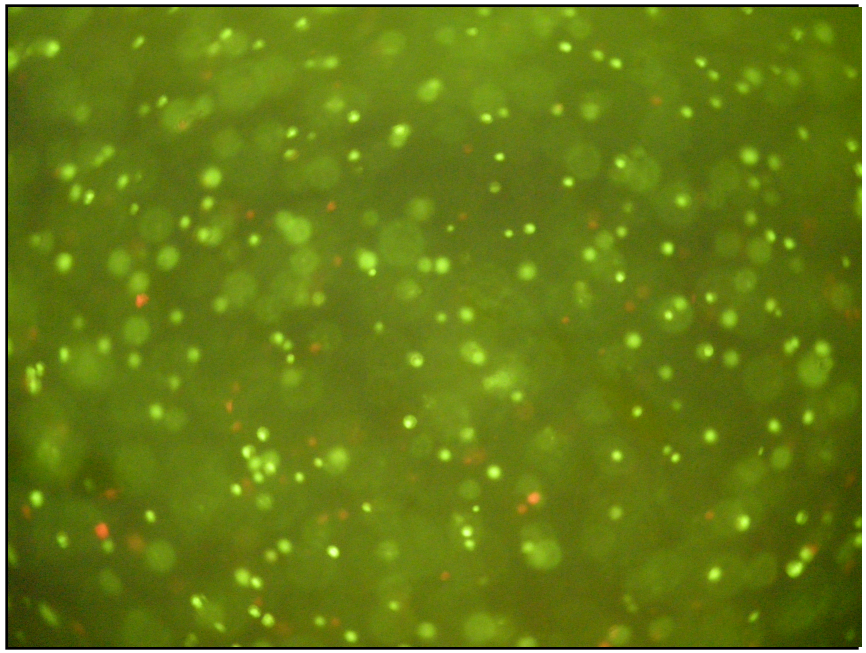
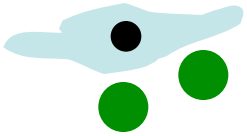
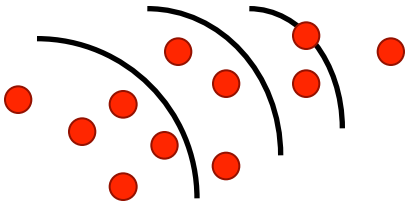


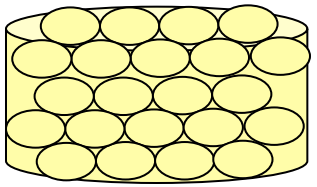
Image from W/F Yellow

Factors affecting cell viability

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

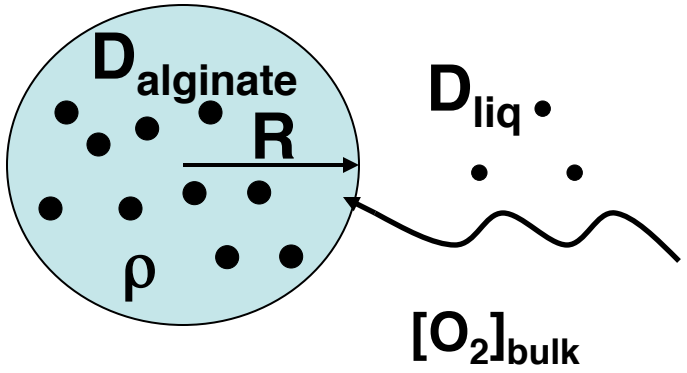


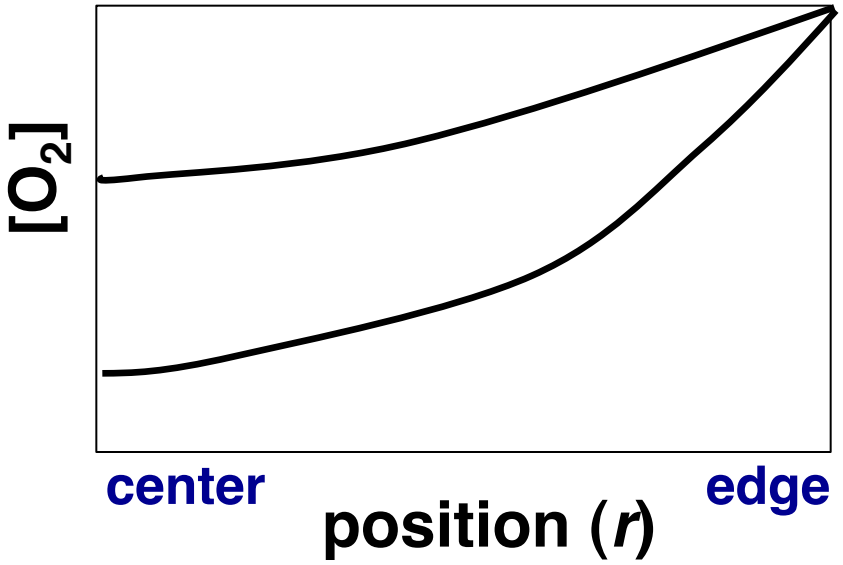




Diffusion in 3D constructs

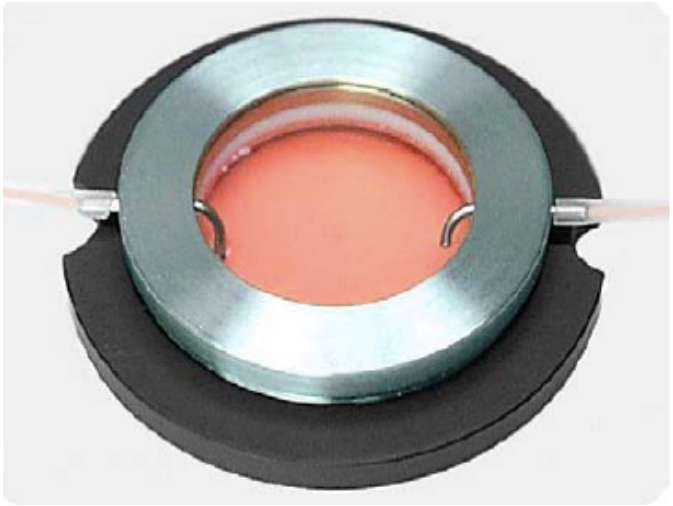
- Nutrients, O_2
- Affected by
  - construct size R
  - cell density ρ
  - diffusivity D
  - conc. in medium $[O_2]_{bulk}$
- Concentration profile
  - can be solved (DE)
  - [O2] ↓ toward center
  - steepness = f(D, ρ, ...)





Significance of diffusion in TE

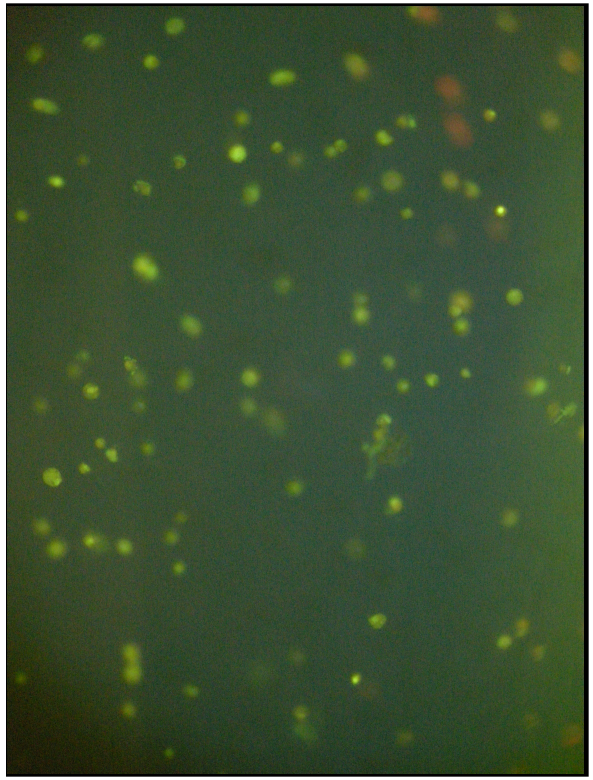
- Characteristic limit ~100 μm
- Diffusion and viability profiles correlated
- How can we make thick tissues?
  - *in vitro*: dynamic/perfusion culture
  - *in vivo*: promote rapid angiogenesis



perfusion system
zeiss.com.sg

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.