Building the Cell Behavior Ontology (CBO)
An Illustrated Guide

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To build the CBO we will strive towards the goals Professor Glazier set

- The working goal
  - Build Top-levels of CBO
- My goal in this talk is to
  - Help guide the development of the ontology
  - Systematize concepts so they can be used
  - To show how to describe images and simulations

This talk is organized into three parts

1. Annotating a Cell Size Growth example
2. Creating a structured definition of Cell Behavior
3. Use cases and challenges going forward

Cell Size Growth is my simple example of how to describe a cell behavior

This 'cell' is growing in size. How can we describe this phenomenon?

	x1	x2	x3	x4
Image				
Time (step)	**15**	**45**	**75**	**115**
Size (1k lattice site)	9.5	17	202	270

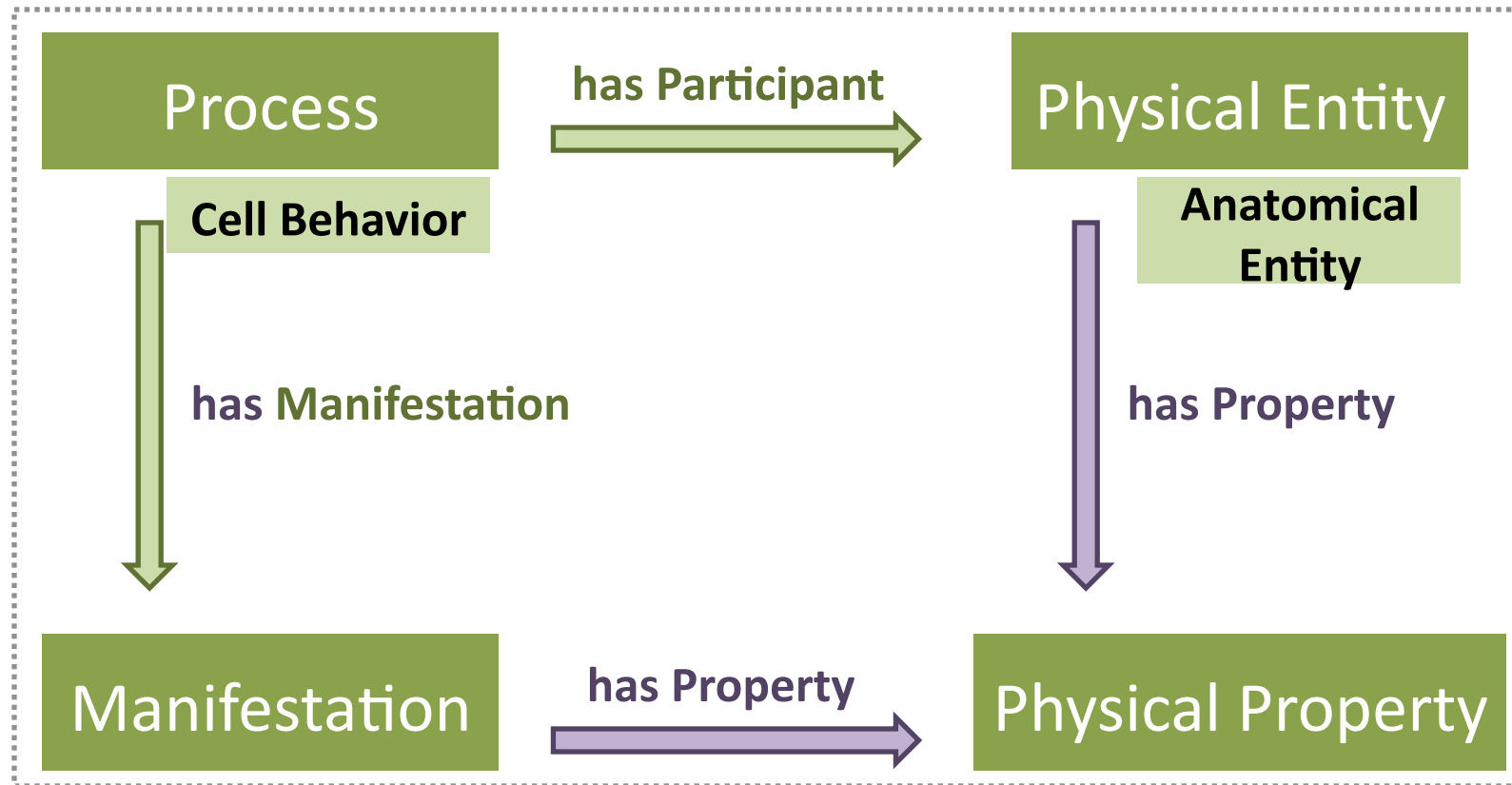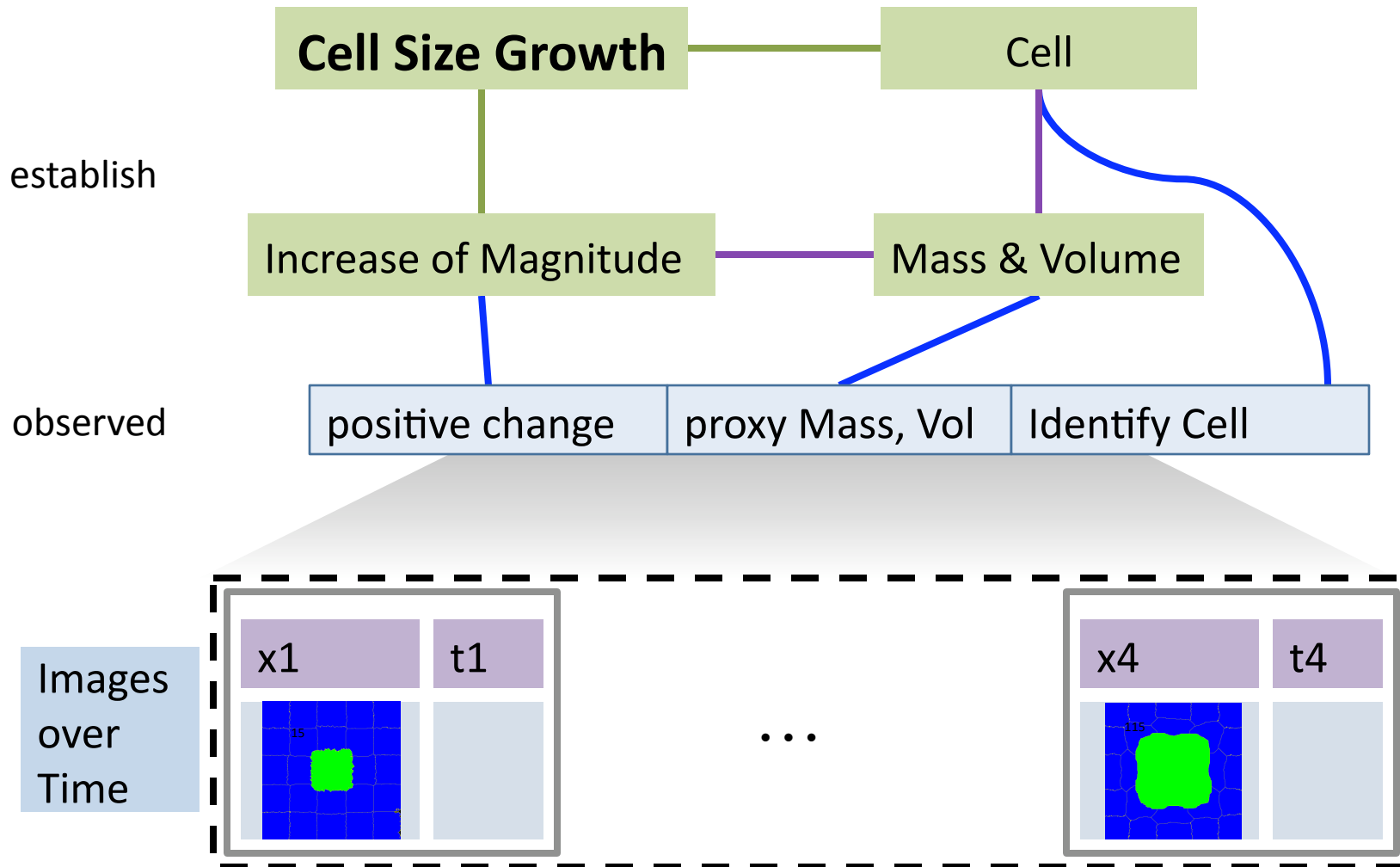**Simulated Cell Size**
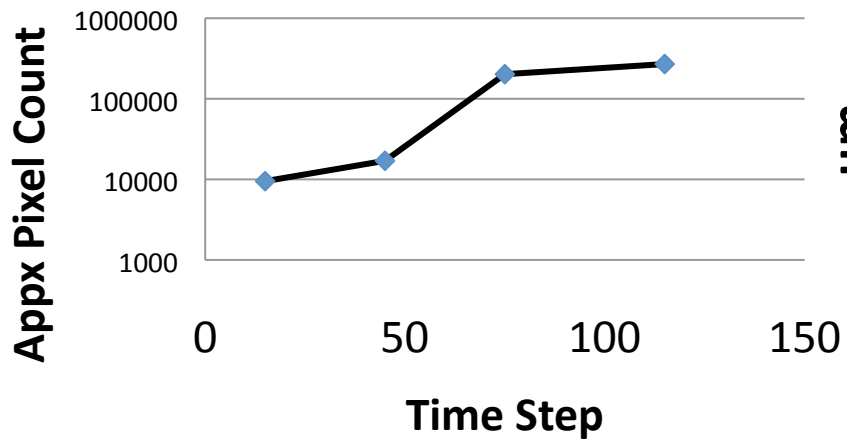
Oocyte Diameter
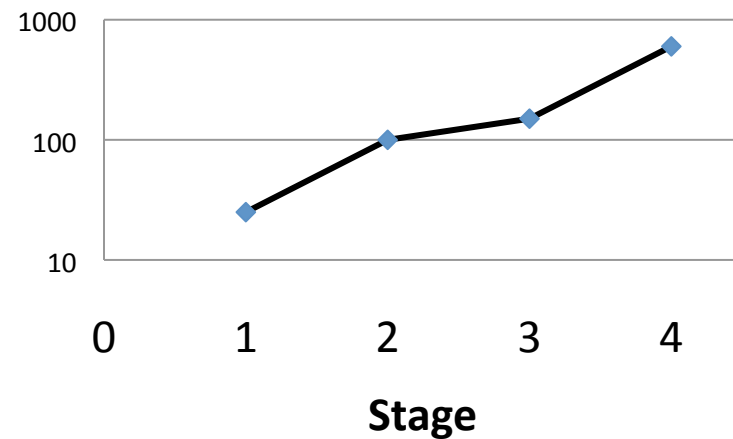
The structure is provided by the foundation of the OPB framework

Data can also be annotated using an ontology as the description

Leevers, Hafen. **Cell growth: Control of Cell Size**. (2004). Ed. Hall, Raff, and Thomas. Cold Spring Harbor. Laboratory Press. 634 pp.

To get an ontology structure we generalize from the example

Leevers, Hafen. **Cell growth: Control of Cell Size**. (2004). Ed. Hall, Raff, and Thomas. Cold Spring Harbor. Laboratory Press. 634 pp.
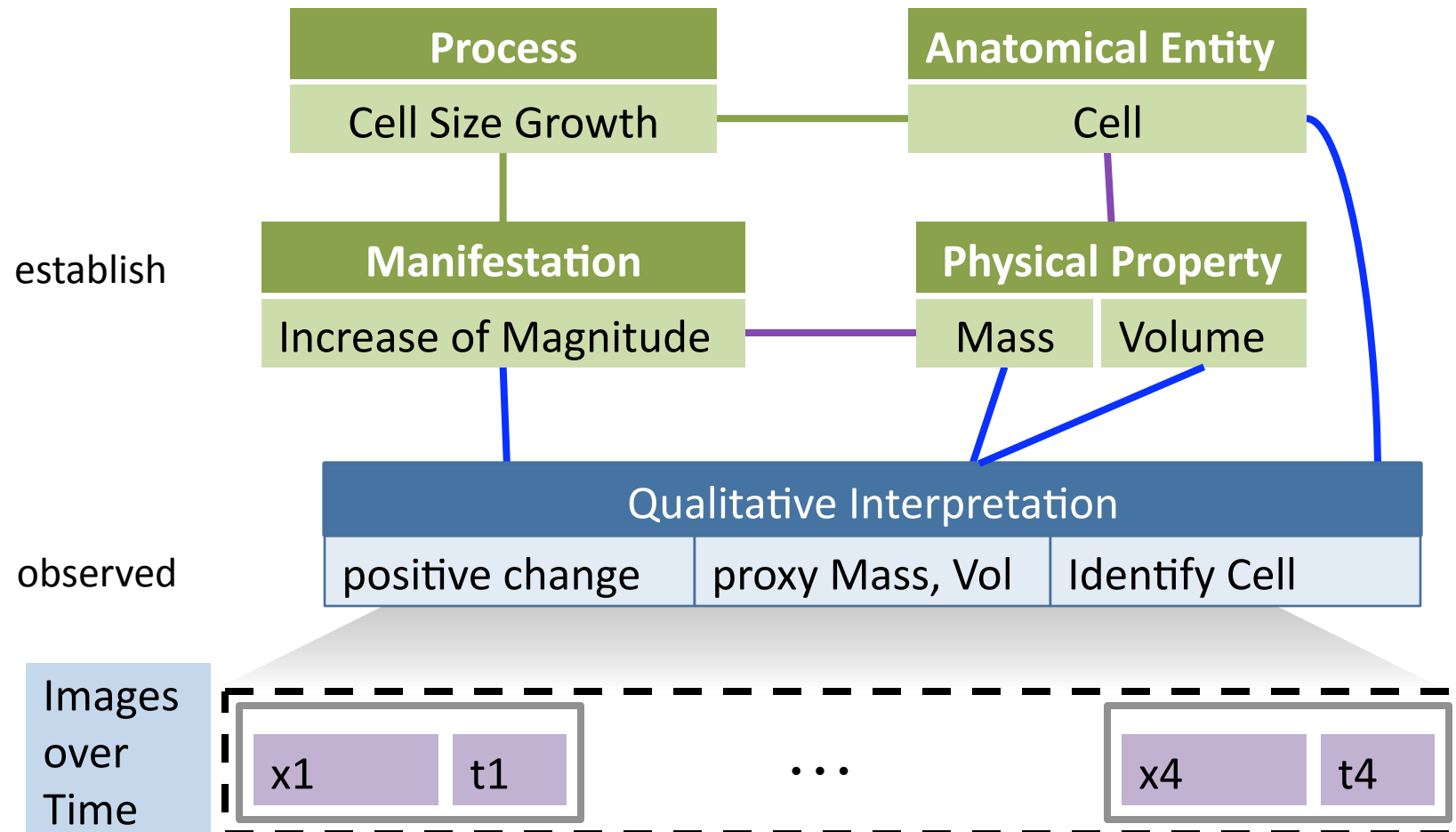
We can make explicit the difference between kinetic v spatial properties

Process		**Anatomical Entity**		**Spatial Region**
Cell Size Growth		Cell		3D Shape

Physical Property

Manifestation	**Kinetic Property**	**Spatial Property**
Increase of Magnitude	Mass	Volume

establish

Qualitative Interpretation		
positive change	proxy Mass, Vol	Identify Cell

observed

Images over Time

| x1 | t1 | ... | x4 | t4 |

Leevers, Hafen. **Cell growth: Control of Cell Size**. (2004). Ed. Hall, Raff, and Thomas. Cold Spring Harbor. Laboratory Press. 634 pp.

Structured descriptions of behaviors can help build the ontology

Junqueira LC, Carneiro J, "Chapter 13. Hematopoiesis" (Chapter). Junqueira LC, Carneiro J: Basic Histology: Text and Atlas, 11e:
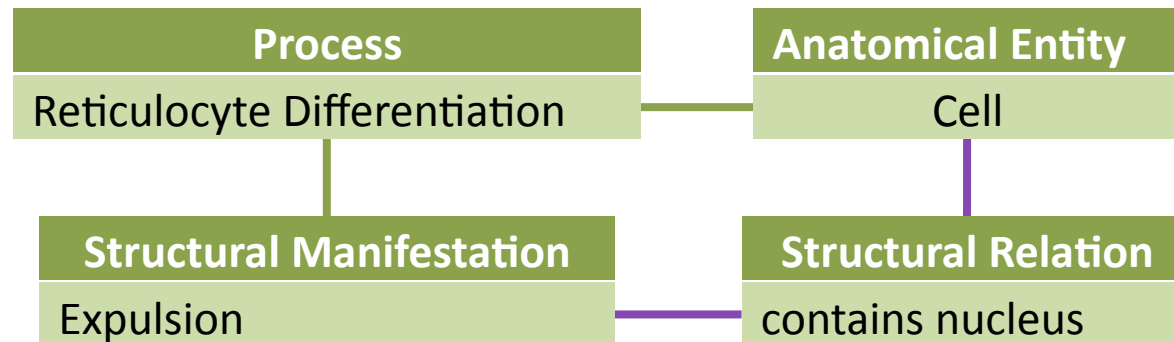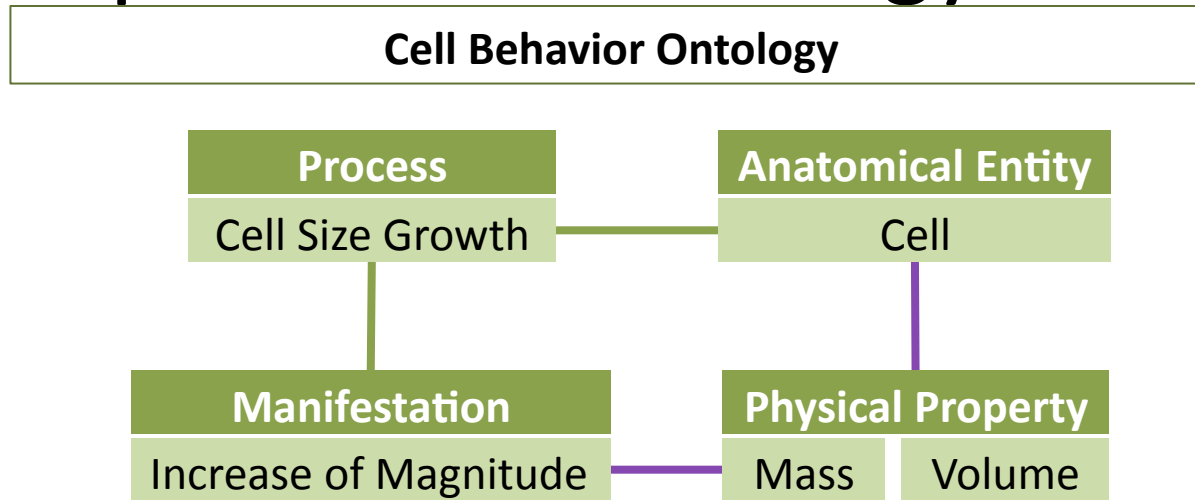
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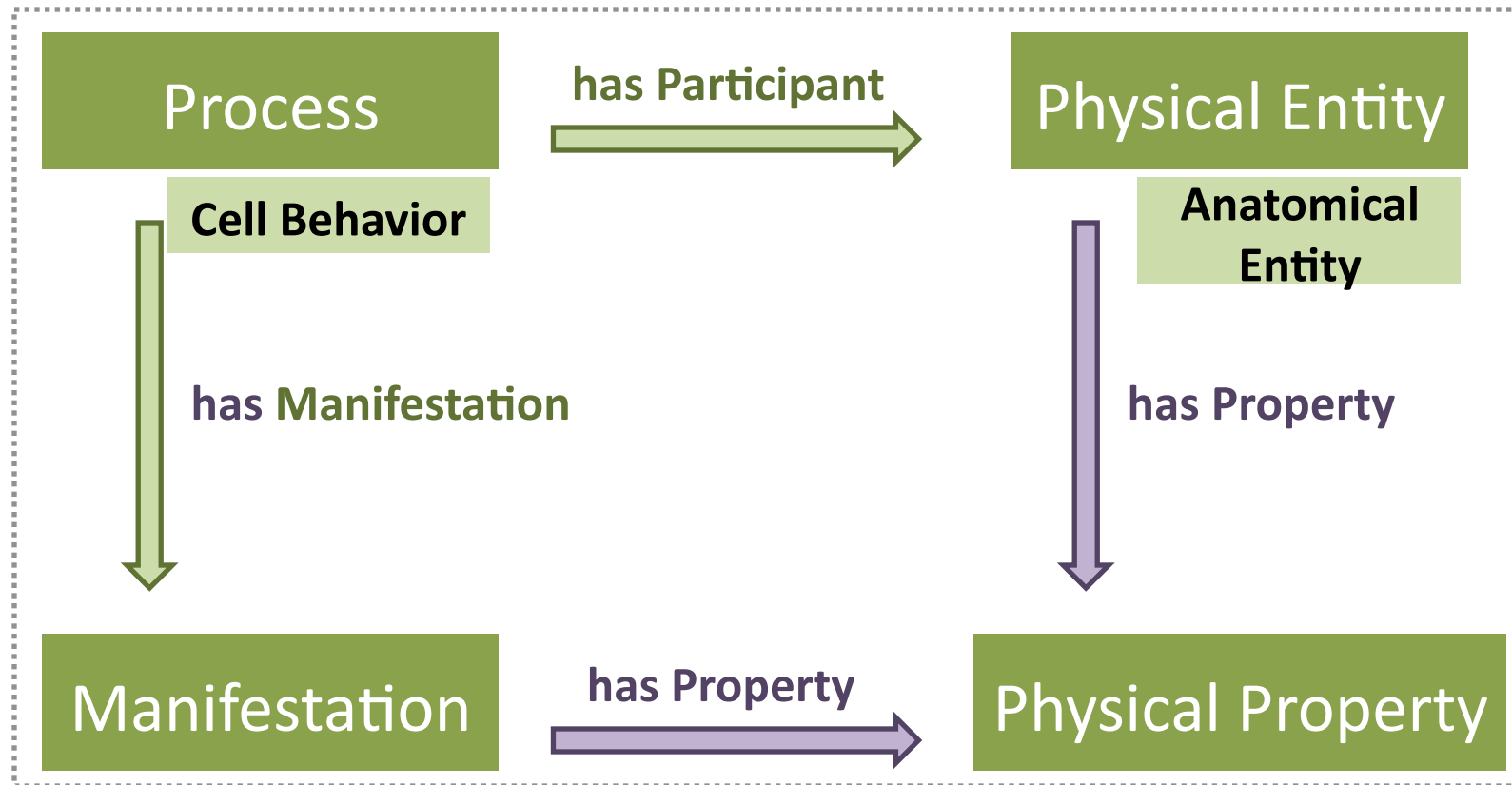
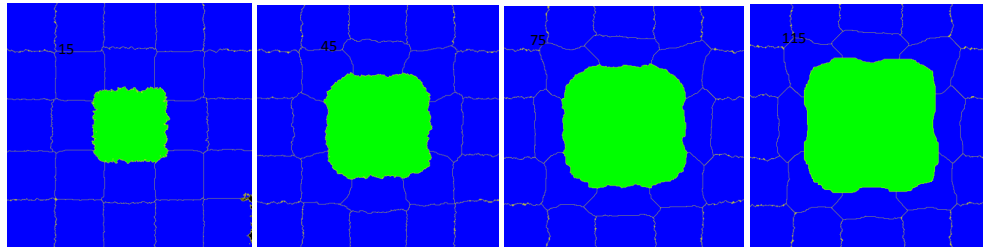To build a consistent CBO each term
needs to be described the same way

Process

Physical Entity

Manifestation

Physical Property
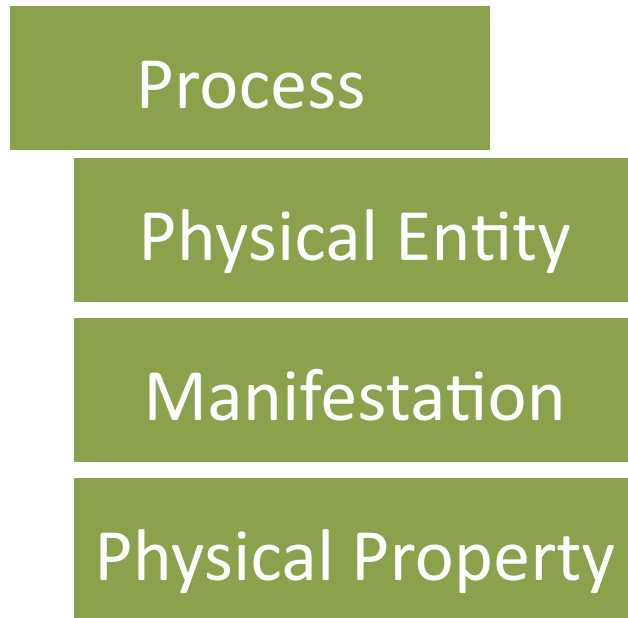
A template set of questions can be used to guide
ontology development

Which entities change during a process?

| Process	has Participant →	Physical Entity

Cell Size Growth

- Kinetic Physical Entity
  - ➤ Structures
  - **Anatomical Entity**
  - Sub-cellular (pseudopods, nuclei)
  - Molecular (cadhedrins, Protein marker X)

- Spatial Entity
  - ➤ Regions
 - Surfaces
  - Shapes

Which properties of the entity are essential to defining the process?

- Kinetic Physical Entity
  – State Property
    - **Mass**
    - Concentration
  – Rate Property
    - Flow Rate
    - Force

- Spatial Property
  – **Volume**
  – Area
  – Locus, Location

Physical Entity

has Property
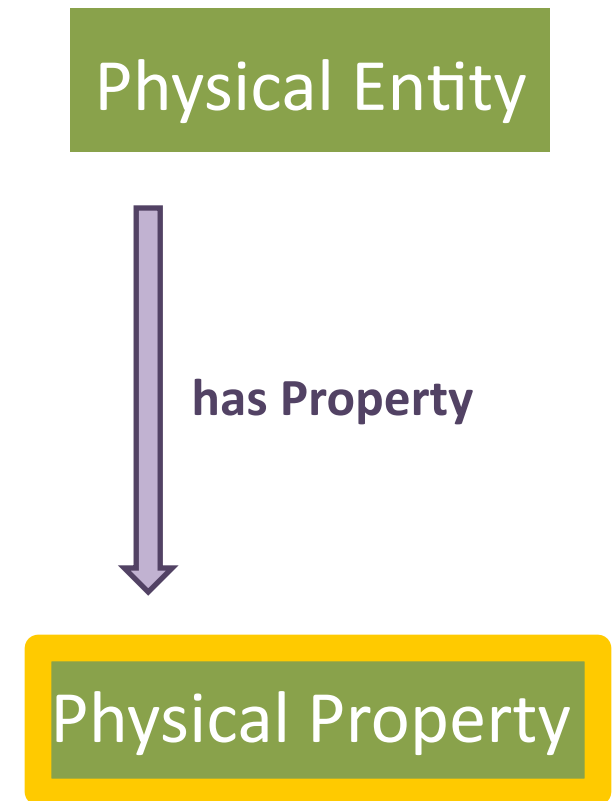
Physical Property

How does each property change with respect to time?

- **Property Manifestation**
  - **Increase**
  - **Asymptotically increasing**
- Structural Manifestation
- Existential Manifestation
  - Fusion
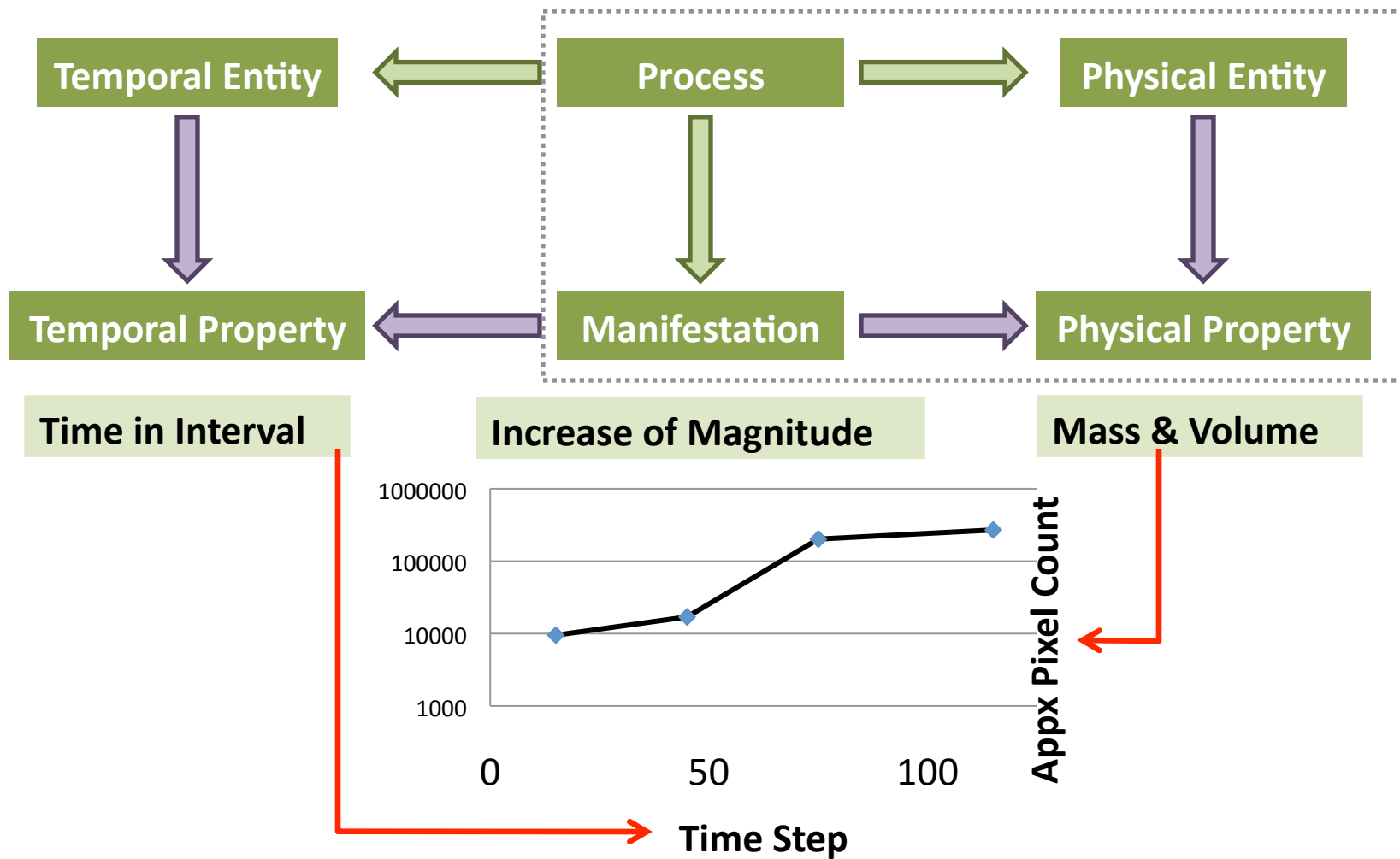 - Appearance
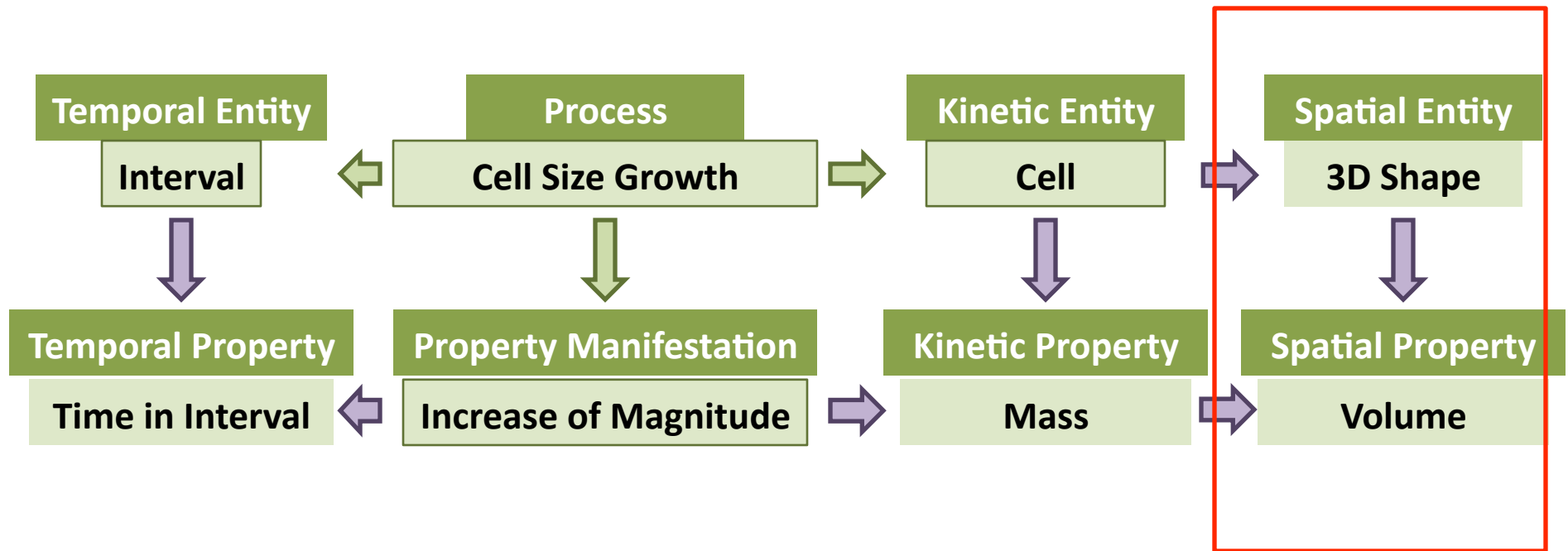
Cell Size Growth
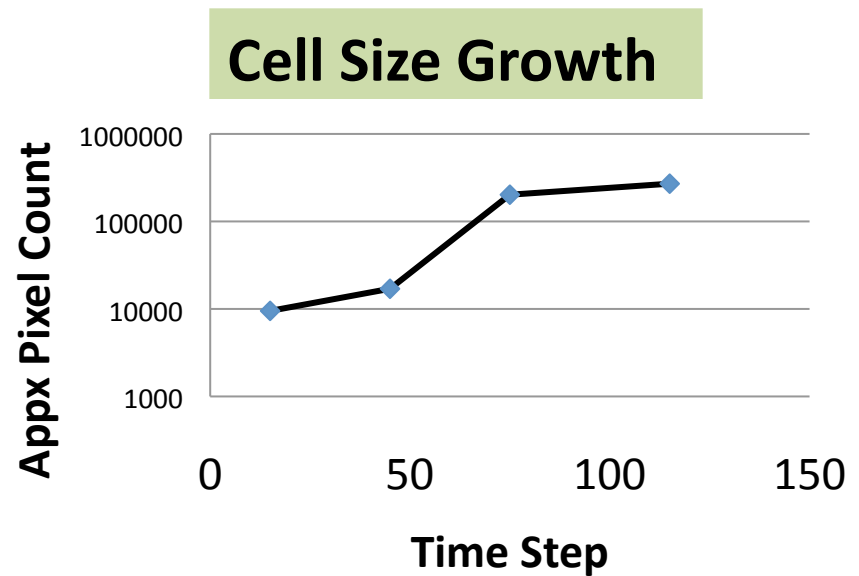
Note:
Possible for a Physical Property to change with respect to another Property and time.

Manifestation → has Property → Physical Property

Processes occur over time, which is often implied, but important

For each Cell Behavior a structured definition is formed

Temporal Entity	Process	Kinetic Entity	Spatial Entity
Interval	Cell Size Growth	Cell	3D Shape

Temporal Property	Property Manifestation	Kinetic Property	Spatial Property
Time in Interval	Increase of Magnitude	Mass	Volume

Differentiation requires starting and ending
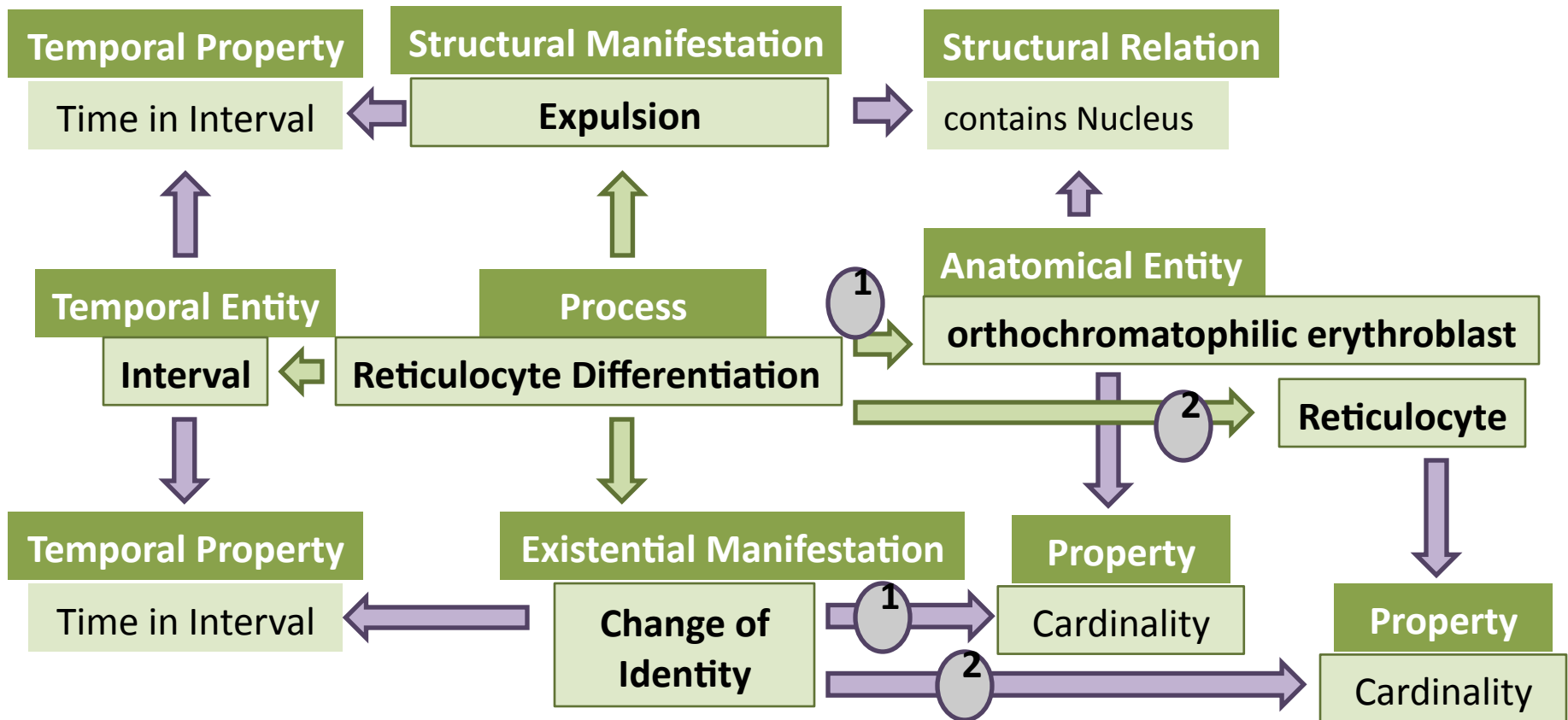
"Simply": Cell Behaviors can be described by answering three questions

1. What **Entities** change during a process?
2. Which **Properties** of the entity are essential to defining the process?
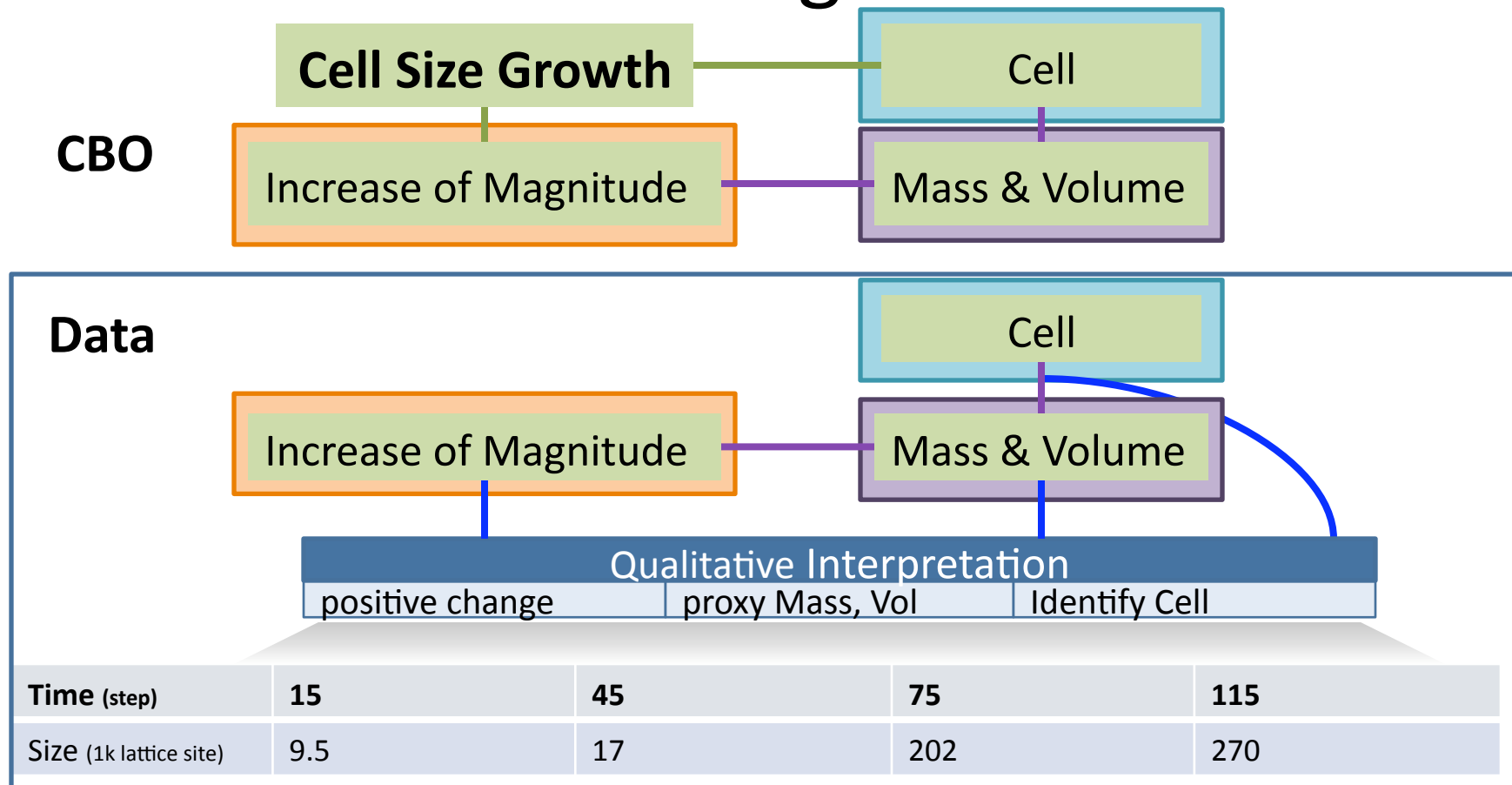3. How does each property **Change** with respect to time?

The CBO built using this structure can be applied in multiple contexts

- Annotate
  - Cellular image time series data
  - Simulation results and models
  * Useful for retrieving them in the future
- Ontology described data can facilitate sharing of defined data in scientific communication

Data can be annotated the underlying definitions of behaviors
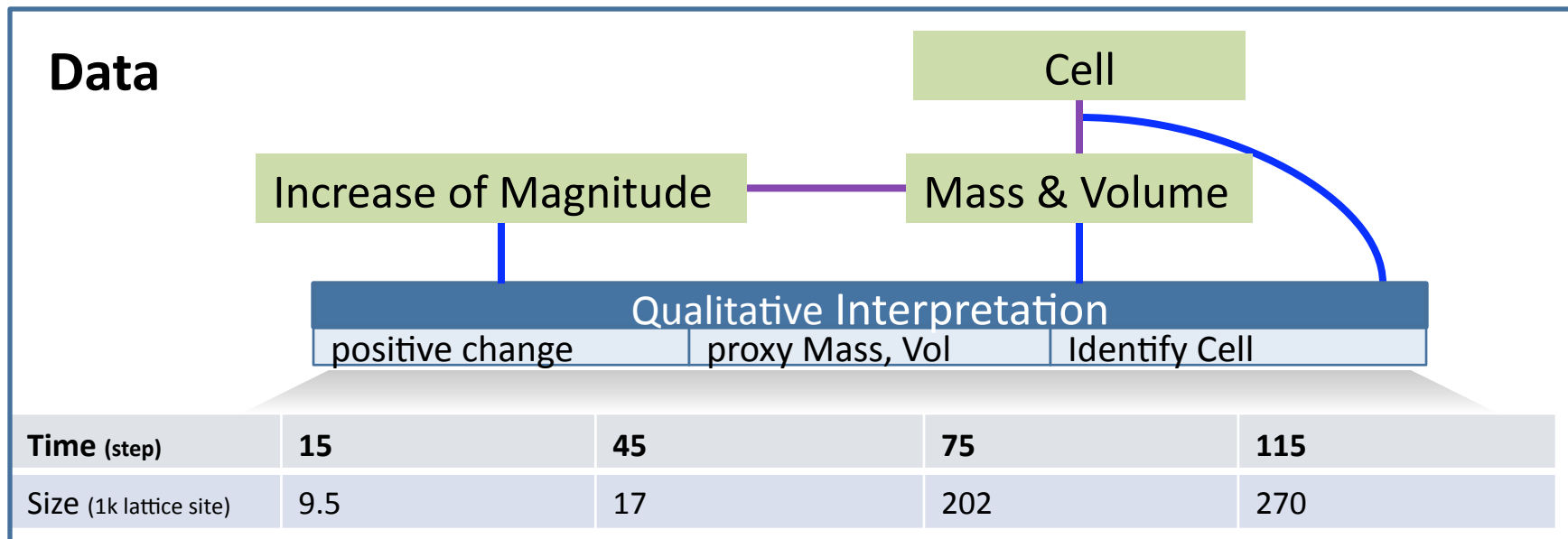
If the CBO is right it will be possible to match data exhibiting the behavior

CBO

Cell Size Growth		Cell
Increase of Magnitude		Mass & Volume

Data

		Cell
Increase of Magnitude		Mass & Volume

Qualitative Interpretation

positive change	proxy Mass, Vol	Identify Cell

Time (step)	15	45	75	115
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- Allows for automated reasoning

Cell Size Growth

The real challenge will be to organize the behaviors into sensible classes

CBO major classes include:

- Adhesion
- Communication
- Existence
- Regionalization
- Transport

⋮

Which factors drive their categorization?

- Structure
- Type of Change
  - Quantitative Property
  - Self Identity
  - Multi Cell Context
 - Relative Location
- Progress of Time

To summarize: In building the CBO we are writing the structured definitions

- cell size growth is an increase of magnitude of the mass and volume of a cell

- Reticulocyte Differentiation is the expulsion of the nucleus

  and

- Reticulocyte Differentiation is the change of identity of a orthochromatophilic erythroblast to Reticulocyte

My preliminary impression of the answers to the questionnaire

- A diversity of perspectives, but
- Consensus on terminology for behaviors

  - cells – move
  - retinoic acid - secretion
  - **Entity- Change**
  - Surface ligand presentation
  - **Location - Entity- Change**

The proposed CBO structure can be organized using 'the square'
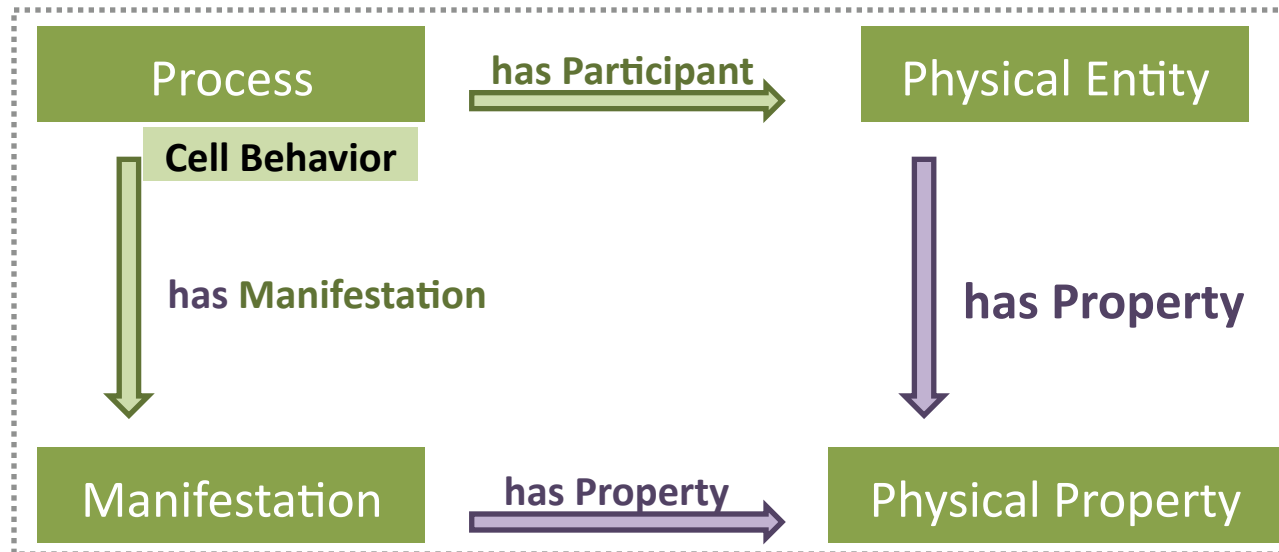
Thank You!

Biocomplexity X and CBO organizers

National Library of Medicine

Colleagues from UW BioEngineering, Indiana University BioComplexity Institute, UW Biomedical and Health Informatics