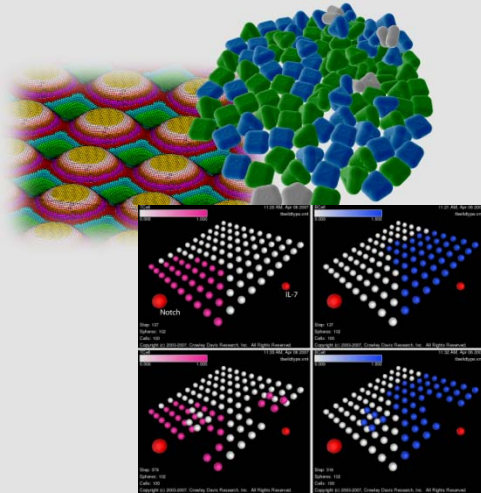


# Virtual Tissues and Bridging Technologies

Richard Newman

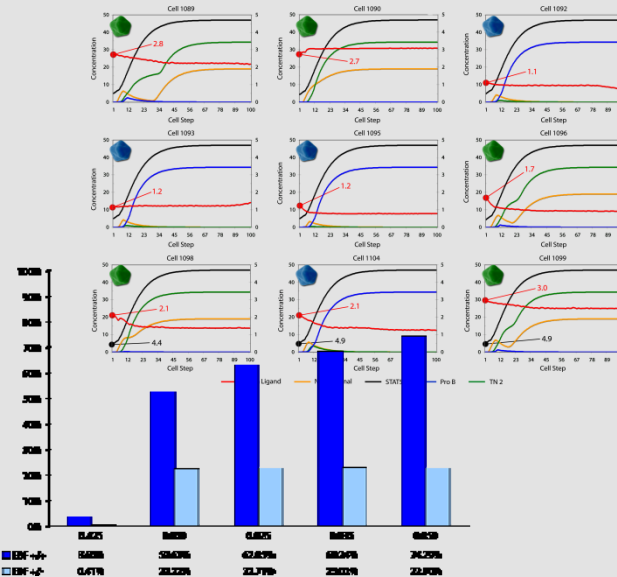


# Predictive utility



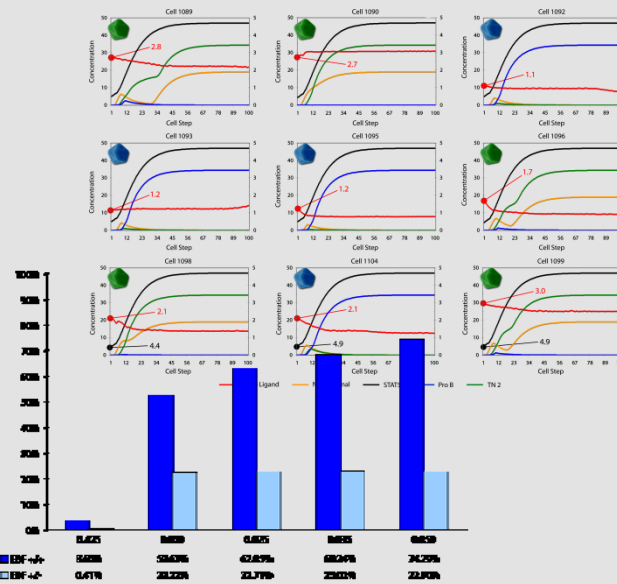
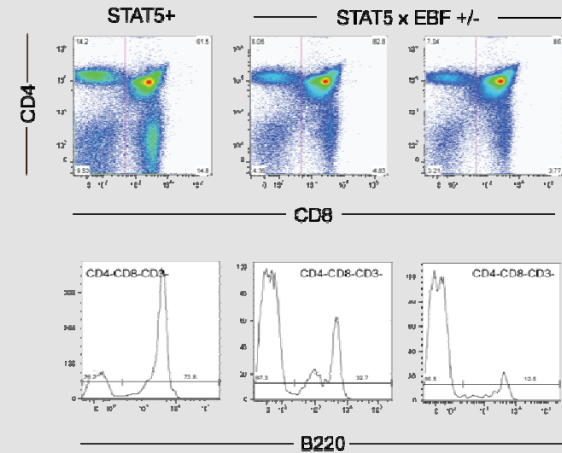
In silico prediction: Percent of thymic B cells is proportional to strength of STAT5 pathway *in vivo*.

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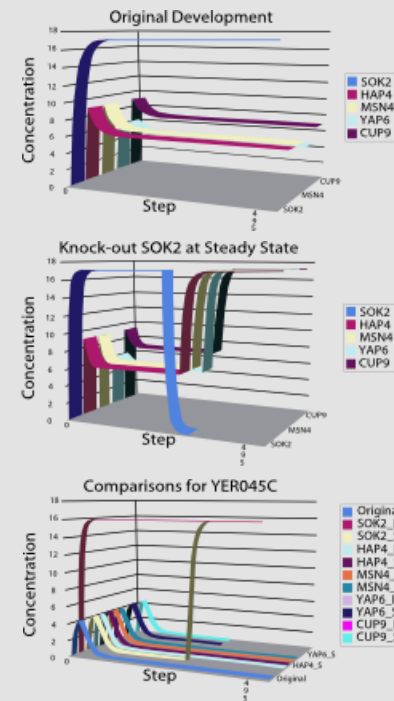
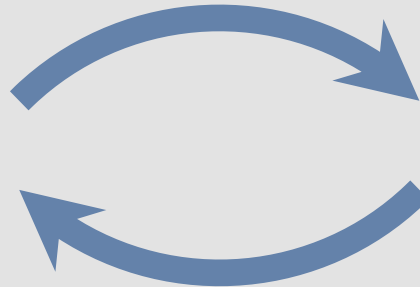
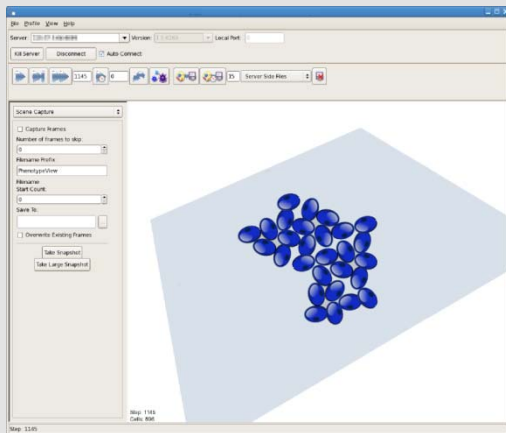
# Predictive utility

In vivo confirmation: Transgenic mice grown at Masonic Cancer Center (UMN) confirm prediction.



Masonic Cancer Center  
UNIVERSITY OF MINNESOTA

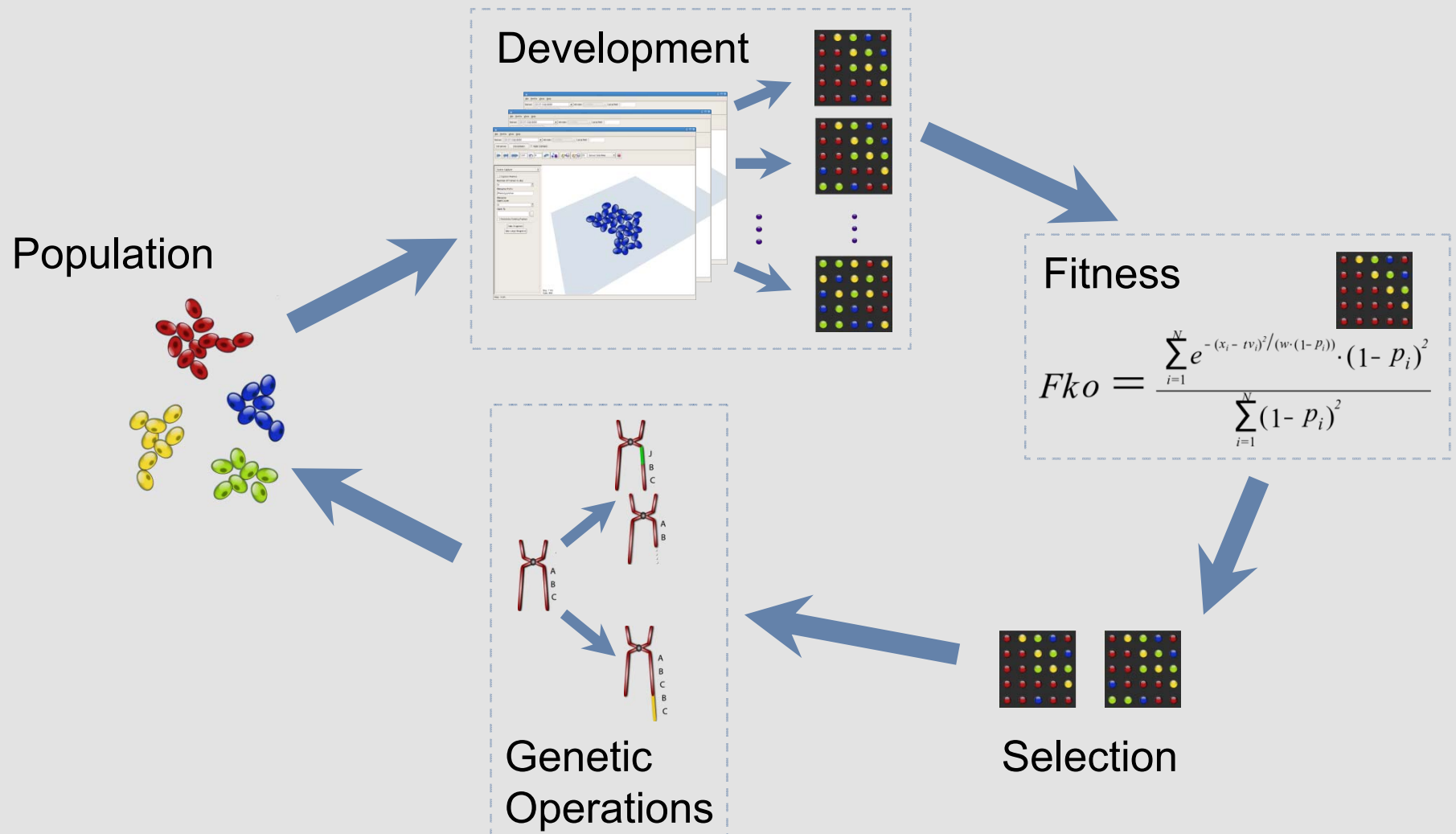
# Experimental utility



# Leveraging virtual tissue

- Collaborative Systems
  - Joining virtual tissues to existing models
  - Building derivative models from earlier versions
- Bioinformatics
  - Mapping known function to raw data
  - Identifying unrecognized effects of known data
- Artificial Intelligence
  - Evolutionary algorithms: searching
  - Machine learning: optimization

# Evolutionary search



# Ignoring something

- Abstraction of detail
- Convention of thought
- Communication of perspective
- Art in design
- Snapshot within progression
- Prioritization of resources

Virtual tissues require some choice of criteria.

# Criteria

- That which is not to be ignored.
- Standard by which a model is judged.

Determining criteria for modeling virtual tissue will reveal questions worth researching.

Even if virtual tissues aren't predictive, trying will be worthwhile.

# Role of biology

- As a **reference**: the objective reality
- As a **discipline**: understanding and theory
- As an **opportunity**: diagnosis and treatment
- As a **culture**: cognitive biases and membership

# Reverse engineering

*Can a Biologist Fix a Radio? – or, What I Learned while Studying Apoptosis*      Yuri Lazebnik  
(2002)

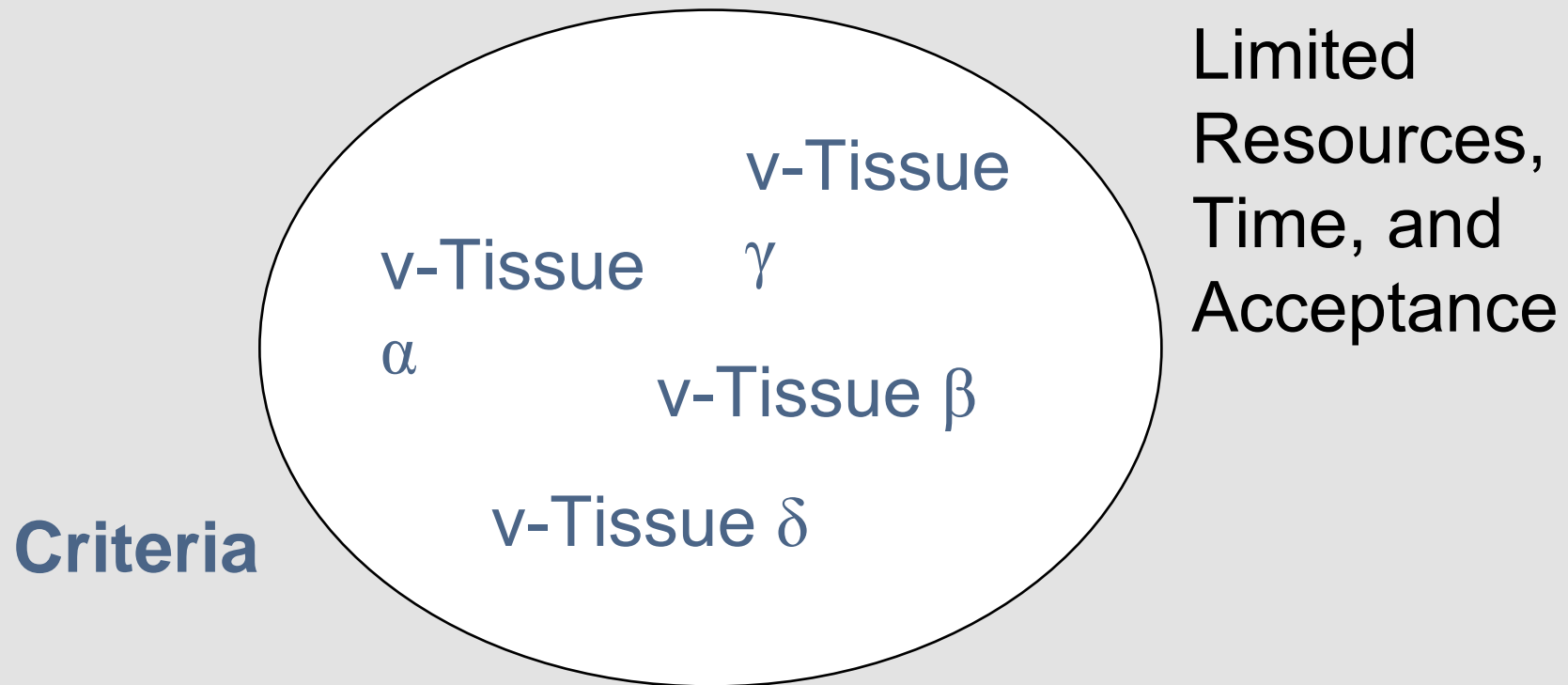
“The language used by biologists...is not unlike that used by stock market analysts. Both are vague...and avoid clear predictions.”

“The question is whether we would be able to understand what we need to learn if we do not use a formal description.”

Criteria: formal description, better language

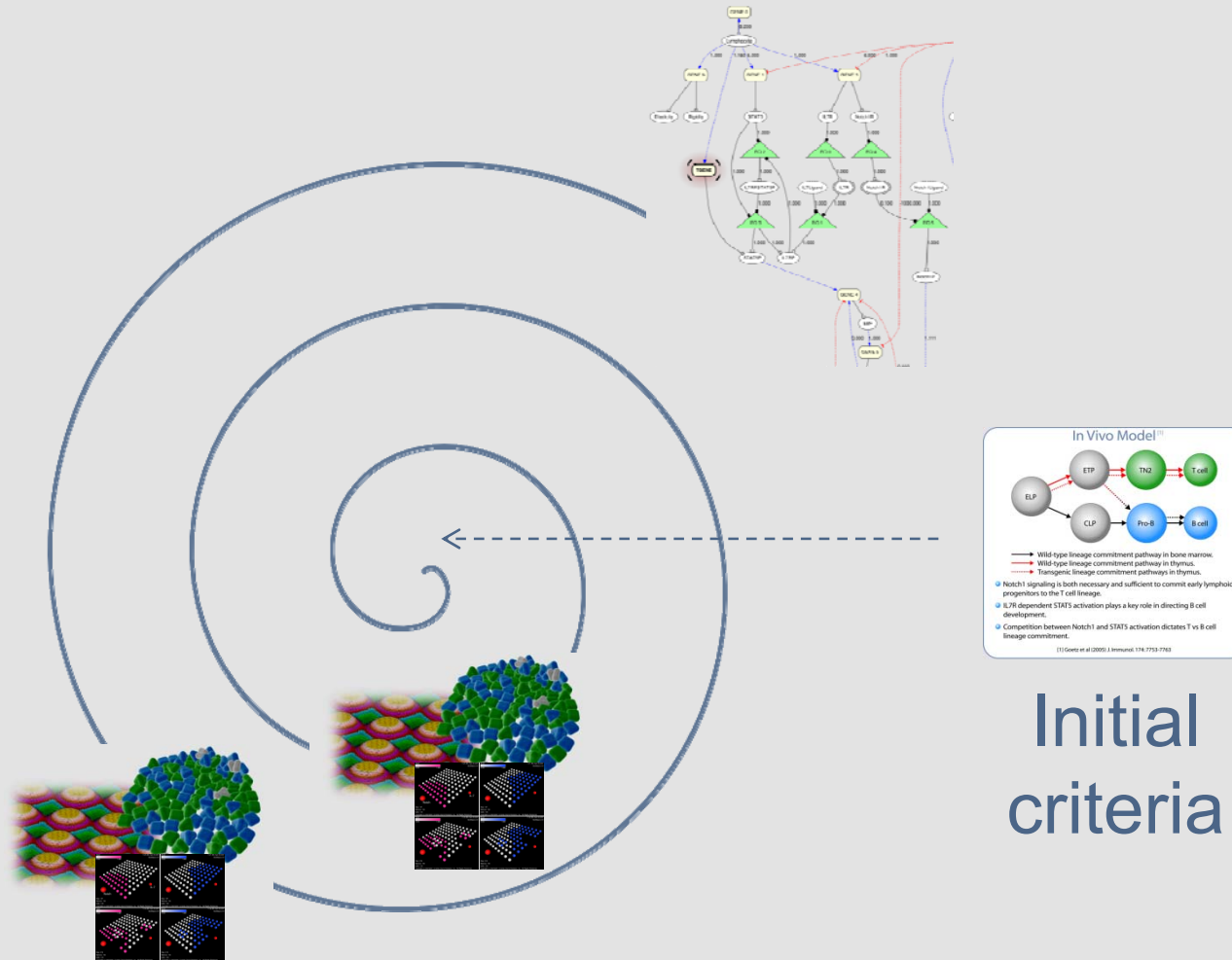


# Selection



Selection by fitness against the  
criteria, explicit and unrealized.

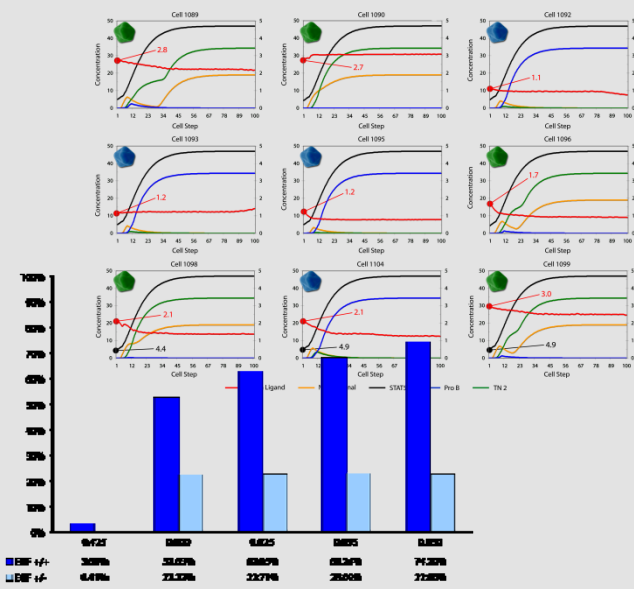
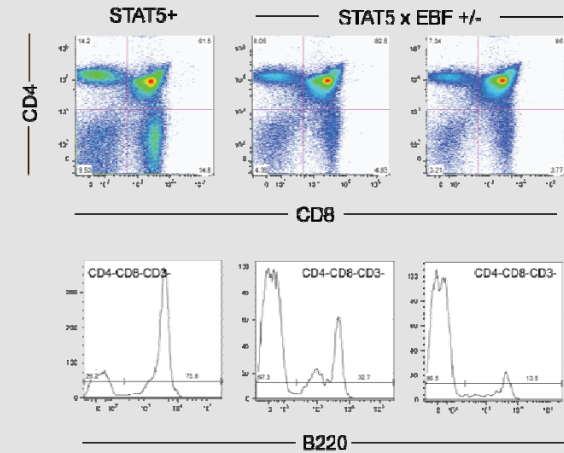
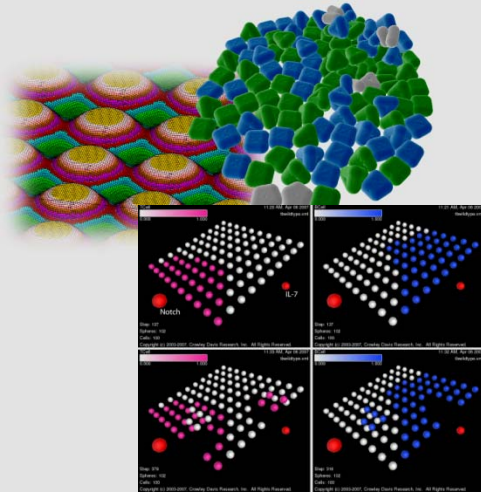
# Iterative improvement



Initial  
criteria

Construction and refinement of baseline model

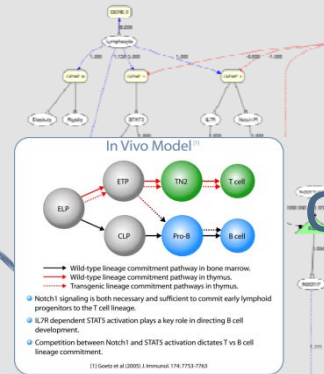
# Validation



new findings inform new criteria for future models

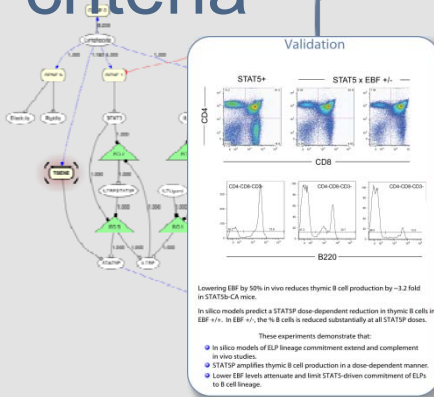
# Iterative improvement

Initial  
criteria



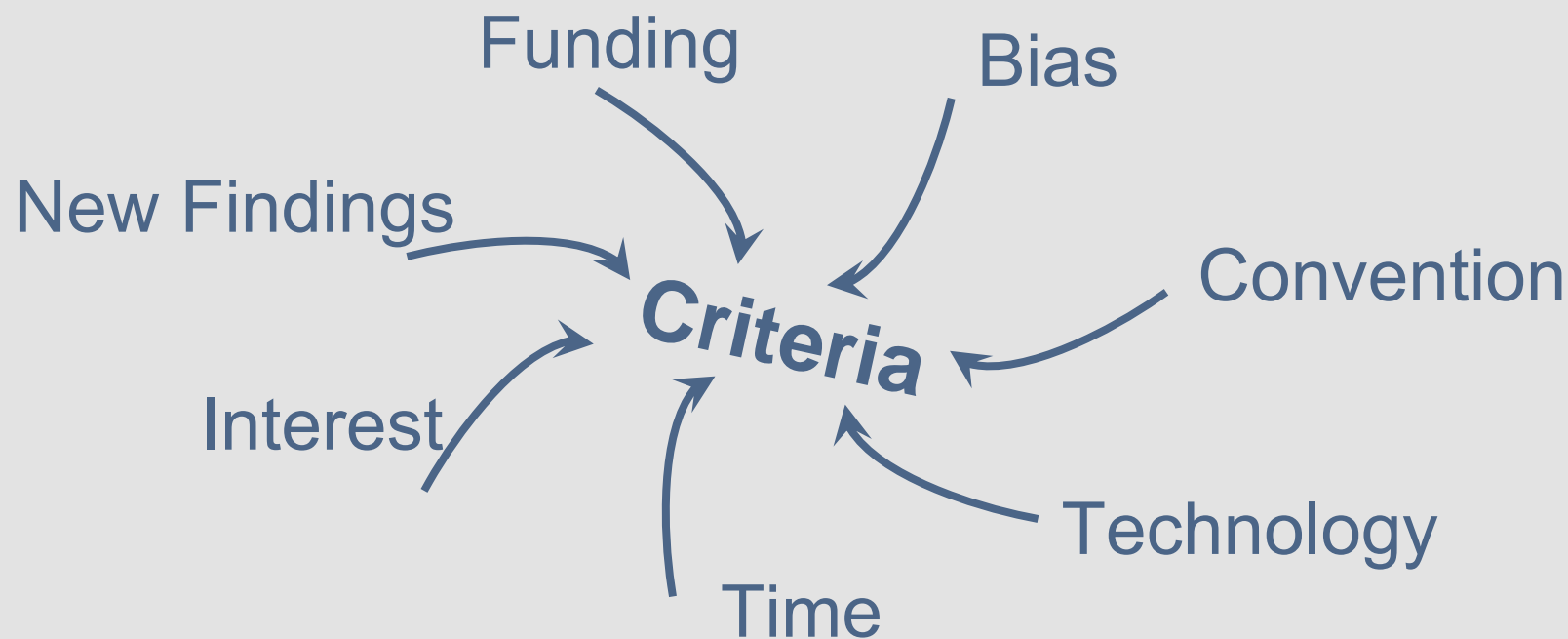
insight into  
living tissue

Improved  
criteria



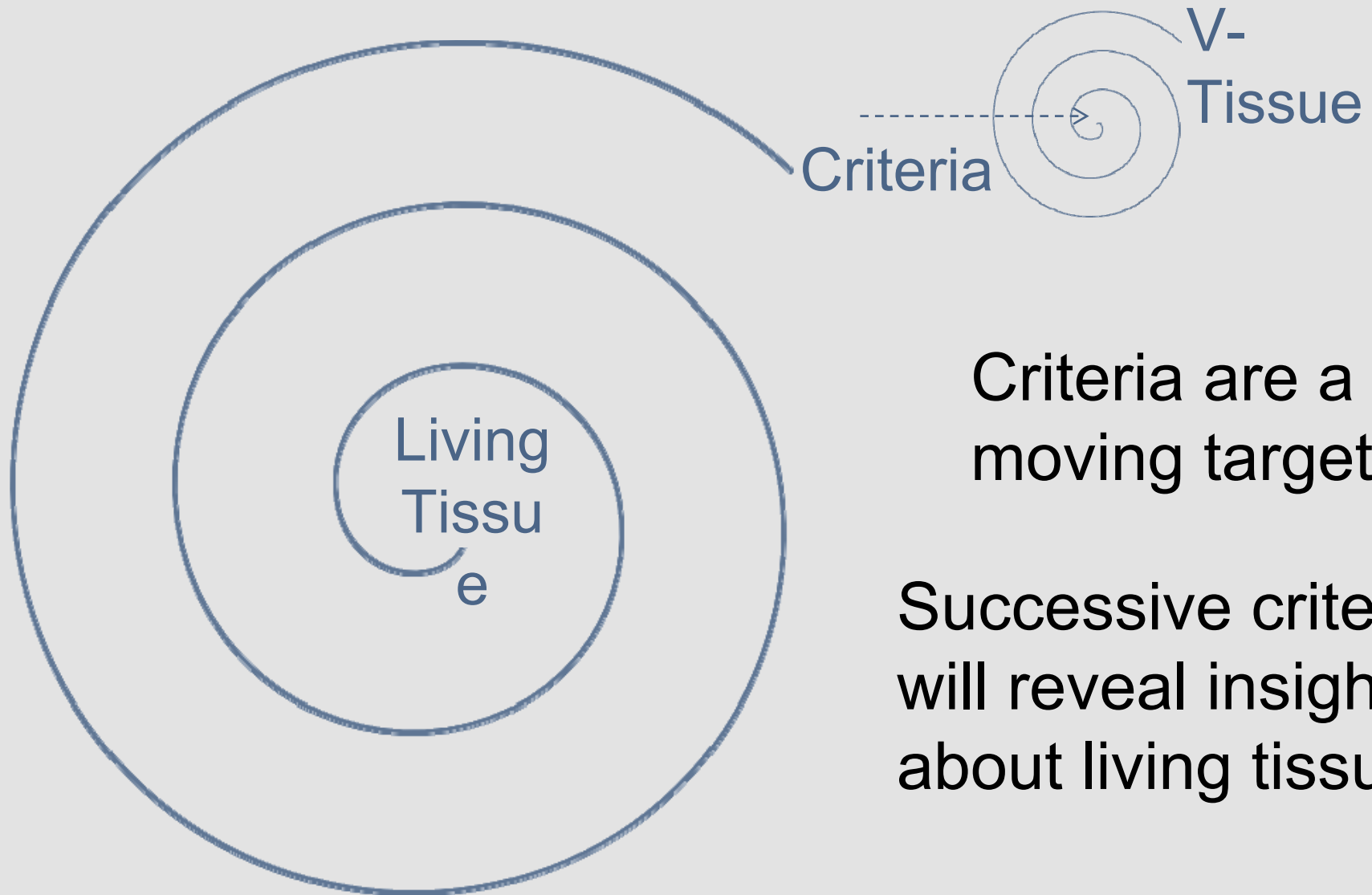
## Improved criteria reveals better understanding

# Pressures



The criteria for what a virtual tissue “ought to be” are constantly changing in a largely uncontrolled environment.

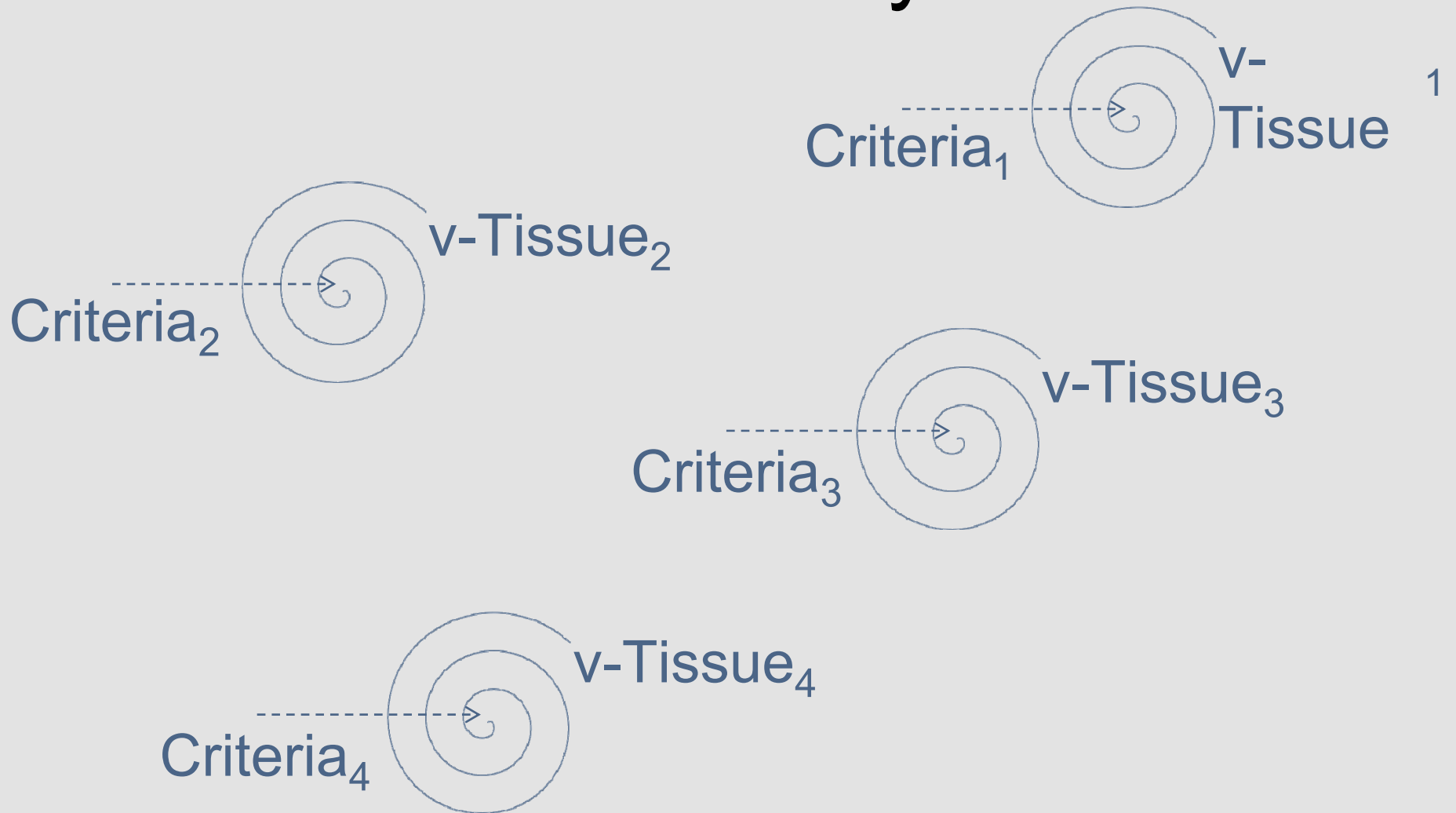
# Evolution



Criteria are a moving target

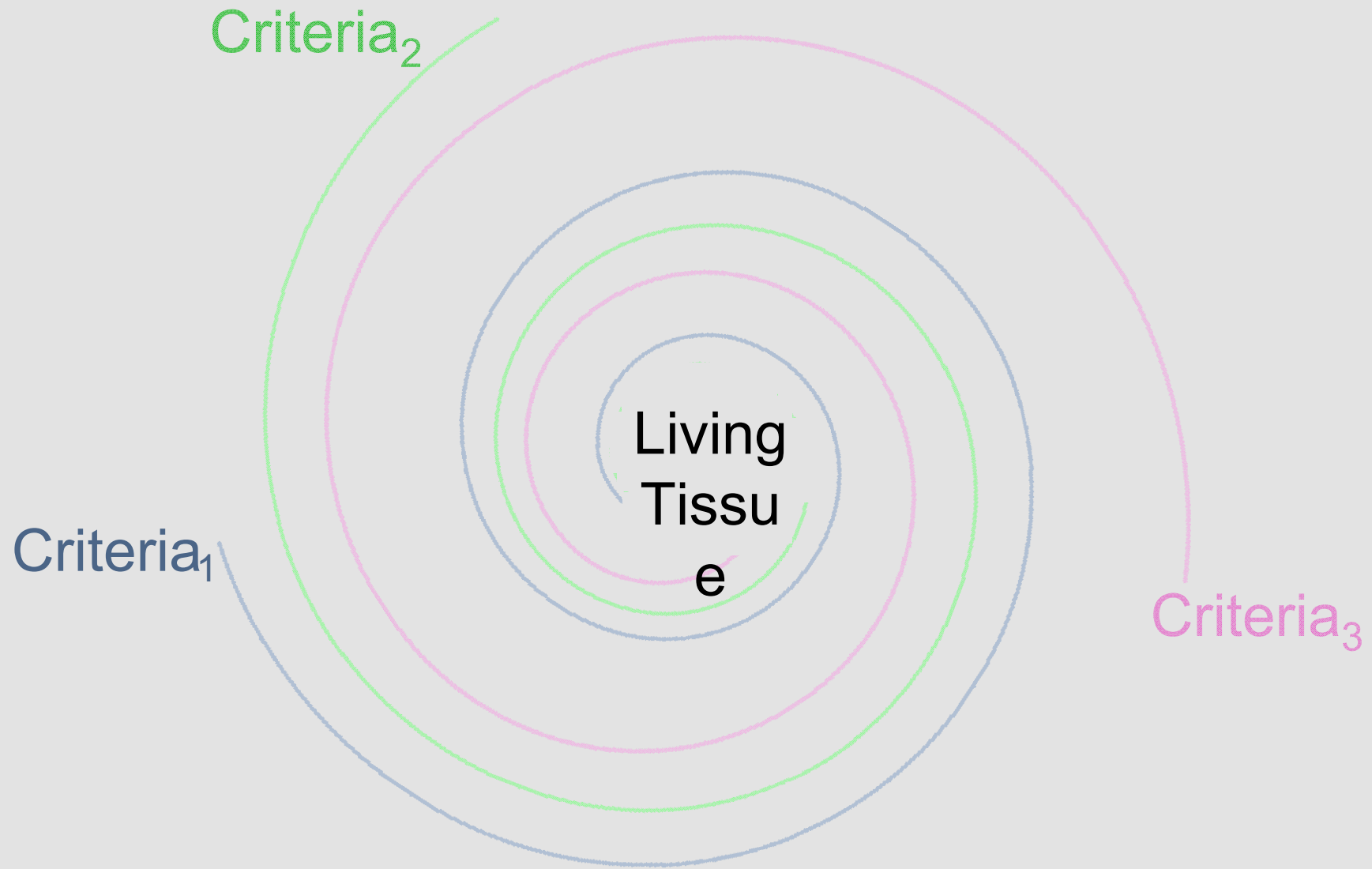
Successive criteria will reveal insight about living tissue

# Diversity



Criteria are not canonical.

# Convergence?



# Mammary acini

- Are *in vitro* acini spherical due to cell regulation or incidental to being grown in suspension?
- How do we recognize “maturity”?
- “Growth”: cell growth or tissue growth? Can we take cell growth for granted?
- Why do interior cells die? Is it because of the lack or presence of something?
- Is growth arrest dependent on polarization or is arrest coincidental to polarization?

# Worth trying

- Criteria by which virtual tissue are judged will be under pressure to evolve toward useful answers.
- Those virtual tissues that flourish will be the ones that best meet all criteria: explicit and implicit.
- Determining criteria will reveal interesting research questions.

Even if virtual tissues aren't predictive, trying will be worthwhile.



CrowleyDavisResearch

Eagle, Idaho

<http://www.cdres.com>



(L to R, F to B)

Ullysses Eoff, Debra Garrett,

Tim Otter, David Zuercher, Mason Vail,

Bill Crowley, Richard Newman, Jeff Habig, Marc Footen,

Tim Andersen (NP)

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