Heart Development

Narrative vs Combinatorial Approach

Narrative Approach

- This is the way we currently build the ontologies

- It stems from a traditional approach to learning

- We read about the process and make a story to describe it

Combinatorial Approach

- Uses the vocabularies from two or more general processes to build a vocabulary for a specific process
- In this case we we use knowledge of heart anatomy and general developmental processes to build a vocabulary for heart development
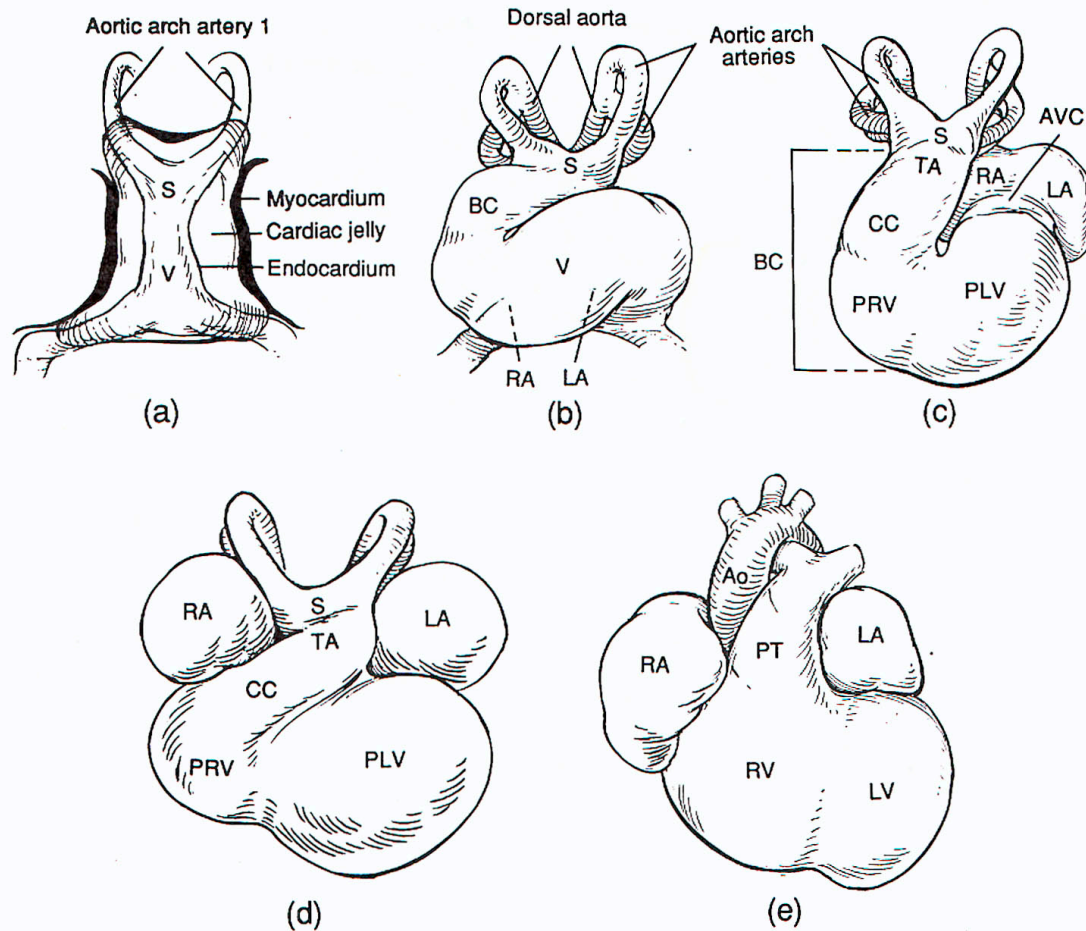
The Test

- Read papers and textbooks to build a vocabulary describing heart development using the narrative approach.

- Take use a combination of terms from heart anatomy with developmental process terms to build a vocabulary describing heart development.

Mouse Heart Development

From The Heart by Margaret Kirby in "Embryos, Genes and Birth Defects". Edited by Peter Thorogood

The Narrative Approach

```
% heart development (sensu mammalia) % organogenesis
 < heart induction  % endoderm/mesoderm induction
 < formation of cardiogenic regions
  < thickening of the cardiogeneic plates
  < formation of cardigenic cells from neural crest
            % development of ectodermal derivatives
  < formation of cardiogenic cells from mesoderm
            % development of mesodermal derivatives
 < formation of heart tube % formation of an
                             epithelial tube
 < formation of layered heart tube
  < endocardium formation
  < myocardium formation
   <heart muscle differentiation
    % ventricular cardiac myocyte differentiation
            % cell differentiation
    % atrial cardiac myocyte differentiation
            % cell differentiation
  < cardiac jelly formation
  < endocardial cushion formation
   % atrial endocardial cushion formation
            < formation of the primitive atrium
   % ventricular endocardial cushion formation
            < formation of the primitive ventrical
 < formation of the dorsal mesocardium
 < folding of the heart tube
  < rightward looping of the heart tube
            < left/right asymmetry determination ; GO:0007368
 < breakdown of the dorsal mesocardium
 < myocardial cell shape changes
 < primitive heart ascention
 < demarcation of the heart tube % pattern formation
  < heart segmentation % segmentation
   < demarcation of the inflow tract
   < demarkation of the outflow tract
   < demarkation of the primitive atrium
   < demarkation of the primitive ventricle
```

```
< formation of the bulbo-ventricular groove
    < formation of the atrio-ventricular groove
  < remodelling of the primitive heart
   < development of the atria
    < cell proliferation in the atrial wall % cell proliferation
    < apoptosis in the atrial wall % apoptosis during
            heart remodelling
   < development of the ventricles
    < cell proliferation in the ventricle walls
            % cell proliferation
    < apoptosis during ventricular wall formation
            % apoptosis during heart remodelling
    < development of the ventricular trabeculae
   < heart septation
    % inter-atrial septation < development of the atria
     < formation of the septum primum
    % formation of the aortico-pulmonary spiral septum
    % inter-ventricular septation
            < development of the ventricles
     < proliferation of myocytes at the compact zone
            % cell proliferation ; GO:0008283
    % separation of atrium from ventricle
     < proliferation of mesenchyme cells
     < development of the atrioventricular valves
      % development of the mitral valve
      % development of the tricuspid valve
   < apoptosis during heart remodelling % apoptosis
   < development of the heart valves
    < formation of the valve cusps
    % development of the aortic valve
    % development of the pulmonary valve
  < development of the coronary vessels
    < coronary vessel vasculogenesis % formation of an
            epithelial tube
    < coronary vessel angiogenesis % angiogenesis
```

Observations: Narrative Approach

- At first look, this ontology looks good. As I read down, the flow is logical and it does a nice job describing heart development.

- As I read through the ontology, I can find areas where I would like to establish more relationships. Eg. Breakdown of the dorsal mesocardium should perhaps be a type of apoptosis.

- We now have to write definitions for all of these terms.

The Combinatorial Approach
Step 1

- Modify the current vocabularies
  - Consolidate the terms in the anatomical dictionary so that each term is represented once and they all have the correct "parts of" and "types of" designations. Primitive structures are "types of".
  - Remove anatomical terms from the Developmental Process Ontology

Original Anatomical Dictionary

702 lines

Stage 11
| | | | heart
| | | | cardiogenic plate (myocardial plate)
Stage 12
| | | | heart
| | | | cardiogenic plate (myocardial plate)
| | | | early primitive heart tube
| | | | | cardiac jelly
| | | | | cardiac muscle (myocardium)
| | | | | endocardial tube
| | | | mesentery
| | | | | dorsal mesocardium (dorsal mesentery of heart)
| | | | | | transverse pericardial sinus
| | | | primitive heart tube
| | | | | bulbus cordis
| | | | | | caudal half
| | | | | | | cardiac jelly
| | | | | | | cardiac muscle (myocardium)
| | | | | | | endocardial tube
| | | | | | rostral half (conotruncus)
| | | | | | | cardiac jelly
| | | | | | | cardiac muscle (myocardium)
| | | | | | | endocardial tube
| | | | | common atrial chamber
| | | | | | cardiac jelly
| | | | | | cardiac muscle (myocardium)
| | | | | | endocardial tube
| | | | | outflow tract

| | | | | | | cardiac jelly
| | | | | | | endocardial tube
| | | | | | | mesenchyme
| | | | | | primitive ventricle (future left ventricle)
| | | | | | | cardiac jelly
| | | | | | | cardiac muscle (myocardium)
| | | | | | | endocardial tube
| | | | sinus venosus
| | | | | left horn
| | | | | right horn
Stage 13
| | | | heart
| | | | bulbus cordis
| | | | | caudal half
| | | | | | cardiac jelly
| | | | | | cardiac muscle (myocardium)
| | | | | | endocardial tube
| | | | | rostral half (conotruncus)
| | | | | | cardiac jelly
| | | | | | cardiac muscle (myocardium)
| | | | | | endocardial tube
| | | | common atrial chamber
| | | | | cardiac jelly
| | | | | cardiac muscle (myocardium)
| | | | | endocardial tube
| | | | mesentery
| | | | | dorsal mesocardium (dorsal mesentery of heart)

Consolidated Anatomical Dictionary

| heart
| %cardiogenic plate
| %primitive heart tube
| | <myocardium
| | <endocardium
| | <cardiac jelly
| <aortic sinus
| <atrio-ventricular canal (ependymal canal)
| <atrio-ventricular cushion tissue (bulbar cushion,ependymal cushion tissue)
| <atrium
| | %primitive atrium
| | %common atrial chamber
| | | <common atrial chamber bulbous cordis
| | | <common atrial chamber, left part
| | | | <common atrial chamber, left part, cardiac muscle (myocardium)
| | | | <common atrial chamber, left part, endocardial lining
| | | | <common atrial chamber, left part, cardiac jelly
| | | <common atrial chamber, right part
| | | | <common atrial chamber, right part, cardiac muscle (myocardium)
| | | | <common atrial chamber, right part, endocardial lining
| | | | <common atrial chamber, right part, cardiac jelly
| | <left atrium
| | | < left atrium auricular region
| | | | <left atrium auricular region cardiac muscle (myocardium)
| | | | < left atrium auricular region endocardial lining
| | | <left atrium cardiac muscle (myocardium)
| | | <left atrium endocardial lining
| | <right atrium
| | | <right atrium auricular region
| | | | <right atrium auricular region cardiac muscle (myocardium)
| | | | <right atrium auricular region endocardial lining
| | | <right atrium cardiac muscle (myocardium)
| | | <right atrium endocardial lining
| | | <right atrium valve
| | | | % right atrium venous valve
| | < interatrial septum
| | | < foramen ovale
| | | < septum primum
| | | | < foramen primum (ostium primum)
| | | | < foramen secundum (ostium secundum)
| | | < septum secundum
| <endocardial tissue
| | <endocardial cushion tissue (bulbar cushion)
| | <bulboventricular groove
| | <bulbus cordis
| | | < bulbus cordis caudal half (myocardium)
| | | | <bulbus cordis caudal half cardiac muscle (myocardium)
| | | | <bulbus cordis caudal half endocardial lining
| | | | <bulbus cordis caudal half cardiac jelly
| | | < bulbus cordis rostral half (conotruncus)
| | | | < bulbus cordis rostral half cardiac muscle (myocardium)
| | | | < bulbus cordis rostral half endocardial lining
| | | | < bulbus cordis rostral half cardiac jelly
| < heart mesentery
| | <dorsal mesocardium (dorsal mesentery of heart)
| | | <dorsal mesocardium transverse pericardial sinus
| <outflow tract
| | <outflow tract aortic component
| | <outflow tract aortico-pulmonary spiral septum
| | | <outflow tract future ascending aorta
| | <outflow tract pulmonary component

Pared-Down Developmental Process

71 Lines

< branching morphogenesis
< organogenesis %organogenesis (sensu Animalia)
 <   development of ectodermal derivatives
 <   development of endodermal derivatives
  < endoderm determination
 <   development of mesodermal derivatives
  < mesoderm cell migration
  < fate determination in mesoderm
 < establishment of a morphogenetic field
  < establishment and maintennance of a gradient
  < diffusion of a morphogen
  < establishment of a gradient source
  < establishment of a gradient sink
  < anchoring of a gradient component
 % morphogenesis of an epithelium
  < formation of epithelial cells
  % morphogenesis of an epithelial sheet
   % formation of an epithelial tube
  < directed cytokinesis of cells within an epithelial sheet
  < cell shape changes within an epithelial sheet
  < movement of cells within an epithelial sheet
  < growth of cells within an epithelial sheet
  < apoptosis of cells within an epithelial sheet
  % morphogenesis of an epithelial tube
   < directed cytokinesis of cells within an epithelial tube
   < cell shape changes within an epithelial tube
   < movement of cells within an epithelial tube
   < growth of cells within an epithelial tube
   < apoptosis of cells within an epithelial tube
  % rearrangement of epithelial cell layers
  % movement of an epithelial sheet
   % delamination
   % epiboly
   % invagination
   % involution

% morphogenesis of a mesenchyme
   < formation of mesenchymal cells
   < movement of mesenchymal cells
% cell differentiation
 < cell committment
 < cell specification
 < cell determination
% pattern formation
 < pattern specification
 < pattern determination
 % axis specification
  % maternal specification of axis
  % zygotic specification of axis
  % dorsal/ventral axis determination % pattern
             determination
   %maternal dorsal/ventral axis determination
             % maternal specification of axis
             % pattern determination
   %zygotic dorsal/ventral axis determination
             % zygotic specification of axis
             % pattern determination
  % anterior/posterior axis determination
             % pattern determination
   % maternal anterior/posterior axis determination
             % maternal specification of axis
             % pattern determination
   % zygotic anterior/posterior axis determination
             % zygotic specification of axis
             % pattern determination
 % segmentation
< embryonic induction
 % juxtacrine inductive signaling
 % paracrine inductive signaling
 % ectoderm/mesoderm interaction
 % epithelia/epithelial induction
 % epithelial/mesenchymal induction
 % ectodrerm/endoderm interaction NEW TERM
 % endoderm/mesoderm interaction NEW TERM
 < tissue remodeling NEW TERM

The Combinatorial Approach

- ## Is the entire cross-product of the DAG necessary?

    - If the anatomical dictionary really describes all of the parts of the heart, then the product of the AD and "development" should describe all of the anatomical aspects of development

    - If the developmental process ontology really describes all aspects of development, then the product of "heart" and the developmental process ontology should describe all of the processes involved in heart development.

    Start with the two top-level cross products

"Heart Anatomy" X "Development"

94 Terms

| heart !!!development!!!
| <cardiogenic plate !!!development!!!
| <primitive heart tube !!!development!!!
| | <myocardium !!!development!!!
| | <endocardium !!!development!!!
| | <cardiac jelly !!!development!!!
| <aortic sinus !!!development!!!
| <atrio-ventricular canal (ependymal canal) !!!development!!!
| <atrio-ventricular cushion tissue (bulbar cushion,ependymal cushion tissue) !!!development!!!
| <atrium !!!development!!!
| | %primitive atrium !!!development!!!
| | %common atrial chamber !!!development!!!
| | | <common atrial chamber bulbous cordis   !!!development!!!
| | | <common atrial chamber, left part !!!development!!!
| | | <common atrial chamber, left part, cardiac muscle (myocardium) !!!development!!!
| | | <common atrial chamber, left part, endocardial lining !!!development!!!
| | | <common atrial chamber, left part, cardiac jelly !!!development!!!
| | | <common atrial chamber, right part !!!development!!!
| | | <common atrial chamber, right part, cardiac muscle (myocardium) !!!development!!!
| | | <common atrial chamber, right part, endocardial lining !!!development!!!
| | | <common atrial chamber, right part, cardiac jelly !!!development!!!
| | <left atrium !!!development!!!
| | | < left atrium auricular region !!!development!!!
| | | | <left atrium auricular region cardiac muscle (myocardium) !!!development!!!
| | | | < left atrium auricular region endocardial lining !!!development!!!
| | | <left atrium cardiac muscle (myocardium) !!!development!!!
| | | <left atrium endocardial lining !!!development!!!
| | <right atrium !!!development!!!
| | | <right atrium auricular region !!!development!!!
| | | | <right atrium auricular region cardiac muscle (myocardium) !!!development!!!
| | | | <right atrium auricular region endocardial lining !!!development!!!
| | | <right atrium cardiac muscle (myocardium) !!!development!!!
| | | <right atrium endocardial lining !!!development!!!
| | | <right atrium valve !!!development!!!
| | | | % right atrium venous valve !!!development!!!
| | < interatrial septum !!!development!!!
| | | < foramen ovale !!!development!!!
| | | < septum primum !!!development!!!
| | | | < foramen primum (ostium primum) !!!development!!!
| | | | < foramen secundum (ostium secundum) !!!development!!!
| | | < septum secundum !!!development!!!
| <endocardial tissue !!!development!!!
| | <endocardial cushion tissue (bulbar cushion) !!!development!!!
| | <bulboventricular groove!!!development!!!

| | <bulbus cordis !!!development!!!
| | | < bulbus cordis caudal half (myocardium) !!!development!!!
| | | | <bulbus cordis caudal half cardiac muscle (myocardium) !!!development!!!
| | | | <bulbus cordis caudal half endocardial lining !!!development!!!
| | | | <bulbus cordis caudal half cardiac jelly !!!development!!!
| | | | < bulbus cordis rostral half (conotruncus) !!!development!!!
| | | | < bulbus cordis rostral half cardiac muscle (myocardium) !!!development!!!
| | | | < bulbus cordis rostral half endocardial lining !!!development!!!
| | | | < bulbus cordis rostral half cardiac jelly !!!development!!!
| < heart mesentery !!!development!!!
| | <dorsal mesocardium (dorsal mesentery of heart) !!!development!!!
| | | <dorsal mesocardium transverse pericardial sinus !!!development!!!
| <outflow tract !!!development!!!
| | <outflow tract aortic component !!!development!!!
| | <outflow tract aortico-pulmonary spiral septum !!!development!!!
| | | <outflow tract future ascending aorta !!!development!!!
| | <outflow tract pulmonary component !!!development!!!
| | | <outflow tract pulmonary component proximal part !!!development!!!
| <pericardium !!!development!!!
| | <fibrous pericardium !!!development!!!
| | <serosal pericardium !!!development!!!
| | | <parietal pericardium !!!development!!!
| | | <visceral pericardium (epicardium) !!!development!!!
|<sinus venosus !!!development!!!
| | <sinus venosus left horn !!!development!!!
| | <sinus venosus right horn !!!development!!!
| <trabeculae carneae !!!development!!!
| <heart valve !!!development!!!
| | %aortic valve   !!!development!!!
| | | <aortic valve leaflets !!!development!!!
| | %mitral valve (bicuspid valve) !!!development!!!
| | | <mitral valve leaflets !!!development!!!
| | %pulmonary valve !!!development!!!
| | | <pulmonary valve leaflets !!!development!!!
| | %tricuspid valve !!!development!!!
| | | <tricuspid valve leaflets !!!development!!!
| |ventricle !!!development!!!
| | %primitive ventricle !!!development!!!
| | | < primirtive ventricle cardiac jelly !!!development!!!
| | <interventricular groove !!!development!!!
| | <interventricular septum (ependymal septum) !!!development!!!

"Heart" X "Dev. Proc."
71 terms

<heart !!!branching morphogenesis!!!

< heart !!!organogenesis!!! %organogenesis (sensu Animalia)   %heart !!!cell differentiation!!!

< heart !!! development of ectodermal derivatives!!!   <heart !!!cell committment!!!

< heart !!! development of endodermal derivatives!!!   <heart !!!cell specification!!!

<heart !!! endoderm determination!!!   <heart !!!cell determination!!!

< heart !!! development of mesodermal derivatives!!!   %heart !!!pattern formation!!!

<heart !!! mesoderm cell migration!!!   <heart !!!pattern specification!!!

<heart !!!fate determination in mesoderm!!!   <heart !!!pattern determination!!!

<heart !!!establishment of a morphogenetic field!!!   %heart !!!axis specification!!!

<heart !!!establishment and maintennance of a gradient!!!   %heart !!!maternal specification of axis!!!

<heart !!!diffusion of a morphogen!!!   %heart !!!zygotic specification of axis!!!

<heart !!!establishment of a gradient source!!!   %heart !!!dorsal/ventral axis determination!!! %heart !!!pattern determination!!!

<heart !!!establishment of a gradient sink!!!   %maternal dorsal/ventral axis determination!!! %heart !!!maternal specification of axis!!!

<heart !!!anchoring of a gradient component!!!   %heart !!!pattern determination!!!

%heart !!!morphogenesis of an epithelium!!!   %zygotic dorsal/ventral axis determination!!! %heart !!!zygotic specification of axis!!!

<heart !!!formation of epithelial cells!!!   %heart !!!pattern determination!!!

%heart !!!morphogenesis of an epithelial sheet!!!   %heart !!!anterior/posterior axis determination %heart !!!pattern determination!!!

%heart !!!formation of an epithelial tube!!!   %heart !!!maternal anterior/posterior axis determination!!! %heart !!!maternal specification of axis!!!

<heart !!!directed cytokinesis of cells within an epithelial sheet!!!   %heart !!!pattern determination!!!

<heart !!!cell shape changes within an epithelial sheet!!!   %heart !!!zygotic anterior/posterior axis determination!!! %heart !!!zygotic specification of axis!!!

<heart !!!movement of cells within an epithelial sheet!!!   %heart !!!pattern determination!!!

<heart !!!growth of cells within an epithelial sheet!!!   %heart !!!segmentation!!!

<heart !!!apoptosis of cells within an epithelial sheet!!!   <heart !!!embryonic induction!!!

%heart !!!morphogenesis of an epithelial tube!!!   %heart !!!juxtacrine inductive signaling!!!

<heart !!!directed cytokinesis of cells within an epithelial tube!!!   %heart !!!paracrine inductive signaling!!!

<heart !!!cell shape changes within an epithelial tube!!!   %heart !!!ectoderm/mesoderm interaction!!!

<heart !!!movement of cells within an epithelial tube!!!   %heart !!!epithelia/epithelial induction!!!

<heart !!!growth of cells within an epithelial tube!!!   %heart !!!epithelial/mesenchymal induction!!!

<heart !!!apoptosis of cells within an epithelial tube!!!   %heart !!!ectodrerm/endoderm interaction!!! NEW TERM

%heart !!!rearrangement of epithelial cell layers!!!   %heart !!!endoderm/mesoderm interaction!!! NEW TERM

%heart !!!movement of an epithelial sheet!!!   <heart !!!tissue remodelling!!!

%heart !!!delamination!!!

%heart !!!epiboly!!!

%heart !!!invagination!!!

%heart !!!involution!!!

%heart !!!morphogenesis of a mesenchyme!!!

<heart !!!formation of mesenchymal cells!!!

<heart !!!movement of mesenchymal cells!!!

The Combinatorial Approach
Step 3

- This ontology creates a very complete picture of heart development, but the picture is of low resolution.

- How do we generate a high-resolution picture?

  – Generate the entire cross product of the two DAGS

  – Use biological knowledge to pick and choose

The Full cross-product

- Would result in every developmental process being assigned to every anatomical term

- From a biological perspective, this may be inappropriate. We know that not every developmental process occurs in the development of every structure.

- We would need to do a lot of culling.

The pick-and-choose approach

- In this approach I have chosen to pick out anatomical terms and combine them with appropriate dev proc terms.

- Rules of the game
  - When an anatomical term is combined with a dev process term and is inserted into process heirarchy it becomes a type of the general process described in "heart X Dev Proc
  - When an anatomical term is combined with a dev process term it retains its relationship within the general process described in heart anatomy X "development"

  The rules insure integrity of the vocabulary. Essentially we are still building a subset of the full cross-products.

Let's take an example of primitive heart tube development.

- The primitive heart tube forms from a mesenchymal to epithelial transition of the cardiogenic plate.
- The epithelial sheet that is formed then forms an epithelial tube.
- The epithelial tube differentiates into three layers: endocardium, myocardium and cardiac jelly.

Here are the areas we are working on

From "Heart Anatomy X Development"

| heart !!!development!!!
| <cardiogenic plate !!!development!!!
| <primitive heart tube !!!development!!!

From "Heart" X "Developmental Process"

%heart !!!morphogenesis of an epithelium!!!
 <heart !!!formation of epithelial cells!!!
 %heart !!!morphogenesis of an epithelial sheet!!!
  %heart !!!formation of an epithelial tube!!!
  <heart !!!directed cytokinesis of cells within an epithelial sheet!!!
  <heart !!!cell shape changes within an epithelial sheet!!!
  <heart !!!movement of cells within an epithelial sheet!!!
  <heart !!!growth of cells within an epithelial sheet!!!
  <heart !!!apoptosis of cells within an epithelial sheet!!!

%heart !!!cell differentiation!!!
 <heart !!!cell committment!!!
 <heart !!!cell specification!!!
 <heart !!!cell determination!!!

The primitive heart tube forms from a mesenchymal to epithelial transition of the cardiogenic plate.

heart !!!development!!!
| <cardiogenic plate !!!development!!!
| <primitive heart tube !!!development!!!
| | < **primitive heart tube !!!morphogenesis of an epithelium!!!**
| | | <**primitive heart tube !!!formation of epithelial cells!!!**

%heart !!!morphogenesis of an epithelium!!!
 % **primitive heart tube !!!morphogenesis of an epithelium!!!**
 <heart !!!formation of epithelial cells!!!
  %primitive heart tube !!!formation of epithelial cells!!!
 %heart !!!morphogenesis of an epithelial sheet!!!
  %heart !!!formation of an epithelial tube!!!
 <heart !!!directed cytokinesis of cells within an epithelial sheet!!!
 <heart !!!cell shape changes within an epithelial sheet!!!
 <heart !!!movement of cells within an epithelial sheet!!!
 <heart !!!growth of cells within an epithelial sheet!!!
 <heart !!!apoptosis of cells within an epithelial sheet!!!
 %heart !!!morphogenesis of an epithelial tube!!!

%heart !!!cell differentiation!!!
 <heart !!!cell committment!!!
 <heart !!!cell specification!!!
 <heart !!!cell determination!!!

The epithelial sheet that is formed then forms an epithelial tube.

heart !!!development!!!

| <cardiogenic plate !!!development!!!

| <primitive heart tube !!!development!!!

| | < **primitive heart tube !!!morphogenesis of an epithelium!!!**

| | | **<primitive heart tube !!!formation of epithelial cells!!!**

| | | **% primitive heart tube !!!morphogenesis of an epithelial sheet!!!**

| | | **< primitive heart tube !!!formation of an epithelial tube!!!**

| | | | **< primitive heart tube !!!directed cytokinesis of cells within an epithelial sheet!!!**

| | | | **< primitive heart tube !!!!cell shape changes within an epithelial sheet!!!**

| | | | **< primitive heart tube !!!movement of cells within an epithelial sheet!!!**

%heart !!!morphogenesis of an epithelium!!!

 % primitive heart tube !!!morphogenesis of an epithelium!!!

 <heart !!!formation of epithelial cells!!!

 %primitive heart tube !!!formation of epithelial cells!!!

%heart !!!morphogenesis of an epithelial sheet!!!

 % primitive heart tube !!!morphogenesis…!!!

 %heart !!!formation of an epithelial tube!!!

 % primitive heart tube !!!formation of an…!!!

 <heart !!!directed cytokinesis of cells within an epithelial sheet!!!

 % primitive heart tube !!!directed cytokinesis…!!!

 <heart !!!cell shape changes within an epithelial sheet!!!

 % primitive heart tube !!!!cell shape changes…!!!

 <heart !!!movement of cells within an epithelial sheet!!!

 % primitive heart tube !!!movement of cells…!!!

%heart !!!cell differentiation!!!

 <heart !!!cell committment!!!

 <heart !!!cell specification!!!

 <heart !!!cell determination!!!

The epithelial tube differentiates into three layers: endocardium, myocardium and cardiac jelly.

heart !!!development!!!
| <cardiogenic plate !!!development!!!
| <primitive heart tube !!!development!!!
| |< **primitive heart tube !!!morphogenesis of an epithelium!!!**
| | | **<primitive heart tube !!!formation of epithelial cells!!!**
| | | **% primitive heart tube !!!morphogenesis of an epithelial sheet!!!**
| | | **< primitive heart tube !!!formation of an epithelial tube!!!**
| | | | < **primitive heart tube !!!directed cytokinesis of cells**
                           within an epithelial sheet!!!
| | | | < **primitive heart tube !!!!cell shape changes**
                           within an epithelial sheet!!!
| | | | < **primitive heart tube !!!movement of cells**
                           within an epithelial sheet!!!
| |< **primitive heart tube !!!cell differentiation!!!**
| | |**<myocardium !!!cell differentitation!!**
| | |**< endocardium !!!cell differentiation!!!**
| | |**<cardiac jelly !!!cell differenttiation!!!**
| | |**<primitive heart tube !!!cell commitment!!!**
| | | | **< myocardium !!!cell commitment!!!**
| | | | **< endocardium !!!cell commitment!!!**
| | | | **< cardiac jelly !!!cell commitment!!!**
| | |**<primitive heart tube !!!cell specification!!!**
| | | | **< myocardium !!!cell specification!!!**
| | | | **< endocardium !!!cell specification!!!**
| | | | **< cardiac jelly !!!cell specification!!!**
| | |**<primitive heart tube !!!cell determination!!!**
| | | | **< myocardium !!!cell determination!!!**
| | | | **< endocardium !!!cell determination!!!**
| | | | **< cardiac jelly !!!cell determination!!!**

%heart !!!cell differentiation!!!
 %primitive heart tube !!!cell differentiation!!!
  % myocardium !!!cell differentiation!!!
  % endocardium !!!cell differentiation!!!
  % cardiac jelly !!!cell differentiation!!!
 <heart !!!cell committment!!!
  % primitive heart tube !!!cell commitment!!!
   % myocardium !!!cell differentiation!!!
   % endocardium !!!cell differentiation!!!
   % cardiac jelly !!!cell differentiation!!!
<heart !!!cell specification!!!
 %primitive heart tube !!!cell specification!!!
  % myocardium !!!cell differentiation!!!
  % endocardium !!!cell differentiation!!!
  % cardiac jelly !!!cell differentiation!!!
<heart !!!cell determination!!!
 % primitive heart tube !!!cell determination!!!
  % myocardium !!!cell differentiation!!!
  % endocardium !!!cell differentiation!!!
  % cardiac jelly !!!cell differentiation!!!

Observations: Cross-product Approach

- On a global level, this approach looks really good. All of the developmental structures are accounted for.

- Not everything is covered. For example there is a great deal of tissue remodeling that occurs late in heart development. Using the process ontologies as they are this is not dealt with well.

- There is no indication of where things come from. Some of this can be handled in the pick-and-choose phase.

- The terms are not user friendly and they are not expressions that biologist would use.

Conclusions:Narrative Approach

- This is clearly the comfortable approach. It is based on the way we learn about things. If we were writing a review, we would use this approach.

- The approach is accurate since all of the terms are picked by hand. However, relationships may not be complete because we tend to think of the terms in isolation. For example, cardiac jelly formation is not defined as cell differentiation. Of course that can be done by inspection after the construction.

- The sense of things being derived from other things can be well represented in this approach.

- This is clearly the approach if we are annotation-driven. It allows great ease of inserting terms as needed.

- It is inherently incomplete and inconsistent.

- Problems are dealt with by hand.

Conclusions: Cross-product approach 1

- This approach is inherently complete as long as the two vocabularies that are used to construct it are complete and consistent.

- It's accuracy can be debated. For example I originally argued that branching morphogenesis wasn't appropriate for heart development…..but then I remembered cardiac vasculature (interesting point).

- It is less complex. Although there are a lot of terms and relationships generated it happens automatically.

- This approach works well if we a trying to describe the whole process.

- Definitions are already written!!!

- Query's will be complete.

Conclusions: Cross-product approach 2
Dealing with Problems

- Most problems are due to incompleteness of the original vocabularies:
  - Heart remodelling: There should be a tissue remodelling term as a part of morphogenesis. It should include all of the processes that are involved. The process will be useful for other organs as well.
  - Cardiac vasculature:needs to become a part of the heart anatomy
  - Derived from concepts: introduce transitional processes into the developmental processes, eg mesenchymal to epithelial transition.
- It is a pain to build these things by hand!!!
  - Design a multiplier tool that allows you to choose two trees and which decendants you'd like to multiply.
- The terms are not user friendly
  - Define synonyms

Questions

- Do we leave it up to each group which procedure they will choose?

- Can we separate out subtrees that can be used to generate the cross products?

- How will we represent the complete ontology at the GO web site?