Honours Project - Appendix

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Cell Model Containment Hierarchy

The top level capsule in the containment hierarchy is called LifeTheUniverseAndEverything, after the book by Douglas Adams (1982). The top of the hierarchy is as follows:

```
LifeTheUniverseAndEverything
. SolarSystem
. . Sun
. . Earth
. . . SimpleEcology
. . . . HumanBeing (me)
. . . . . Eye
. . . . . Mouth
. . . . . Lung
. . . . . CirculatorySystem
. . . . . NervousSystem
. . . . . DigestiveSystem
. . . . Lettuce
. . . . BodyOfWater (lake)
. . . . Atmosphere
. . . . Land
```

Figure 1, Figure 2 and Figure 3 show the top of the hierarchy as modeled visually in RRT.

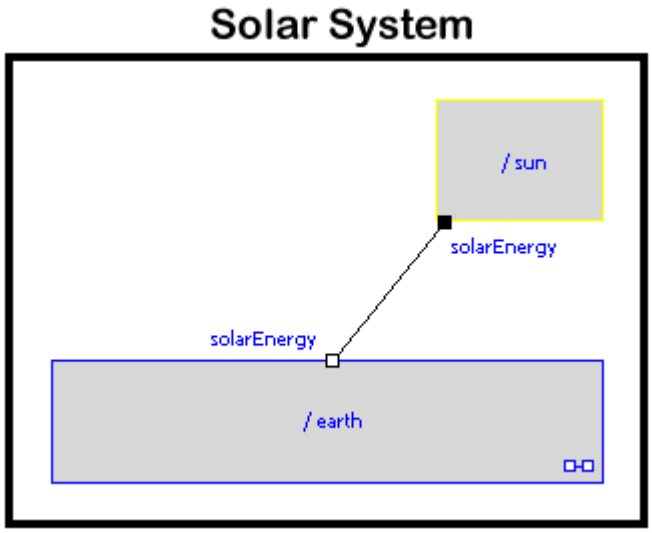

Figure 1 - The Solar System capsule contains the Sun and the Earth.

In the Simple Ecology of Figure 2, the Atmosphere functions as a storehouse for the Oxygen and Carbon Dioxide needed by plants and animals. The lake is a Body of Water that serves as a usable storehouse of Water. The Land includes Soil where Organic Matter is broken down for recycling. Lettuce is a plant that uses some of the received Solar Energy to drive the conversion of Water and Carbon Dioxide into sugars such as Sucrose and Glucose. Some of the other Photons in the Solar Energy are reflected off the Lettuce, and are sent to me as Visible Light. I am a Human Being. I breath Oxygen, drink Water, watch the world around me, process the information that I can sense, eat Lettuce, and eliminate Wastes.

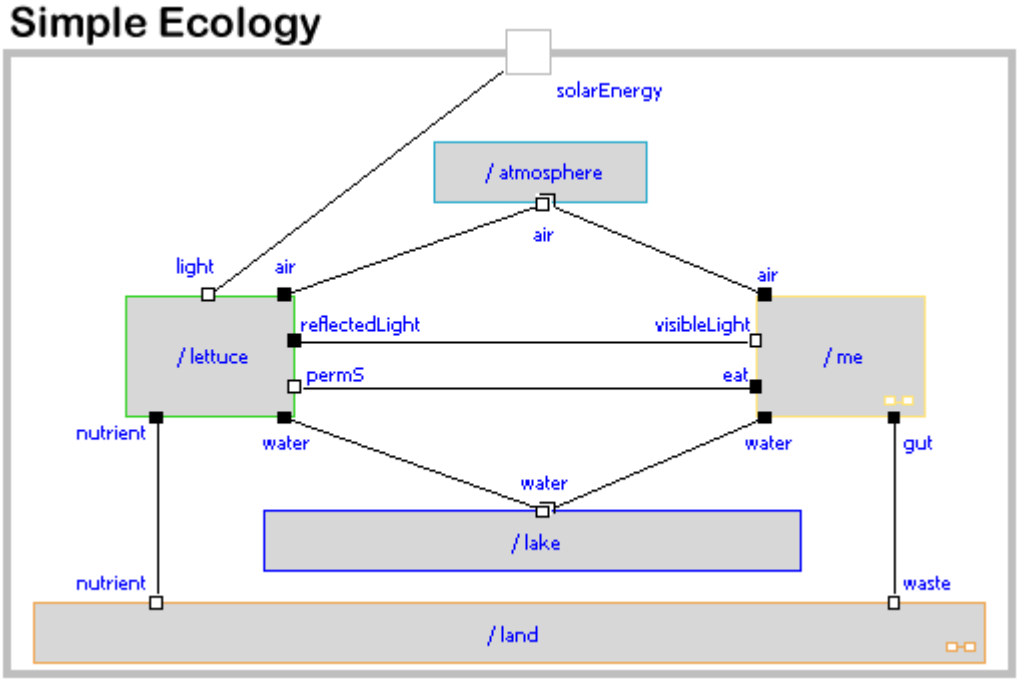

Figure 2 - Simple Ecology.

My body, as modeled in Figure 3, includes many different systems including Lungs for breathing, Eyes for seeing, a Mouth for eating, and a Digestive System for digesting the food. I have a Circulatory System for moving the breathed air and digested food to where it's needed, and a Nervous System to convert sensory images from the Eyes and other sensors into actions by Muscles within the Mouth and other parts of the body.

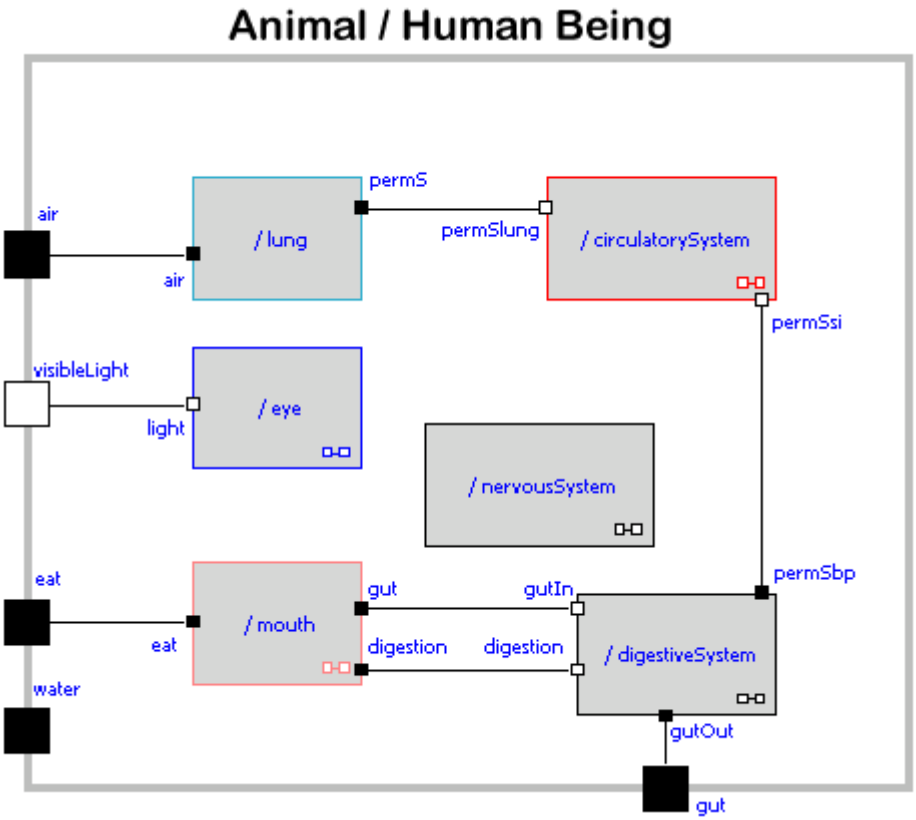

Figure 3 - Human Being.

The part of the containment hierarchy beneath HumanBeing is as follows. Entities with an asterisk (*) at the end may exist as multiple instances.

HumanBeing

. **Eye**
. . RetinaConesAndRods
. . . Cone
. . . Rod

. **Mouth**
. . Muscle
. . . SkeletalMuscleCell

. **Lung**

. **CirculatorySystem**
. . Artery (pulmonaryArtery)
. . . BloodPlasma*
. . Capillary (pCapillary)
. . . BloodPlasma*
. . Vein (pulmonaryVein)
. . . BloodPlasma*
. . BoneMarrow
. . . Erythrocyte*
. . Heart
. . . LeftAtrium
. . . RightAtrium
. . . TheArrowOfTime
. . . LeftVentricle
. . . . BloodPlasma*
. . . . . Erythrocyte*
. . . RightVentricle
. . Artery*
. . . BloodPlasma*
. . Capillary*
. . . BloodPlasma*
. . Vein*
. . . BloodPlasma*
. . NeuronCapillaryConnectors

. **NervousSystem**
. . CentralNervousSystem (cns)
. . . Brain
. . . . ForeBrain
. . . . . Diencephalon
. . . . . Thalamus
. . . . . LateralGeniculateNucleus
. . . . . Neuron
. . . . . Astrocyte
. . . . . HypoThalamus
. . . . . Retina
. . . . . BipolarCell
. . . . . GanglionCell
. . . . . Cerebrum
. . . . . CerebralCortex
. . . . . PrimaryVisualCortex
. . . . . Neuron
. . . . . MotorCortex
. . . . . Neuron
. . . . MidBrain
. . . . HindBrain
. . . SpinalCord
. . . . SpinalCordCervicalRegion
. . . . . VentralHornLeft*
. . . . . MotorNeuron*
. . . . . VentralHornRight*
. . . . . MotorNeuron*
. . . . SpinalCordThoracicRegion
. . . . SpinalCordLumbarRegion
. . . . SpinalCordSacralRegion
. . . . SpinalCordCoccygealRegion
. . PeripheralNervousSystem (pns)
. . . DorsalRootGanglion
. . . . FreeNerveEndingNeuron
. . Synapses
. . . SynapticCleft*
. . . . SynapticCleftFluid
. . . . Enzyme

. **DigestiveSystem**
. . Esophagus
. . Stomach
. . . Food
. . SmallIntestine
. . . MucosalCell
. . . DigestedFood
. . Colon
. . . LargeIntestine
. . . Rectum

The next part of the containment hierarchy is the domain of the cell itself:

```
EukaryoticCell

. Nucleus
. . Nucleoplasm
. . . Nucleolus
. . . . Fibril
. . . . Granule
. . . . RnaPolymeraseI
. . . Chromosome
. . . . Dna
. . . Nucleosol
. . . TranscriptionComplexII
. . . . RnaPolymeraseII
. . . . TfIID
. . . . TfIIB
. . . . TfIIE
. . . . TfIIF
. . . . TfIIH
. . . TranscriptionComplexIII
. . . RegulatoryComplex
. . . . Ctf
. . . . Sp1
. . NuclearEnvelope
. . . NuclearPore
. . . . Transporter
. . . . NuclearPoreAqueousChannel
. . . NuclearOuterMembrane
. . . . NuclearOuterBilayer
. . . PerinuclearSpace
. . . NuclearInnerMembrane
. . . . NuclearInnerBilayer
. . NuclearLamina

. Cytoplasm
. . Cytosol
. . . Water
. . RoughEr
. . . ErMembrane
. . . . ErBilayer
. . . CisternalSpace
. . . . ErFluid
. . SmoothEr
. . . ErMembrane
. . . . ErBilayer
. . . CisternalSpace
. . . . ErFluid
. . Mitochondrion
. . . MitochondrialDualMembrane
. . . . MitochondrialOuterMembrane
. . . . . MitochondrialOuterBilayer
. . . . MitochondrialIntermembraneSpace
. . . . . MitochondrialIntermembranesol
. . . . MitochondrialInnerMembrane
. . . . . MitochondrialInnerBilayer
. . . . . PyruvateTransporter
. . . Matrix
. . . . Matrixsol
. . . . Enzyme*
. . . . Ribosome
. . Ribosome
. . Enzyme*
. . MRna
. . GolgiComplex
. . . GolgiSaccule*
. . . GolgiMembrane
. . . . GolgiBilayer
. . . GolgiSpace
. . . . GolgiFluid
. . Vesicle
. . CytoSkeleton

. CellMembrane
. . CellBilayer
. . . LipidDisintegration
. . . LipidLayer (2)
. . . . Lipid*
. . . . . LipidPolarHead
. . . . . LipidNonPolarTail
. . Transporter (and/or Channel)
```

A Eukaryotic Cell is the type of cell found in all plants and animals, including humans. Each cell has a thin Cell Membrane as a boundary between itself and the outside world, Cytoplasm where the bulk of its metabolic processing takes place, and an inner Nucleus where genetic activity takes place.

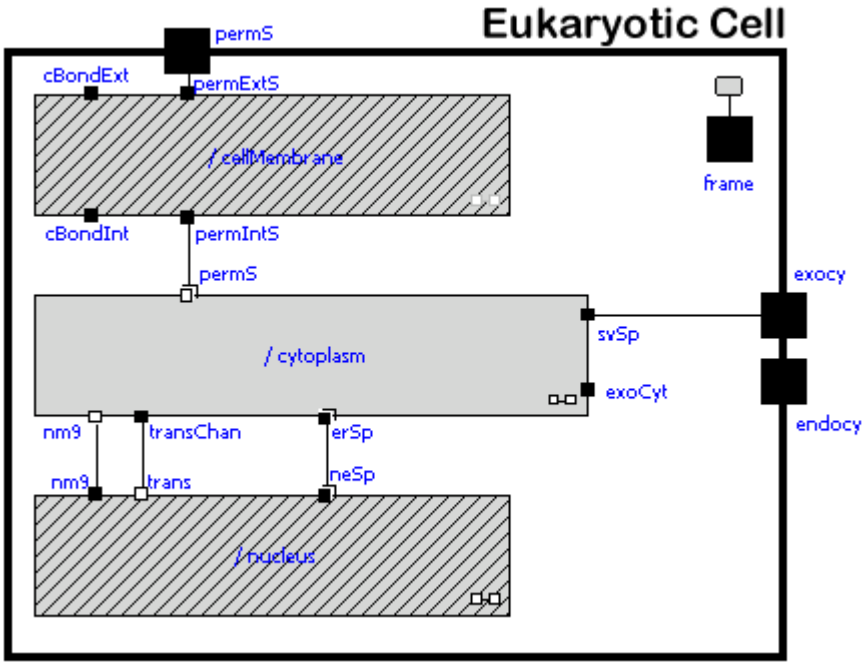

Figure 4 - Eukaryotic Cell.

The Cytoplasm contains many important entities in the Cell Model. The Cytosol contains Small Molecules. Each type of Enzyme converts substrate molecules in the Cytosol into products, which in turn are used as substrates by other enzymes. The many Mitochondria in the system are organelles that perform part of the metabolic processing of the cell. The Ribosome and Messenger RNA (mRNA) increase the number of enzymes of specific types as specified by the DNA.

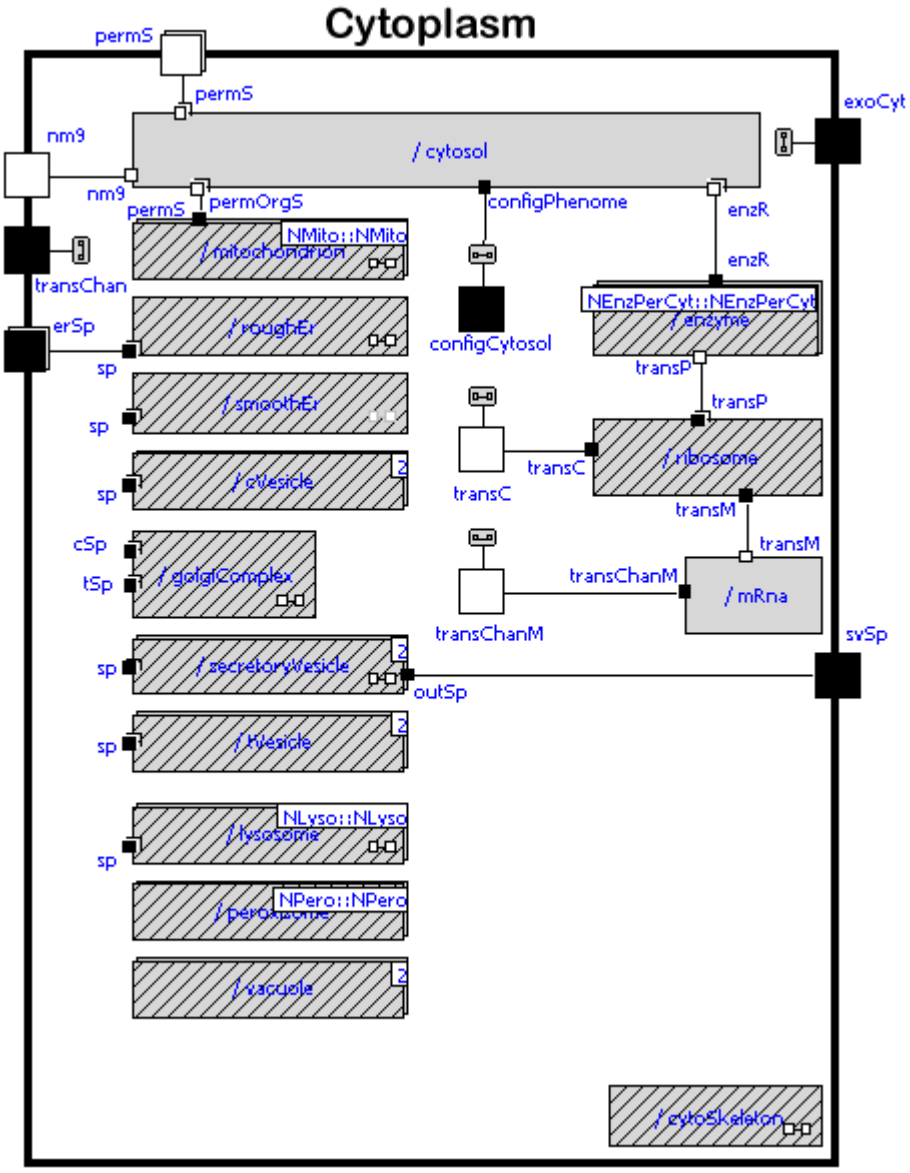

Figure 5 - Cytoplasm.

Neurons are specialized cells that extend the cell containment hierarchy as follows:

```
MotorNeuron

. NeuronCellBody
. . Nucleus
. . . Nucleoplasm
. . . . Nucleolus
. . . . . Fibril
. . . . . Granule
. . . . . RnaPolymeraseI
. . . . Chromosome
. . . . . Dna
. . . . Nucleosol
. . . . TranscriptionComplexII
. . . . . RnaPolymeraseII
. . . . . TfIID
. . . . . TfIIB
. . . . . TfIIE
. . . . . TfIIF
. . . . . TfIIH
. . . . TranscriptionComplexIII
. . . . RegulatoryComplex
. . . . . Ctf
. . . . . Spl
. . . NuclearEnvelope
. . . . NuclearPore
. . . . . Transporter
. . . . . NuclearPoreAqueousChannel
. . . . NuclearOuterMembrane
. . . . . NuclearOuterBilayer
. . . . NuclearInnerMembrane
. . . . . NuclearInnerBilayer
. . . NuclearLamina
. . Cytoplasm
. . CellMembrane
. . . CellBilayer

. Dendrites
. . Dendrite
. . . DendriteMembrane
. . . . DendriteBilayer
. . . . NmdaReceptor
. . Dendrite
. . . DendriteMembrane
. . . . DendriteBilayer
. . . . NmdaReceptor

. Axon
. . AxonHillock
. . AxonSegment
. . . AxonMembrane
. . . . AxonBilayer
. . AxonSegment
. . . AxonMembrane
. . . . AxonBilayer
. MyelinCell

. TerminalButtons
. . TerminalButton*
. . . TerminalButtonPlasm
. . . . SynapticVesicle
. . . . . SynapticVesicleMembrane
. . . . . . SynapticVesicleBilayer
. . . . . . Synaptotagmin
. . . . . SynapticVesicleSpace
. . . . . . SynapticVesicleFluid
. . . . Endosome
. . . . . EndosomeMembrane
. . . . . . EndosomeBilayer
. . . . . EndosomeSpace
. . . . . . EndosomeFluid
. . . . TerminalButtonFluid
. . . TerminalButtonMembrane
. . . . TerminalButtonBilayer
. . . . VoltageGatedCaChannel
```

Neurons are implemented in the Cell Model by placing a Eukaryotic Cell inside a container and adding Dendrites, Axons, and Terminal Buttons. In Figure 6, neuronCellBody is the Eukaryotic Cell. Motor Neron is one type of Neuron.

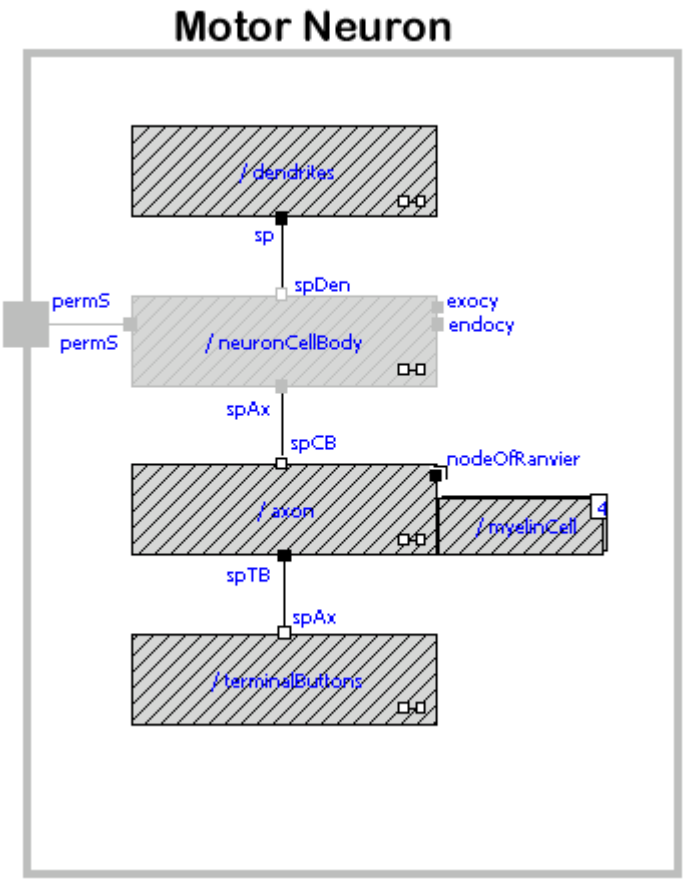

Figure 6 - Motor Neuron.

Some non-biological infrastructure is also required in the model. This is thought of as an artificial nanotechnology that could exist in the real world and is being simulated in RRT. The nanotechnology components are as follows:

```
LifeTheUniverseAndEverything
. ConfigurationAgent
. MmfAgent
. . MmfReflector
. ActiveObjectScheduler
```

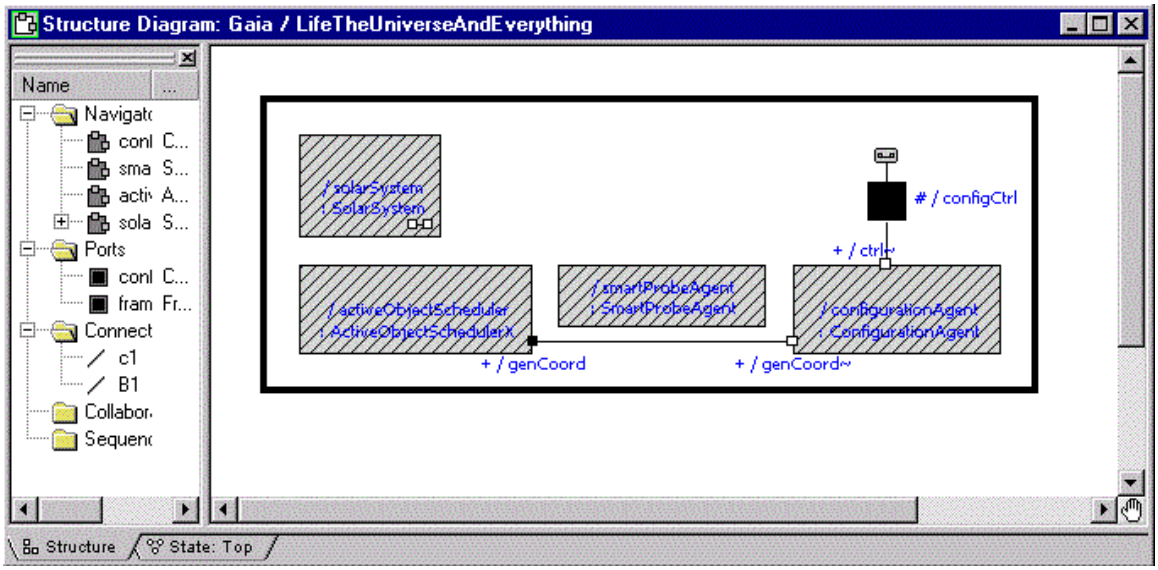

Figure 7 - Cell Model. Top level of containment hierarchy.

When the complete RRT simulation is running, there are between 100,000 and 1,000,000 capsules in the complete containment hierarchy. The number varies depending on how many instances of each component is created. The * to the right of many entities indicates that multiple instances may exist. The size of the model is only constrained by the memory and processing capability of the computer that it runs on.

In addition to RRT capsules, the model also includes more traditional C++ classes. These are used to represent small molecules, and are also important at the non-biological computer implementation level.

Note that everything in the containment hierarchy, other than the nanotechnology entities, corresponds to something in the natural world.

The cell is the main focus of the Cell Model. Much of the containment hierarchy is part of the environment of an individual cell. These higher levels can be thought of as a set of systems that are of biological interest in their own right, as a way of integrating the cells into their natural environment, or as a test harness for the various types of cell.

A test harness is an essential part of any computer system, and may be more complex than the system itself. A test harness is a structure built around a system that allows complete testing of every entity within the system. In the case of the Cell Model it makes sense to build the test harness using entities and interfaces that actually exist in the physical world inhabited by cells. The result is that it is not at all clear where the system ends and its environment begins. One of the strengths of RRT is that a system and its test environment/harness are constucted in the same way, and that any system can be readily embedded within a larger system.

The more levels removed from the level of the cell itself, the less detail is contained within the model. At the level of the Sun for example, there is only a simple timer that transmits photons on a regular basis. The simple Lettuce entity receives the photons which it uses to either simply construct sucrose sugars, or reflects the photons into the Eye of the HumanBeing. Lake, Atmosphere and Land are similarly very simple in structure.

Cell Model Inheritance Hierarchy

The major capsules involved in superclass/subclass relations are shown below.

```
Animal
  HumanBeing
Atrium
  LeftAtrium
  RightAtrium
BloodVessel
  Artery
    SpinalArtery
  Capillary
  Vein
    SpinalVein
CelestialBody
  Earth
  Sun
EndoplasmicReticulum
  RoughEr
  SmoothEr
EukaryoticCell
  AstrocyteCellBody
  Erythrocyte
  MucosalCell
  MuscleCellBody
  NeuronCellBody
InternalSpace
  CisternalSpace
  EndosomeSpace
  GolgiSpace
  LysosomeSpace
  PerinuclearSpace
  PeroxisomeSpace
  SecretoryVesicleSpace
  SynapticVesicleSpace
LgNeuroreceptor
  AmpaKainateReceptor
  GabaAReceptor
  NicotinicAChReceptor
  NmdaReceptor
LipidBilayer
  AxonBilayer
  CellBilayer
  ChloroplastBilayer
  DendriteBilayer
  EndosomeBilayer
  ErBilayer
  GolgiBilayer
  LysosomeBilayer
  MitochondrialInnerBilayer
  MitochondrialOuterBilayer
  MitochondrialOuterMembrane
  NuclearInnerBilayer
  NuclearOuterBilayer
  PeroxisomeBilayer
  SecretoryVesicleBilayer
  SynapticVesicleBilayer
  TerminalButtonBilayer
  VacuoleBilayer
LipidDisintegration
Membrane
  AxonMembrane
  CellMembrane
  MucosalCellMembrane
  ChloroplastMembrane
  DendriteMembrane
  EndosomeMembrane
  ErMembrane
  GolgiMembrane
  LysosomeMembrane
  MitochondrialInnerMembrane
  MitochondrialOuterMembrane
  NuclearInnerMembrane
  NuclearOuterMembrane
  PeroxisomeMembrane
  SecretoryVesicleMembrane
  SynapticVesicleMembrane
  TerminalButtonMembrane
  VacuoleMembrane
MyelinCell
  Oligodendrocyte
  SchwannCell
NervousSystemEntity
  Brain
  CeliacGanglion
  CentralNervousSystem
  Cerebellum
  CerebralCortex
  Cerebrum
  Diencephalon
  DorsalHornLeft
  DorsalHornRight
  DorsalRootGanglion
  ForeBrain
  HindBrain
  HypoThalamus
  InferiorMesentericGanglion
  LateralGeniculateNucleus
  Medulla
  MidBrain
  MotorCortex
  ParasymOrganGanglion
  PeripheralNervousSystem
  Pons
  PrimaryVisualCortex
  Retina
  RetinaConesAndRods
  SpinalCord
  SpinalCordRegion
    SpinalCordCervicalRegion
    SpinalCordCoccygealRegion
    SpinalCordLumbarRegion
    SpinalCordSacralRegion
    SpinalCordThoracicRegion
  SympatheticChain
  SympatheticChainGanglion
  Thalamus
  VentralHornLeft
  VentralHornParasym
  VentralHornRight
  VentralHornSym
Neuron
  CentralNeuron
  AfferentCentralNeuron
  BipolarCell
  GanglionCell
  EfferentCentralNeuron
  InterNeuron
  SpinalInterNeuron
  MotorNeuron
  SensoryReceptorNeuron
```

```
  FreeNerveEndingNeuron
  MechanoReceptorNeuron
  MeissnerCorpuscleNeuron
  MerkelsDiskNeuron
  MuscleSpindleNeuron
  PacinianCorpuscleNeuron
  RuffinisCorpuscleNeuron
  PhotoReceptorNeuron
  Cone
  Rod
Plant
  Lettuce
PhotoReceptor
  ConeOuterSegment
  RodOuterSegment
Solution
  CellularSolution
  ChloroplastFluid
  Cytosol
  EndosomeFluid
  ErFluid
  GolgiFluid
  LysosomeFluid
  Matrixsol
  MitochondrialIntermembranesol
  Nucleosol
  PerinuclearFluid
  PeroxisomeFluid
  SecretoryVesicleFluid
  SynapticCleftFluid
  SynapticVesicleFluid
  TerminalButtonFluid
  GaseousSolution
Solvent
  Water
TranscriptionComplex
  TranscriptionComplexI
  TranscriptionComplexII
  TranscriptionComplexIII
TransportProtein
  PyruvateTransporter
  SucroseTransporter
Ventricle
  LeftVentricle
  RightVentricle
VoltageGatedChannel
  VoltageGatedCaChannel
  VoltageGatedKChannel
  VoltageGatedNaChannel
```

Cell Model Active Objects

In an ideal RRT system, only leaf level capsules have ongoing behavior. Other levels often have initial configuration behavior, but do nothing after they are initially created.

In the following 21-level containment hierarchy, only the MitochondrialOuterBilayer capsule is an active object. All the rest are just containers.

```
LifeTheUniverseAndEverything → SolarSystem → Earth → SimpleEcology →
HumanBeing → NervousSystem → CentralNervousSystem → Brain → ForeBrain →
Diencephalon → Thalamus → LateralGeniculateNucleus → Neuron →
NeuronCellBody → Cytoplasm → Mitochondrion → MitochondrialDualMembrane →
MitochondrialOuterMembrane → MitochondrialOuterBilayer → LipidLayer →
Lipid → LipidPolarHead
```

Cell Model Small Molecule Data Structure

The following are all the small molecules found in the Cell Model. These are found in molTypeData.dat, and in SmallMoleculeDc.h, and in all small molecule data structures pointed to by enzymes, transport proteins, lipid bilayers, and other active objects.

Sugars
Fructose
Galactose
Glucose
Lactose
Maltose
Mannose
Sucrose

Polysaccharides
Glycogen
Starch

Alcohols
Ethanol

Aldehydes
Acetaldehyde

Glycolytic Pathway Intermediates
DihydroxyacetonePhosphate
Fructose_1x6_Biphosphate
Fructose_2x6_Biphosphate
Fructose_6_Phosphate
Galactose_1_Phosphate
Glucose_1_Phosphate
Glucose_6_Phosphate
Glyceraldehyde_3_Phosphate
GlycerolPhosphate
Mannose_6_Phosphate
PhosphoEnolPyruvate
UDP_Galactose
UDP_Glucose
X1x3_BisphosphoGlycerate
X2_PhosphoGlycerate
X3_PhosphoGlycerate

Tricarboxylic Acid (TCA) Intermediates
A_Ketoglutarate
Citrate
Fumarate
Isocitrate
Malate
Oxaloacetate
SuccinylCoa
Succinate

ATP
Adp
Amp
Atp
Gdp
Gtp
Camp

Common small molecules
CarbonDioxide
Oxygen
Water

Coenzymes
AcetylCoA
CoA
Fad
Fadh
Nad
Nadh

Organic Acids
Lactate
Pyruvate

Miscellaneous Small Molecules
Glycerol
Phosphate

Neurotransmitters
Acetylcholine
Glutamate
Aspartate
Gaba
Glycine
Dopamine
Norepinephrine
Epinephrine
Serotonin
Histamine
MethionineEnkephalin

Ions
Ca
Cl
E
H
HCO
K
Na

Lipids
Phosphatidic_Acid
Ethanolamine
Phosphatidyl_Ethanolamine
PE_InVicinity

Circulatory System

In the Circulatory System capsules are active objects, with the function of getting cells, enzymes, transporters, and membranes into position so they can operate on small molecules. Arteries and Veins circulate the Blood Plasma which contains Erythrocytes (red blood cells) a type of Eukaryotic Cell. The Heart pumps the Blood Plasma, and the Bone Marrow manufactures Eryhtrocytes. In the Cell Model, the Circulatory System functions as a way to move Eukaryotic Cells from one environment to another to test their ability to take-up and release oxygen, carbon dioxide, and glucose. Oxygen is picked up in the Lung, Glucose is picked up in the Small Intestine, and both molecules are released in the Brain. This happens without the Erythrocytes ever knowing what part of the body they are located in. It only depends on the relative concentrations of chemicals as the Erythrocytes are pumped from through the system.

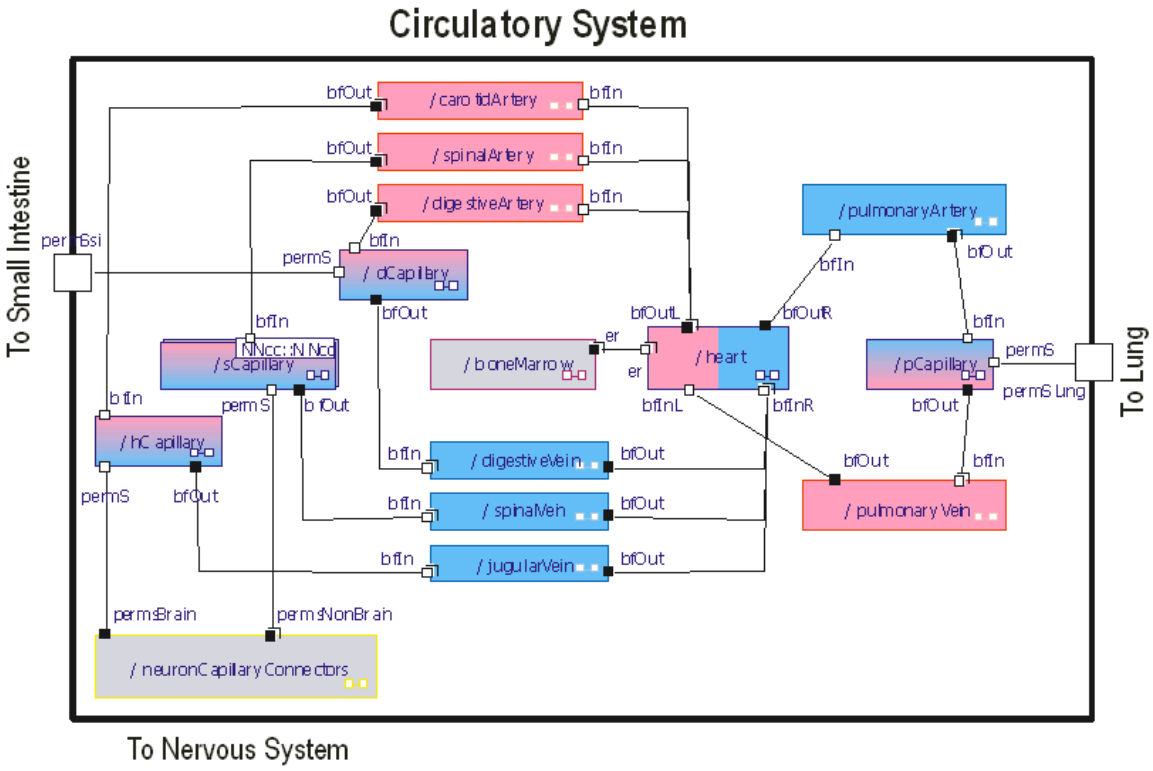

Figure 8 - Circulatory System.