

# Multi-scale, Agent-based Modeling for Human Anatomy and Physiology

## Challenges and Opportunities

Christian Jacob

*Evolutionary & Swarm Design Group*

Dept. of Computer Science

Dept. of Biochemistry & Molecular Biology

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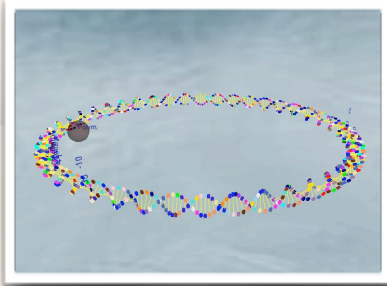




## “Traffic Swarms” — Discovery Channel (2006)

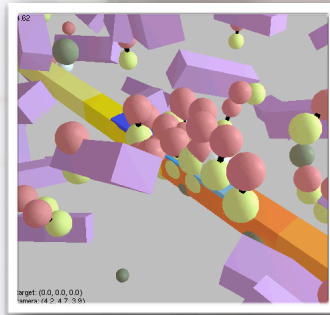


### Lactose Operon



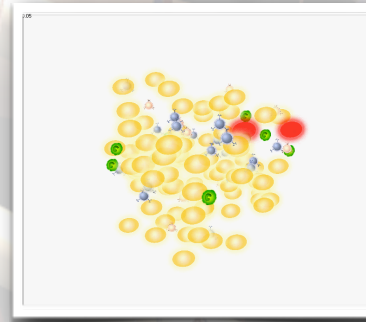
Ian Burleigh

### $\lambda$ Switch



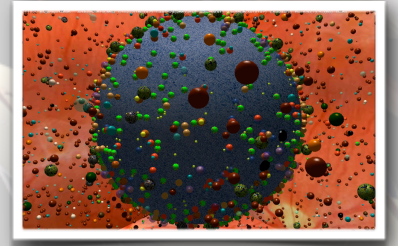
G. Tsui, A. Barbasiewicz

### Immune System



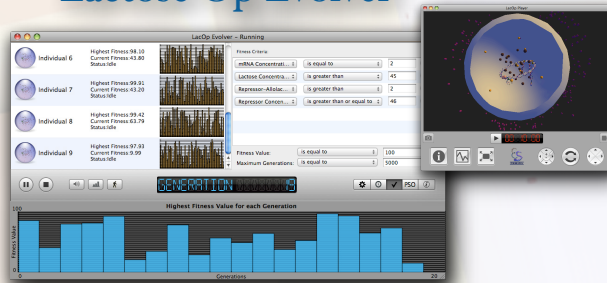
Karel Bergmann, Scott Steil

### Complement System



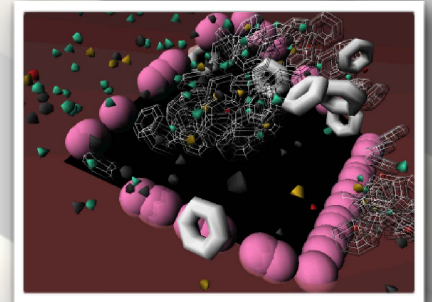
Carey Gingras, Dr. Rolando Feyt

### Lactose Op Evolver



Ryan Moniz

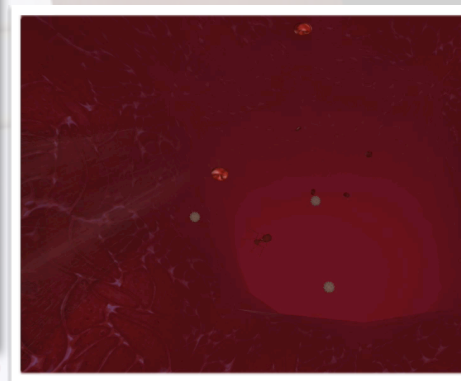
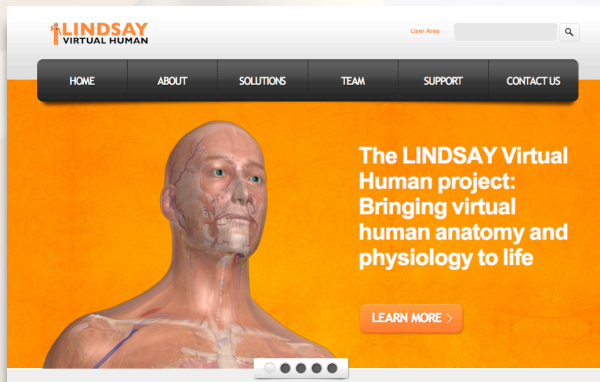
### Blood Clotting



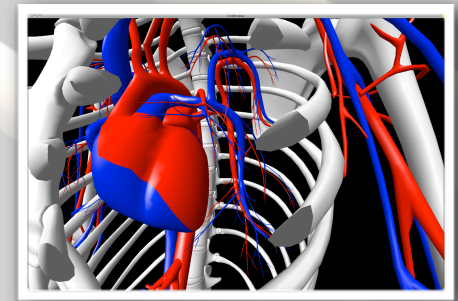
S. Chan, M. Templeton, G. Rowe, R. Degraaf, A. Punj



### LINDSAY



Scott Novakowski

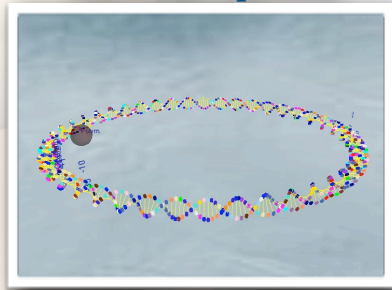


Vlad Sarpe

### Creative Swarms

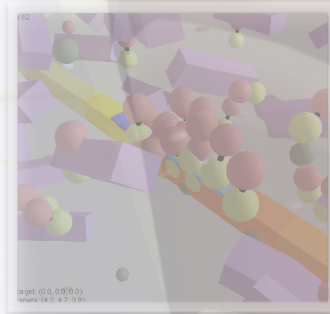


### Lactose Operon



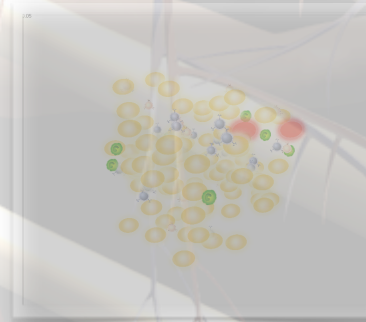
Ian Burleigh

### $\lambda$ Switch



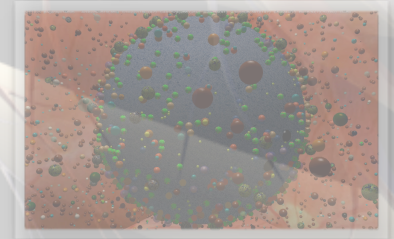
G. Tsui, A. Barbasiewicz

### Immune System



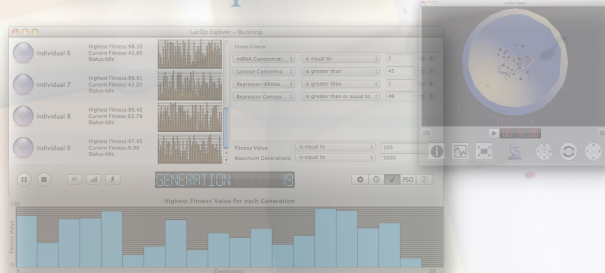
Karel Bergmann, Scott Steil

### Complement System



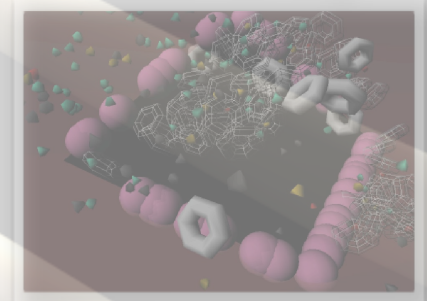
Carey Gingras, Dr. Rolando Feyt

### Lactose Op Evolver



Ryan Moniz

### Blood Clotting



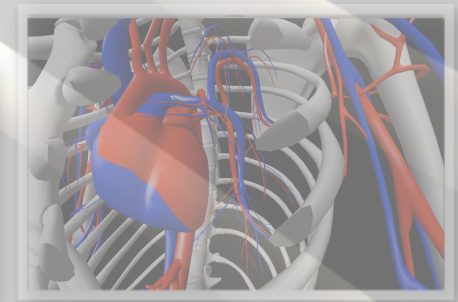
S. Chan, M. Templeton, G. Rowe, R. Degraaf, A. Punj



### LINDSAY



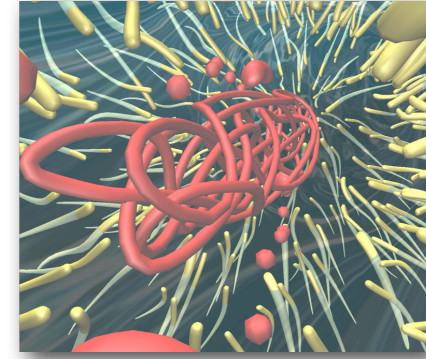
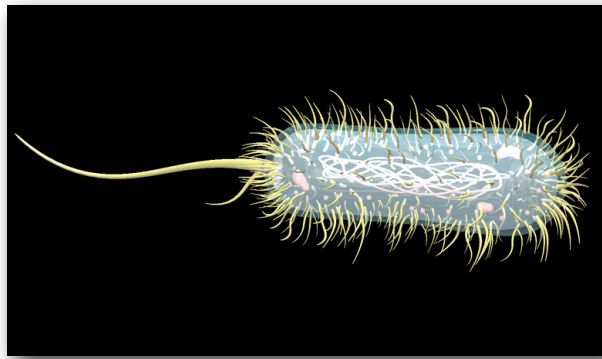
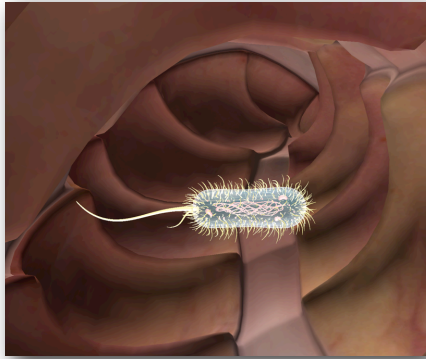
Scott Novakowski



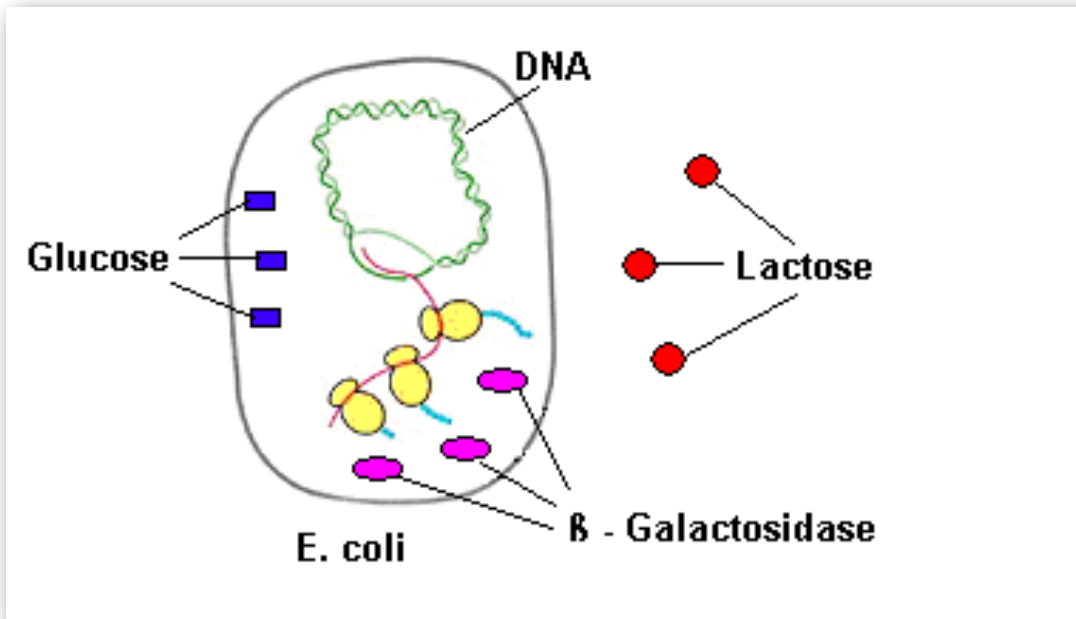
Vlad Sarpe



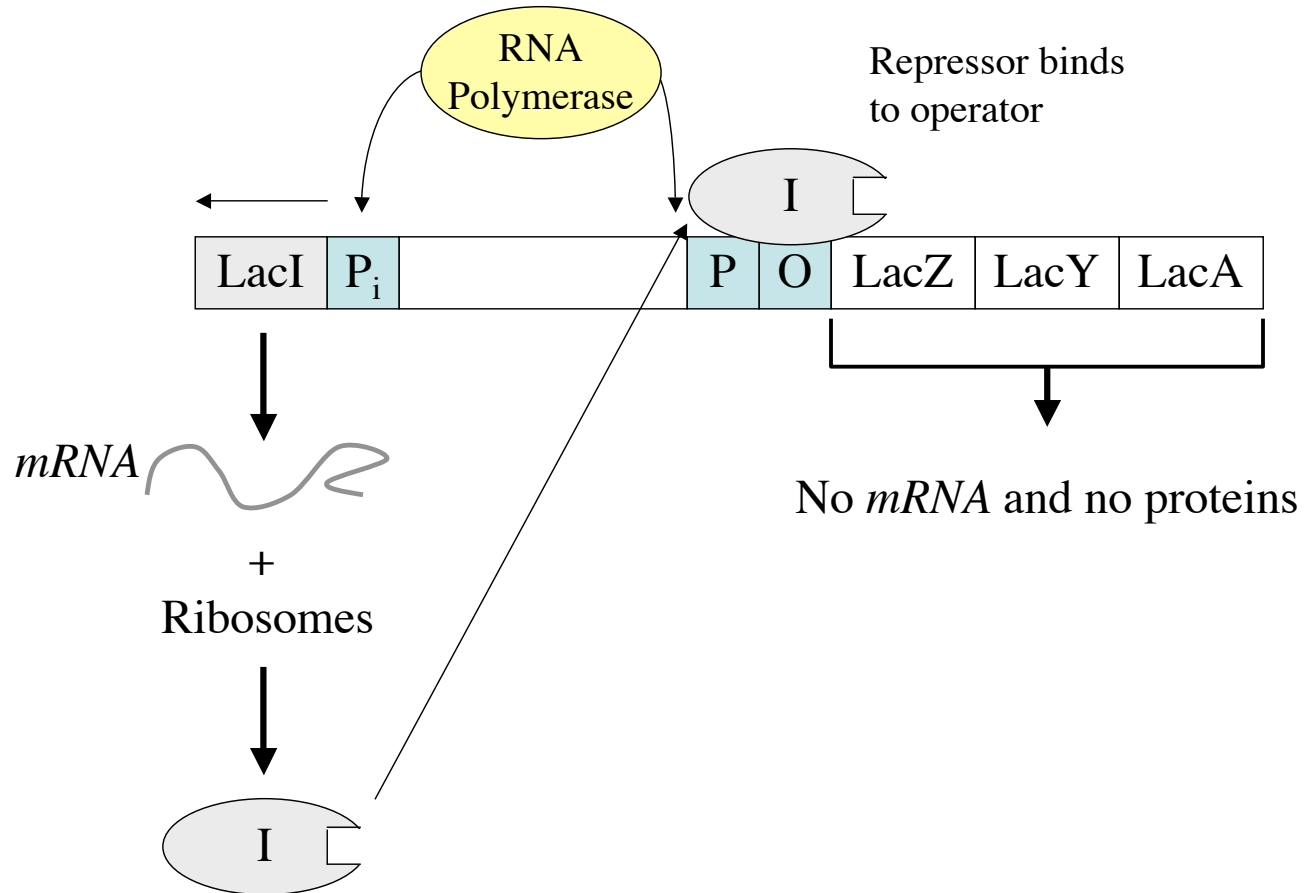
# E. coli and Lactose



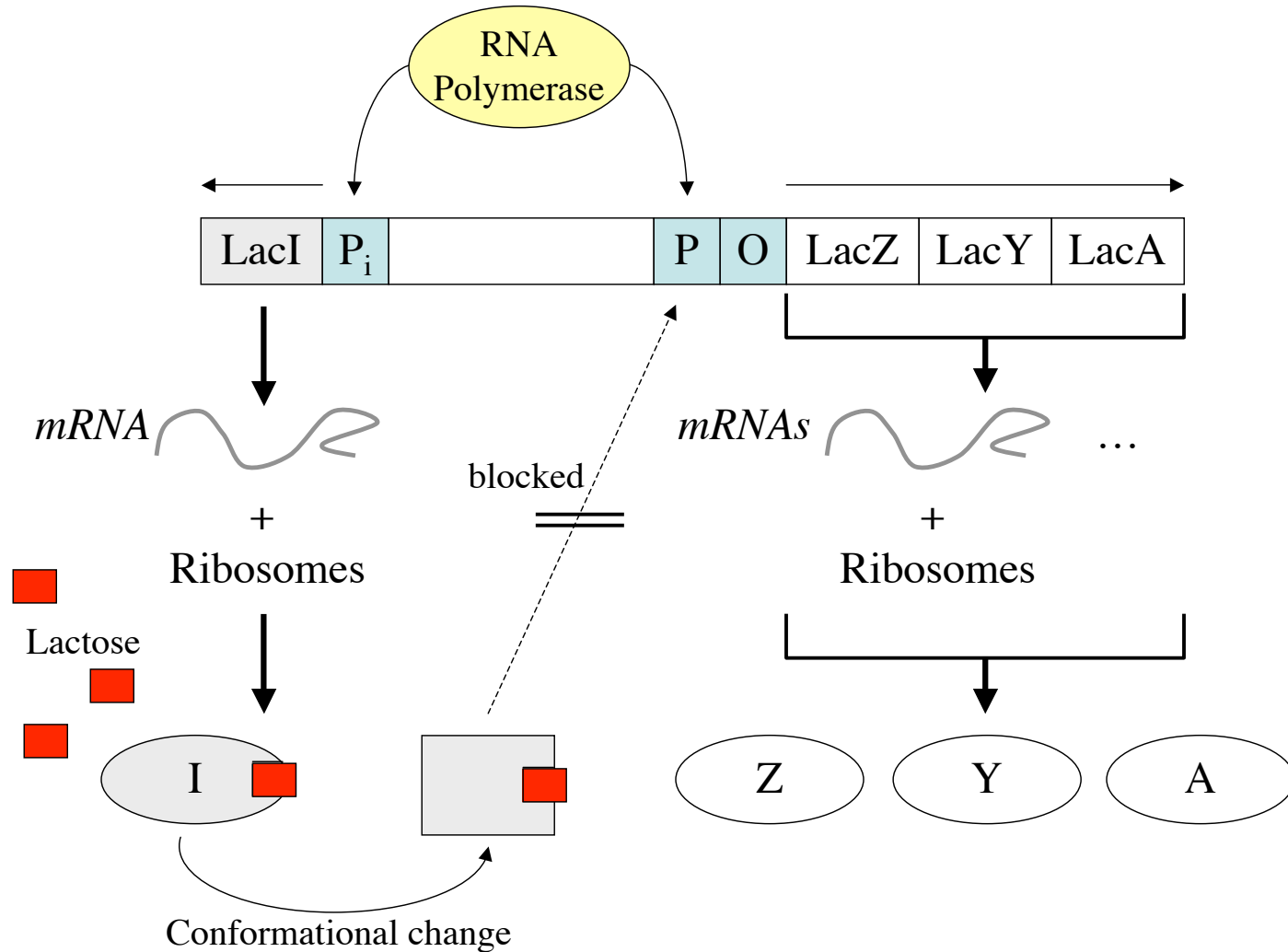
Afshin Esmaeili, 2010



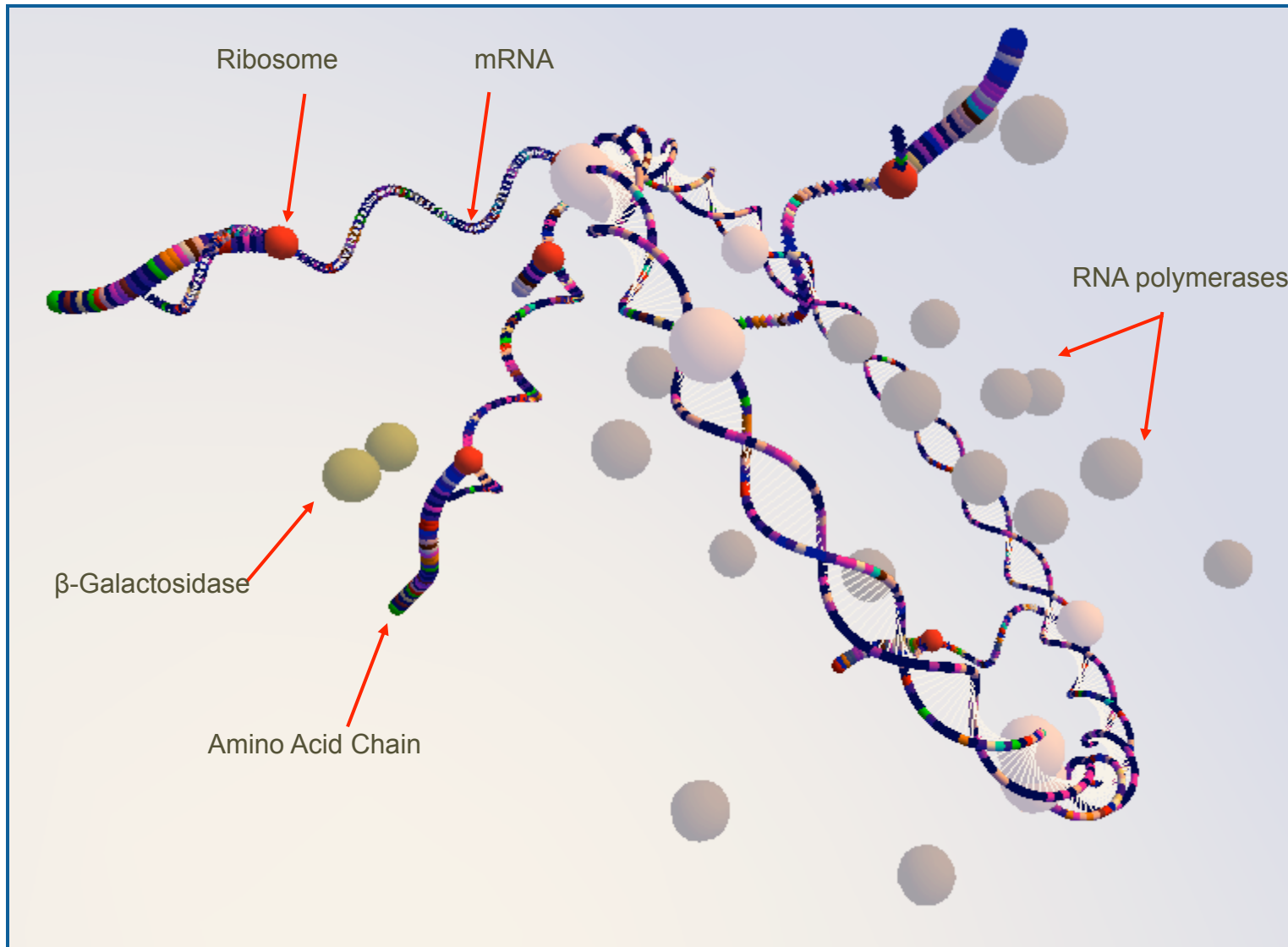
# Turning the *Lac* Operon Off



# Turning the *Lac* Operon On

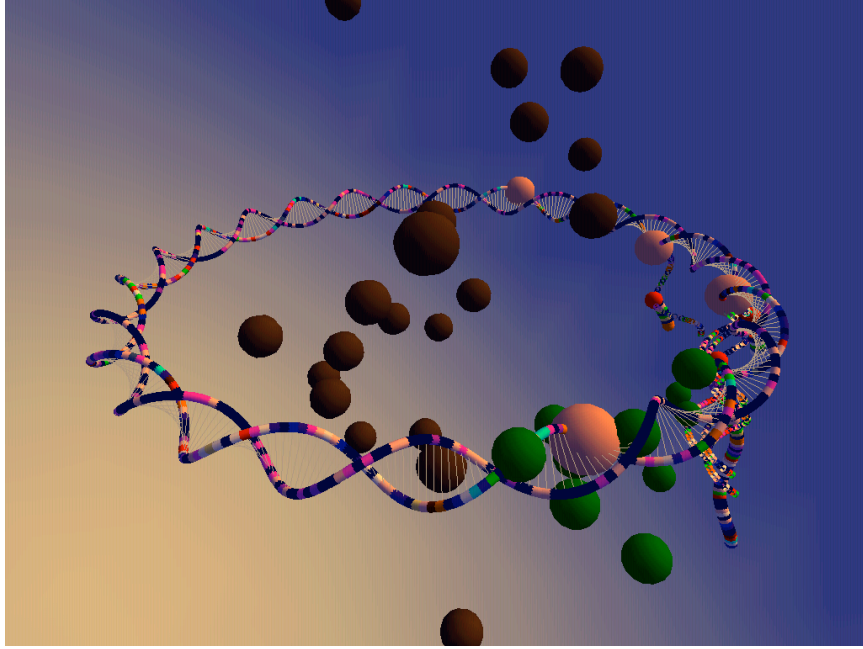


# Transcription and Translation

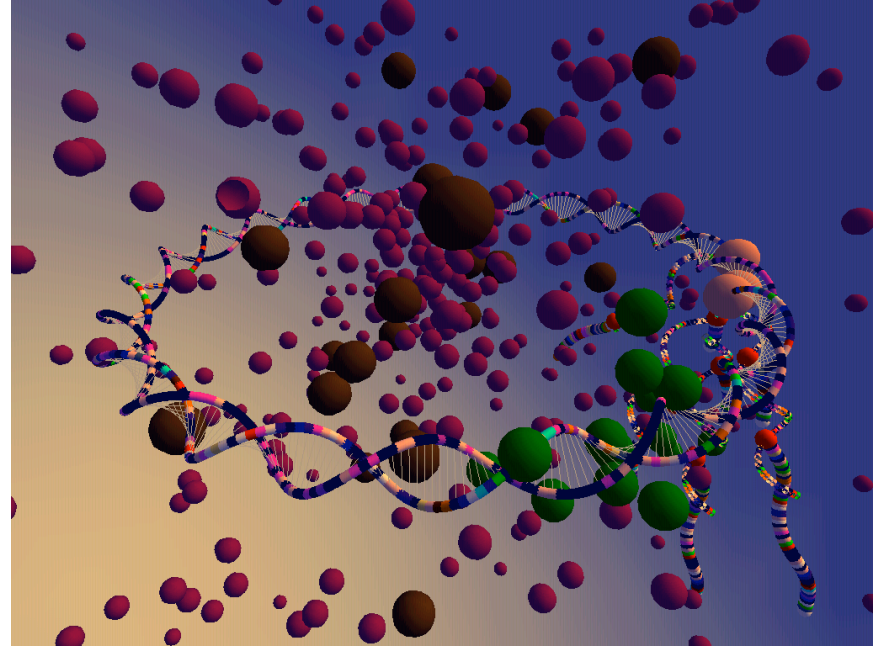


Ian Burleigh, 2004

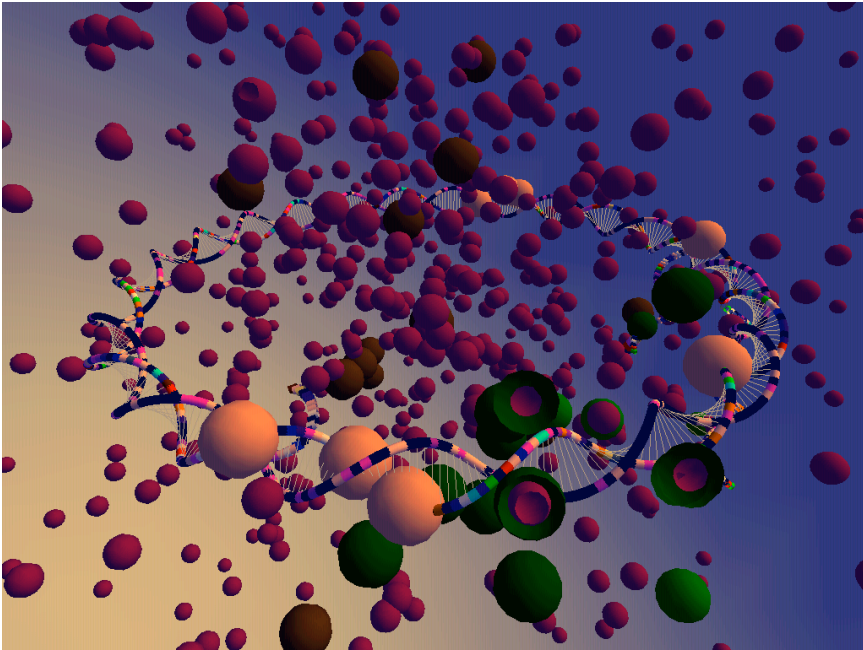




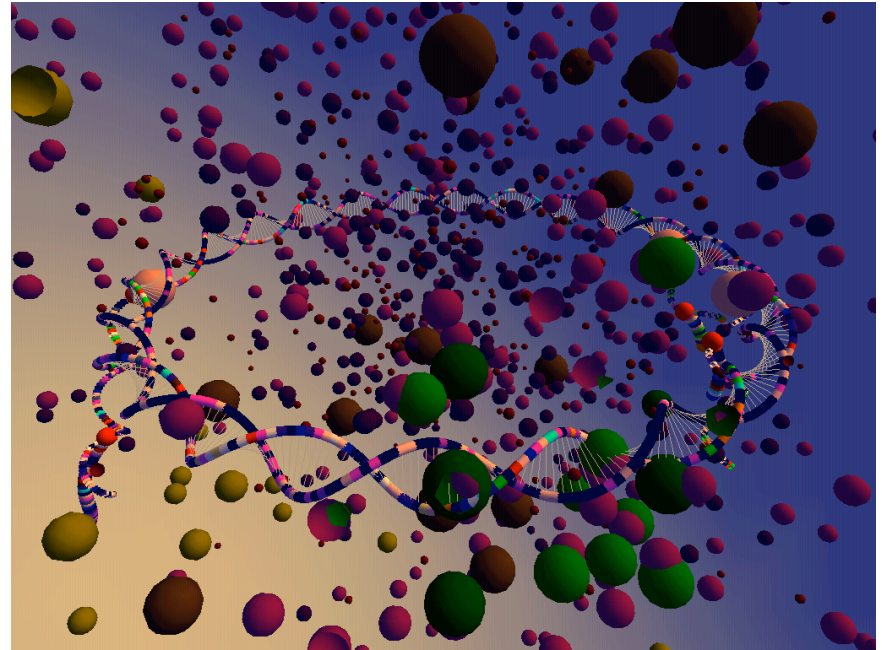
Repressors block RNA polymerase from *LacZ* transcription.



Lactose is introduced into the system.



Lactose binds to repressors. Rep-lac complexes are formed.



Most lactose split into glucose and galactose.



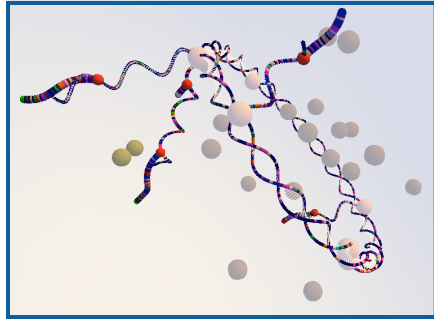
# Lactose Operon in the CAVE

*Sun Centre of  
Excellence for  
Visual Genomics*

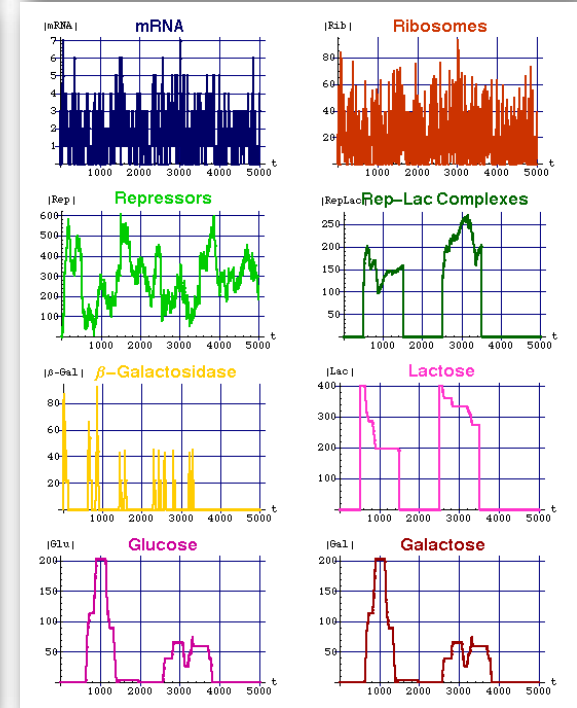
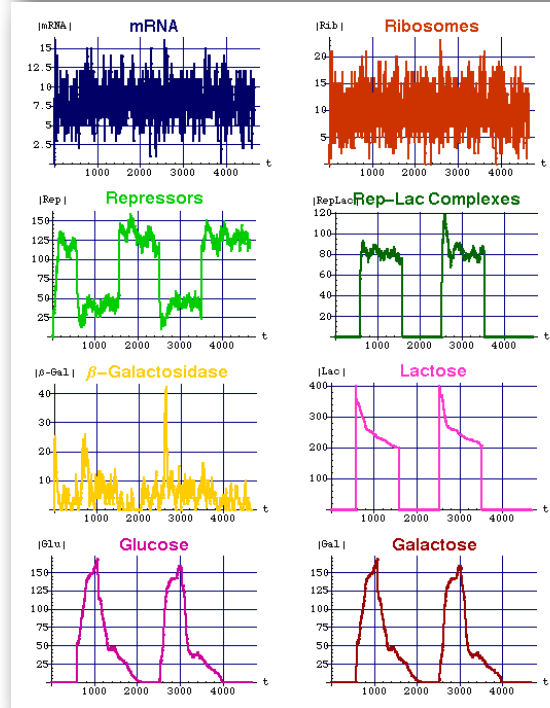
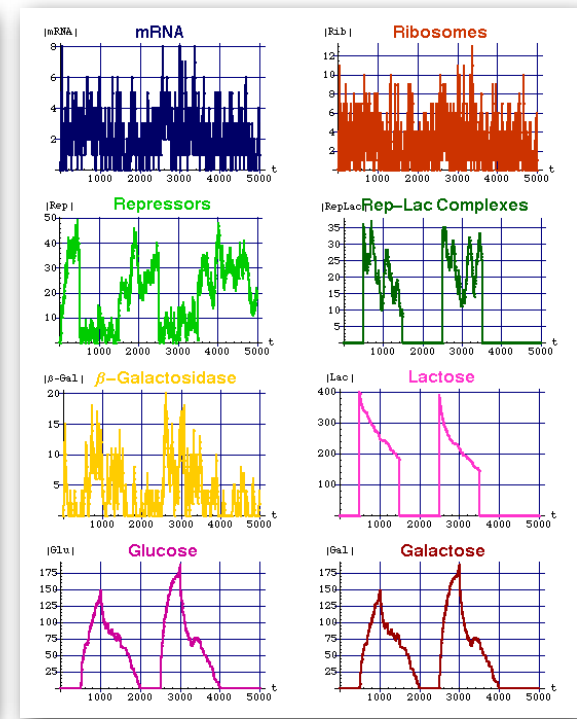
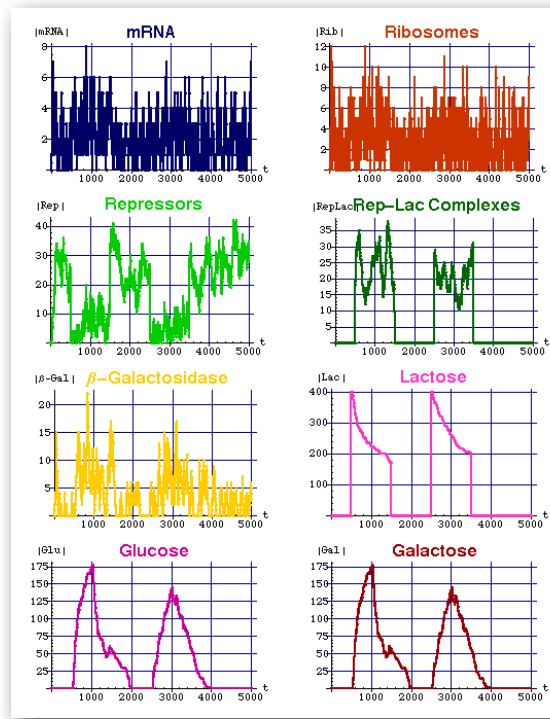
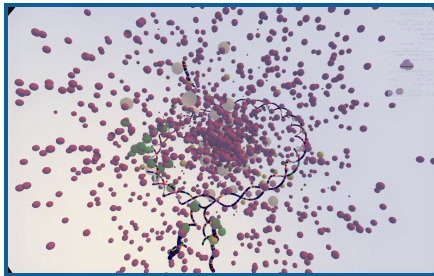
Fac. of Medicine  
Univ. of Calgary

Director:  
Dr. Christoph Sensen

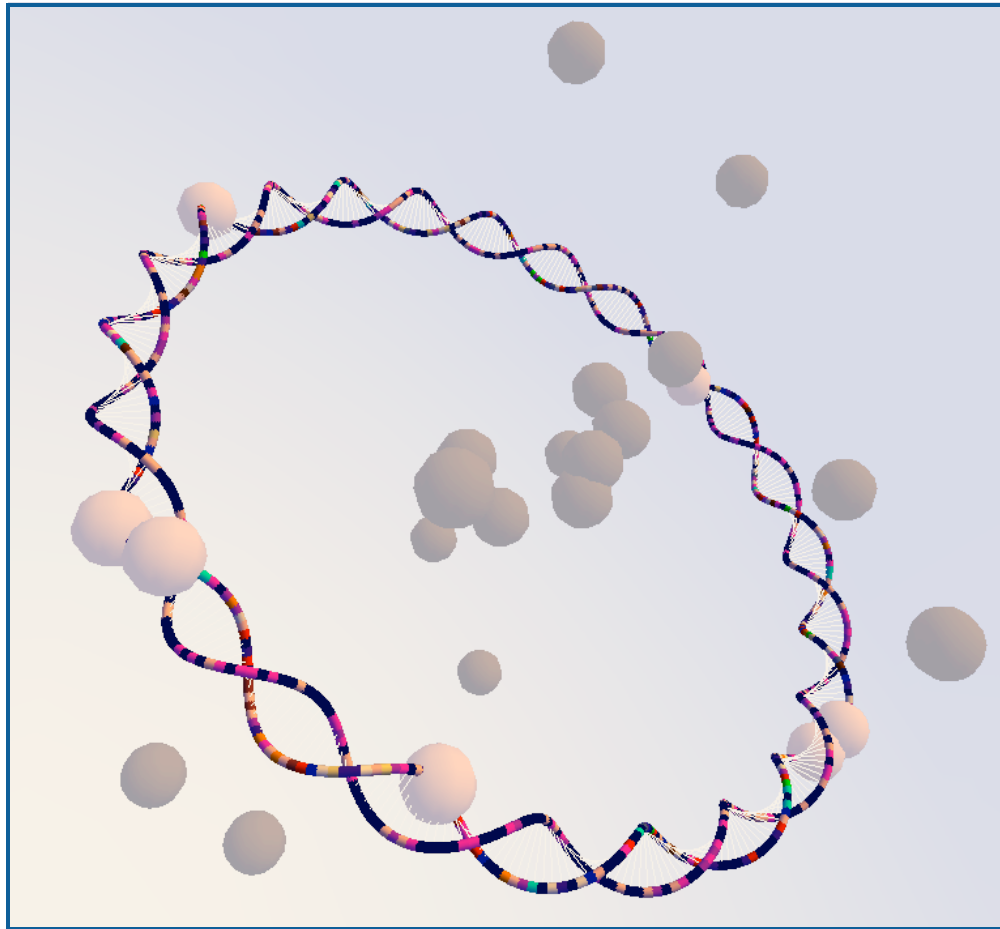




# Lac Operon Simulation: Analysis



# Lactose Operon 3D



Circular DNA with RNA polymerases

```

case state of
  FLOATING:
    if near DNA:
      attach to nearest DNA codon
      state = DOCKED
    else:
      move randomly within cell

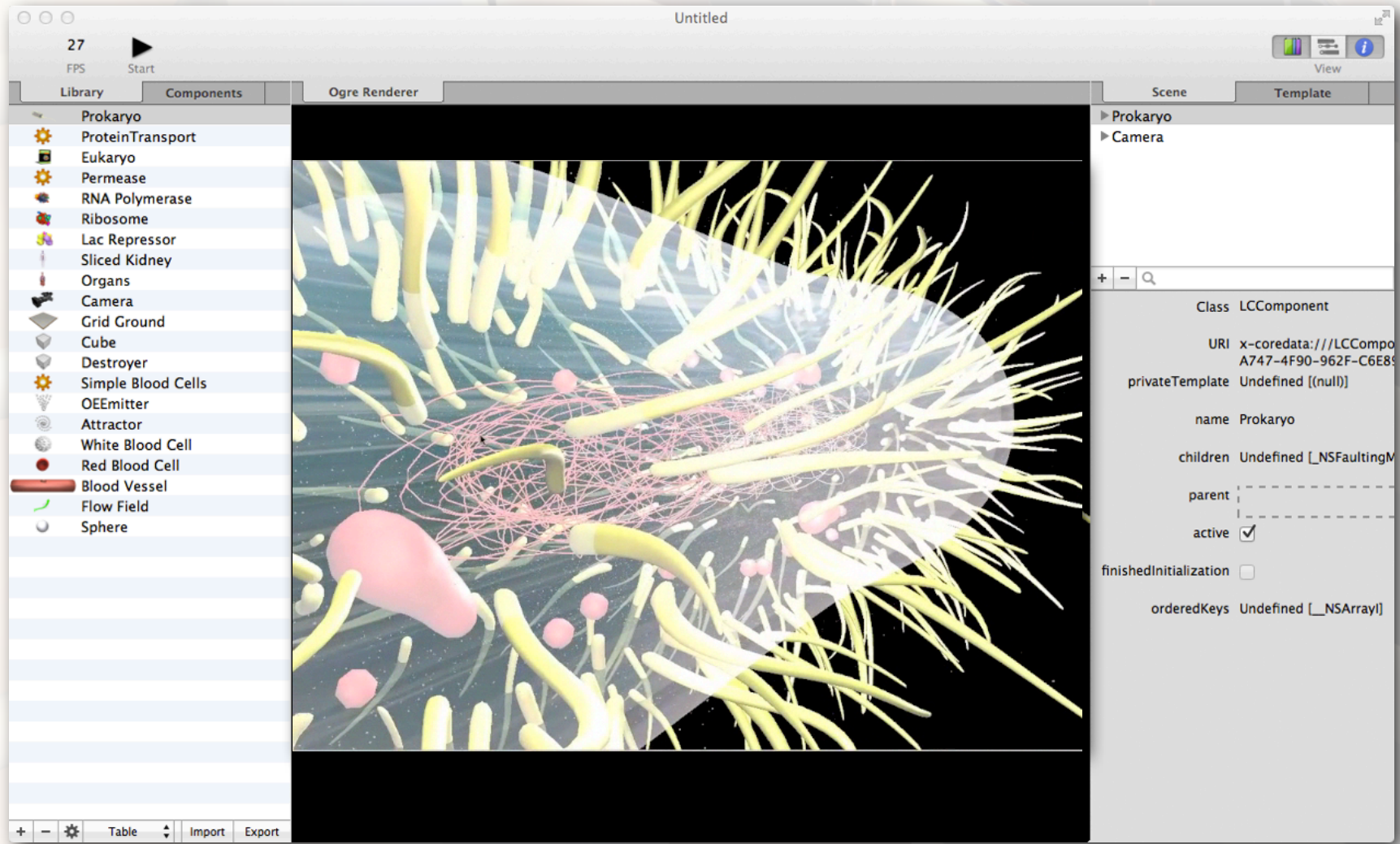
  DOCKED:
    if promoter region is reached:
      state = READY_TO_TRANSCRIBE
    else:
      move along DNA to next codon

  READY_TO_TRANSCRIBE:
    create an empty mRNA molecule
    state = TRANSCRIBING

  TRANSCRIBING:
    if stop codon is reached:
      release constructed mRNA
      state = DETACHED
    else if blocked by repressor:
      destroy partial mRNA
      state = DETACHED
    else:
      move to next codon
      append codon mRNA

  DETACHED:
    detach self from DNA
    move randomly
    state = FLOATING
end case
  
```

# Interactive Virtual E. coli



Afshin Esmaeili, 2011



DESIGN

Christian Jacob and his ESD Team — University of Calgary

SWARM-DESIGN.org

# Interactive Virtual E. coli



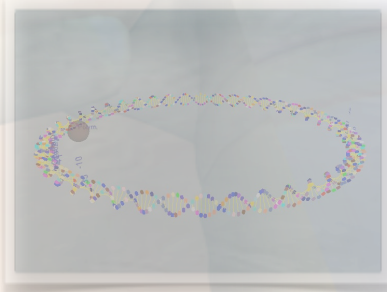
The screenshot shows a software window titled "Untitled" with a menu bar (File, Edit, View) and a toolbar. The main area is divided into three panels:

- Library:** A list of components including Prokaryo, ProteinTransport, Eukaryo, Permease, RNA Polymerase, Ribosome, Lac Repressor, Sliced Kidney, Organs, Camera, Grid Ground, Cube, Destroyer, Simple Blood Cells, OEEmitter, Attractor, White Blood Cell, Red Blood Cell, Blood Vessel, Flow Field, and Sphere.
- Ogre Renderer:** A central 3D view showing a detailed, textured model of an E. coli cell with numerous flagella and a long tail.
- Scene/Template:** A right-hand panel showing the selected component's properties. It includes fields for Class (LCCComponent), URI, privateTemplate, name (Prokaryo), children, parent, active (checked), finishedInitialization, and orderedKeys.

Afshin Esmaeili, 2011

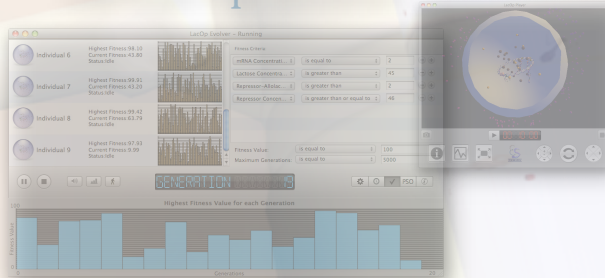


### Lactose Operon



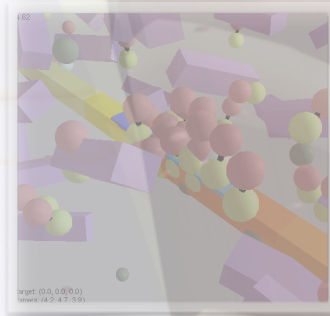
Ian Burleigh

### Lactose Op Evolver



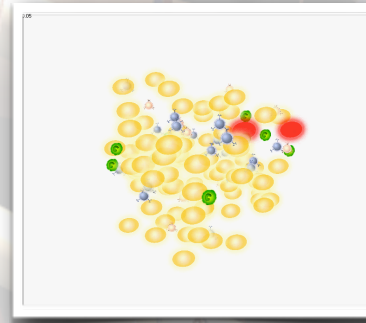
Ryan Moniz

### $\lambda$ Switch



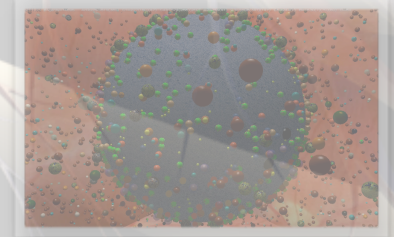
G. Tsui, A. Barbasiewicz

### Immune System



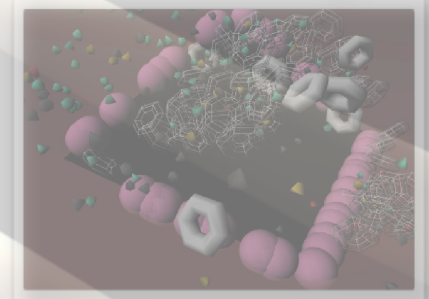
Karel Bergmann, Scott Steil

### Complement System

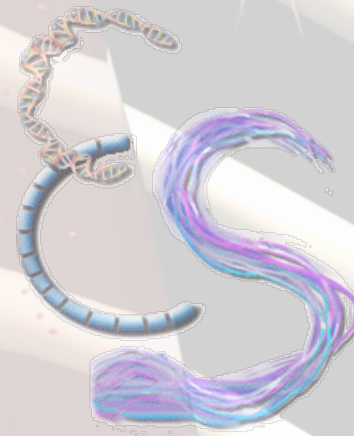


Carey Gingras, Dr. Rolando Feyt

### Blood Clotting



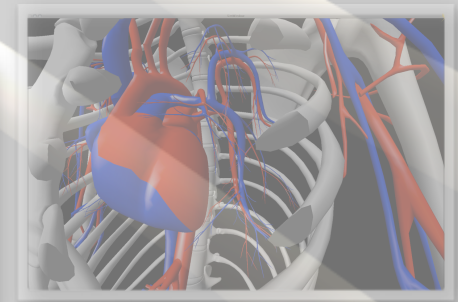
S. Chan, M. Templeton, G. Rowe, R. Degraaf, A. Punj



### LINDSAY



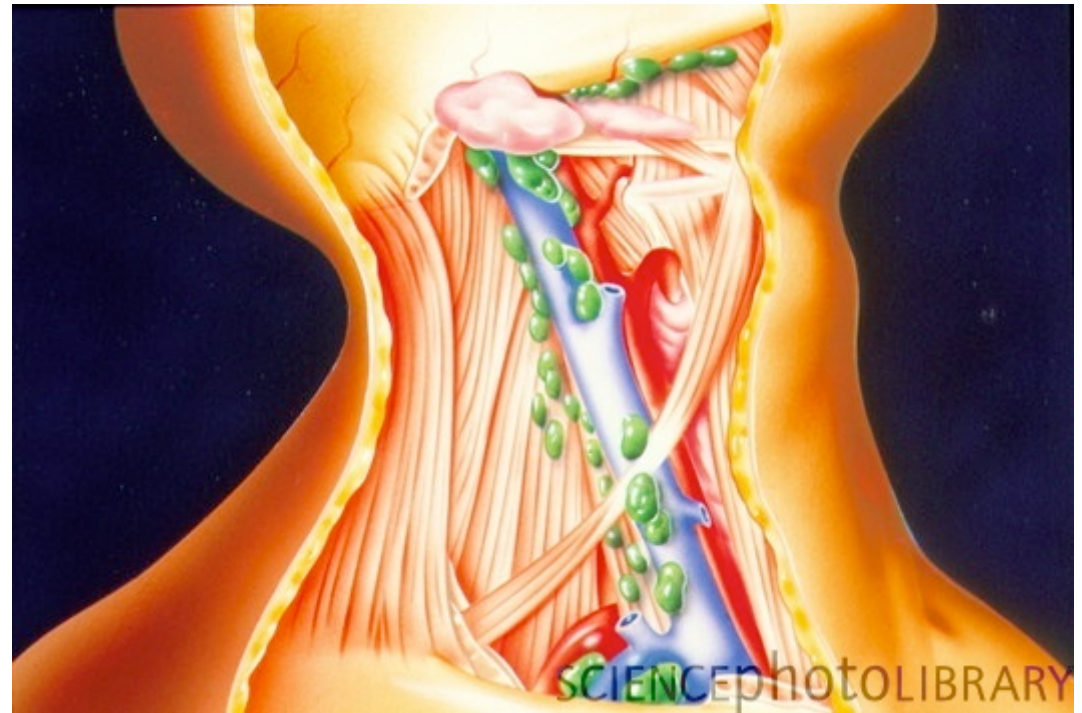
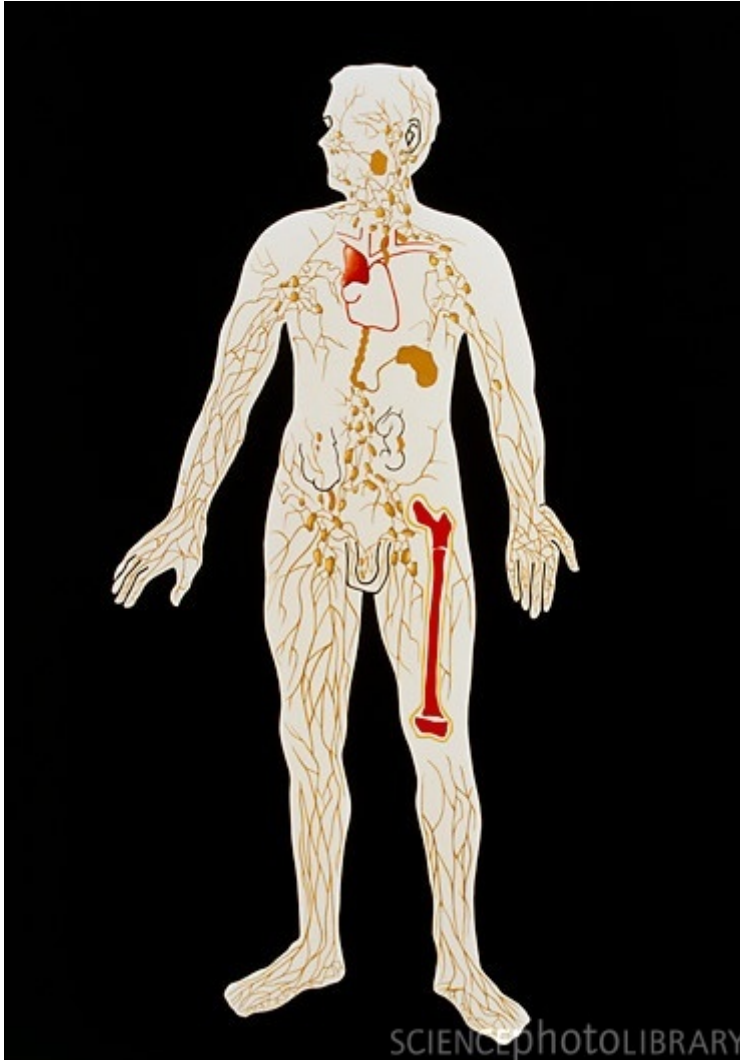
Scott Novakowski



Vlad Sarpe

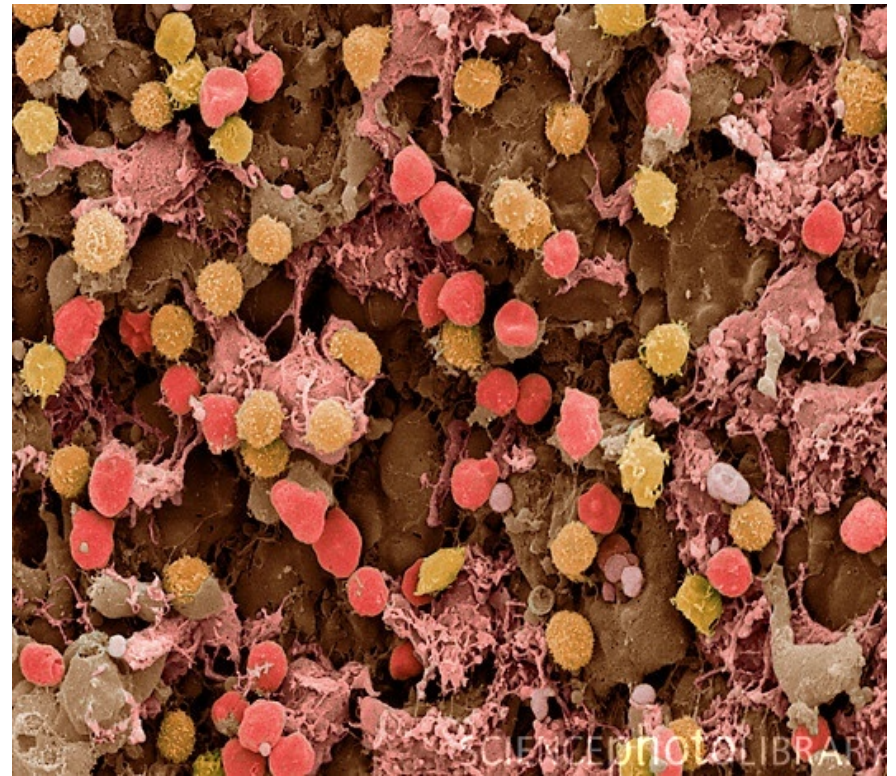


# Human Lymphatic System

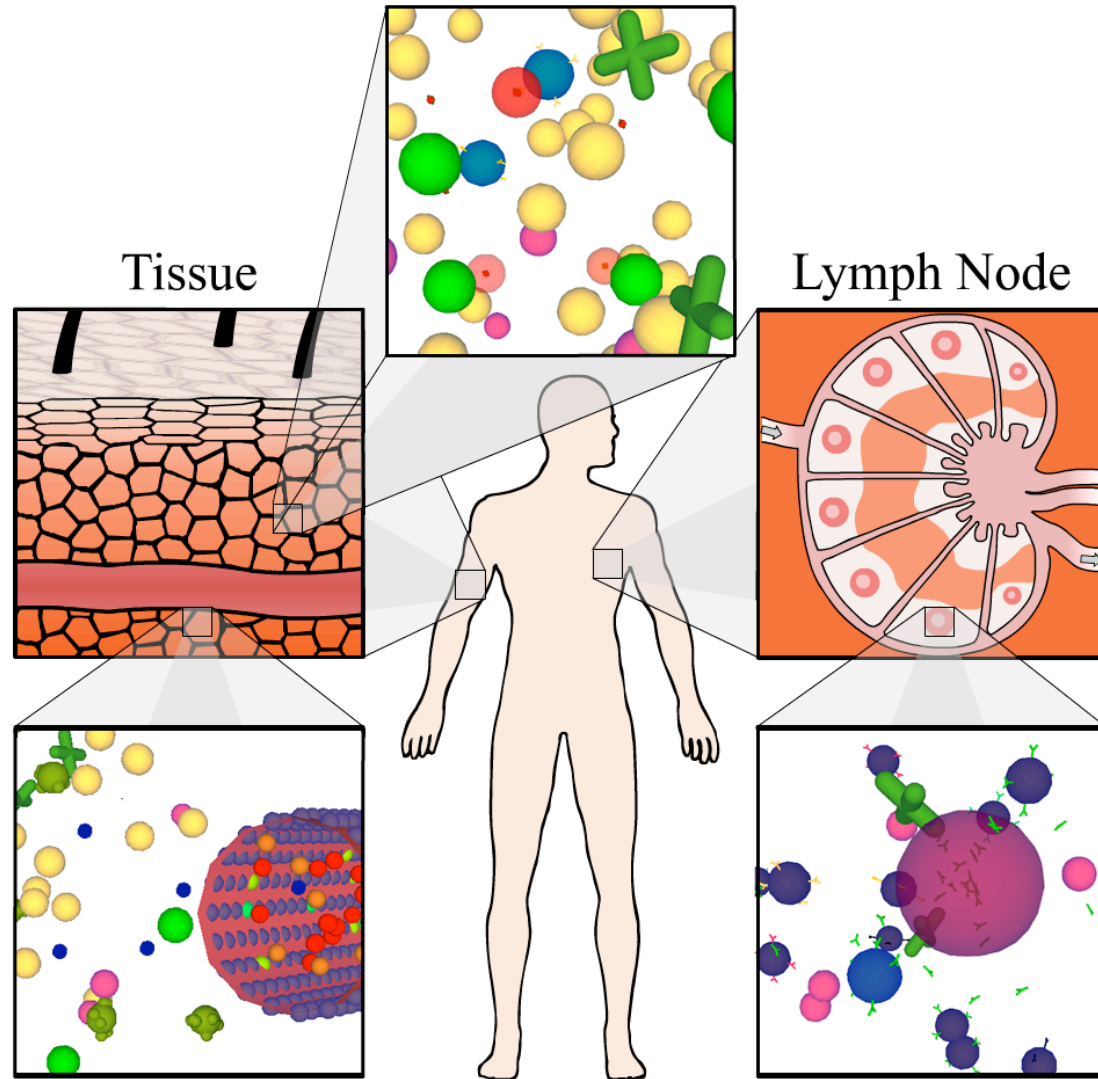




# Lymph Node

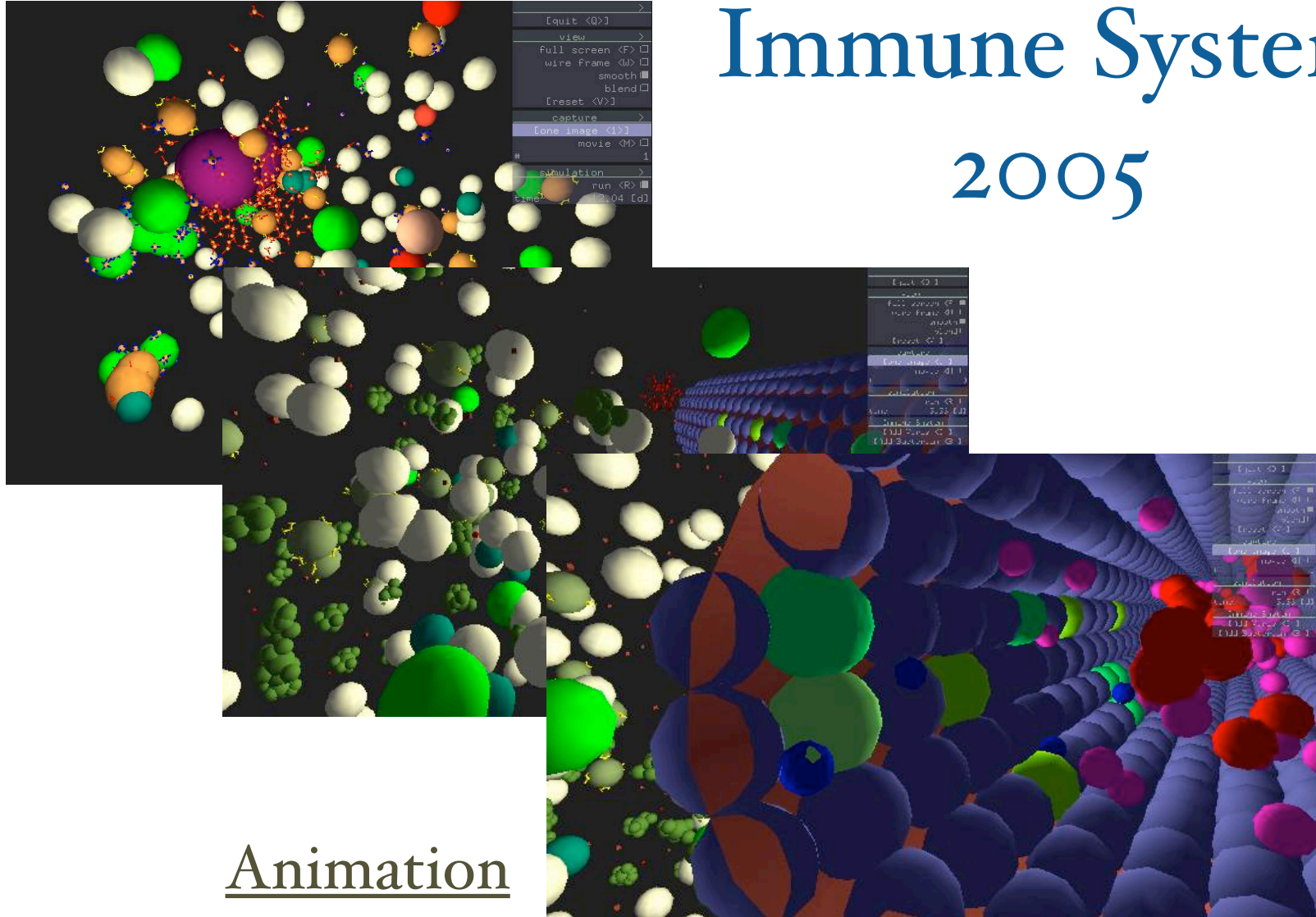


# Towards a Hierarchical Immune System Model



IS 2005

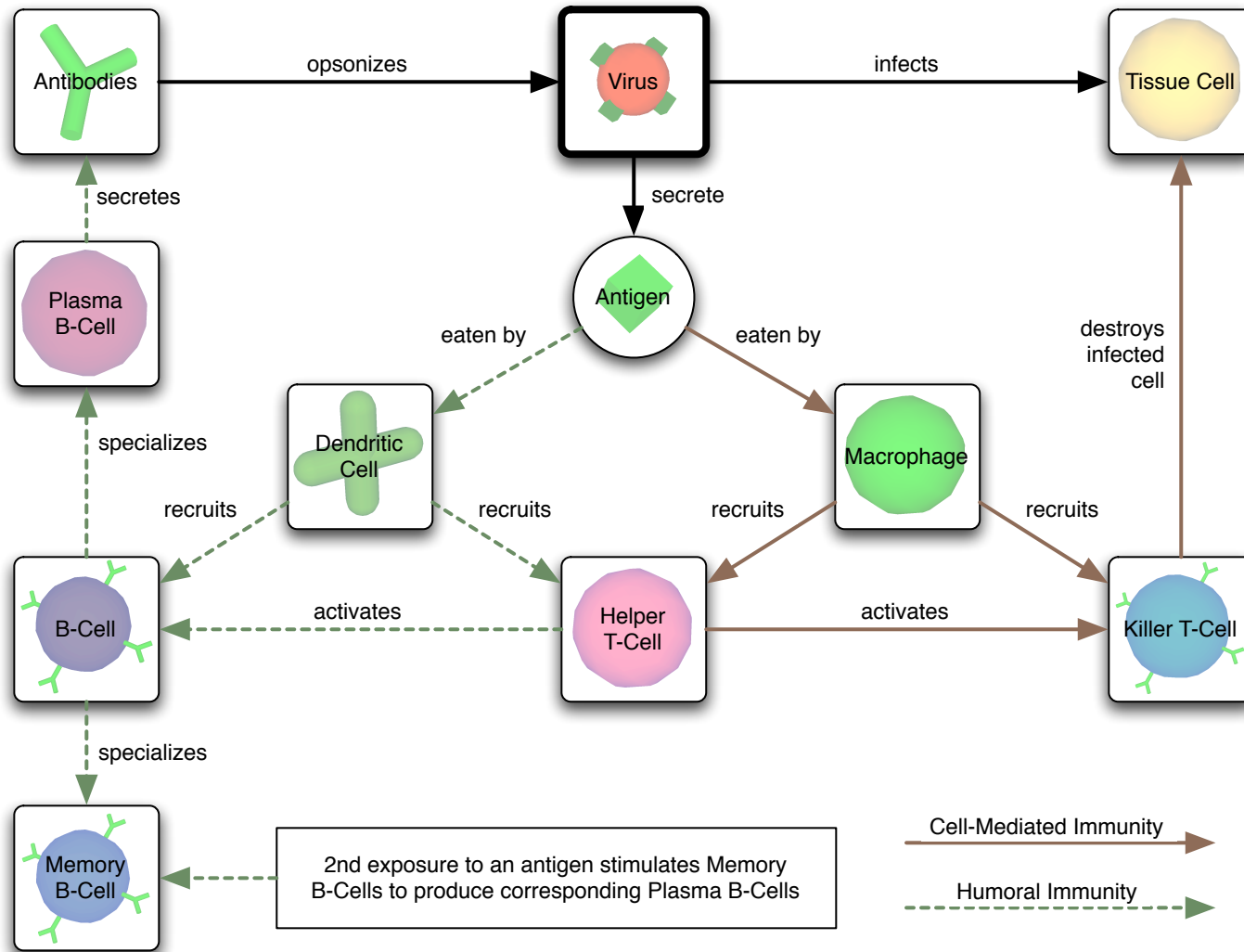
# Immune System 2005



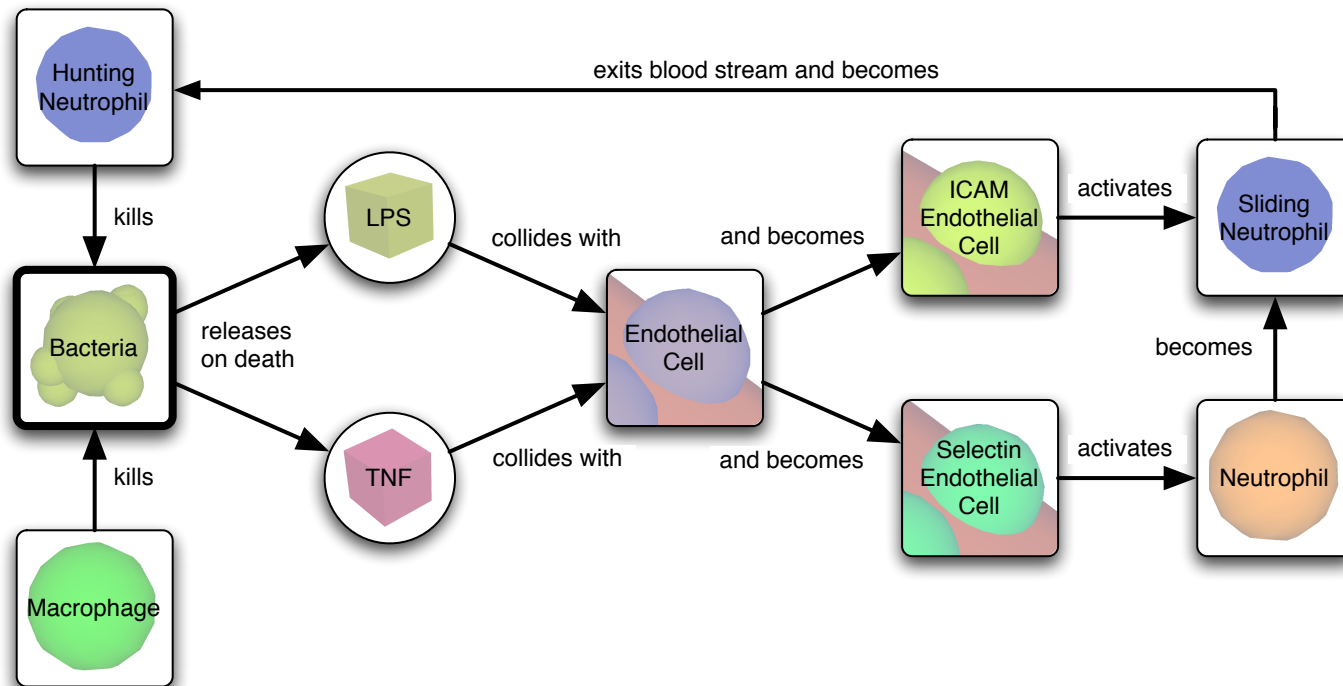
Animation

Karel Bergmann, 2005

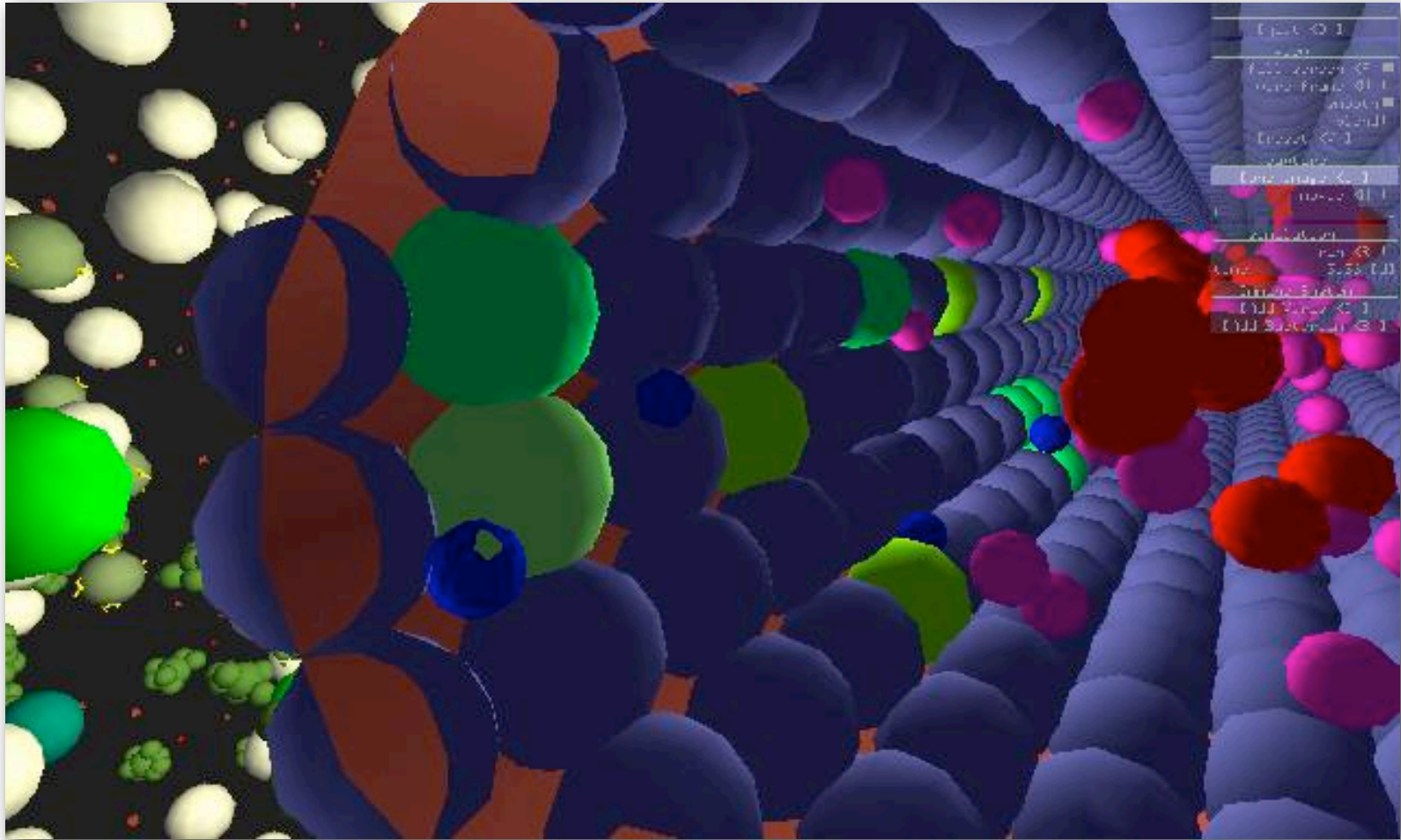
# Viral Infection



# Bacterial Infection

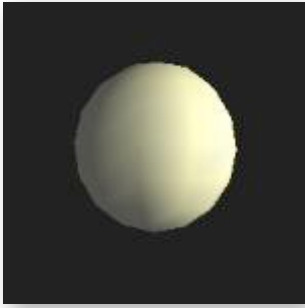


# IS 2005: Bacterial Infection (2)

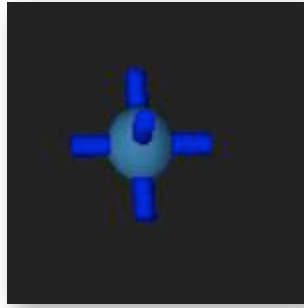


Karel Bergmann, 2005

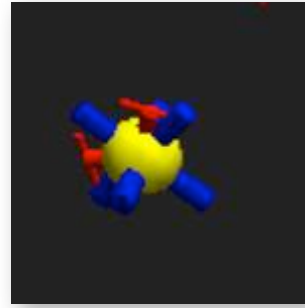
Interior of a blood vessel during a bacterial infection:  
**Red blood cells** and **neutrophils** move through the blood vessel.  
 Some neutrophils are rolling along the inside surface. **Endothelial cells** at different stages of stimulation.



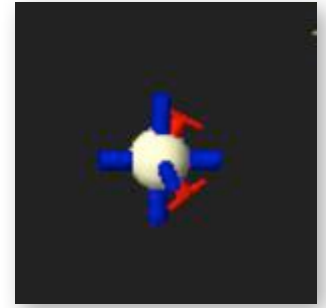
Tissue cell



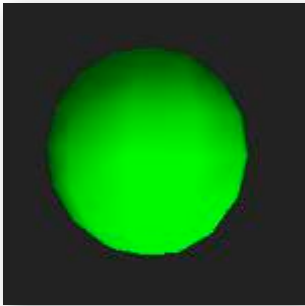
Virus



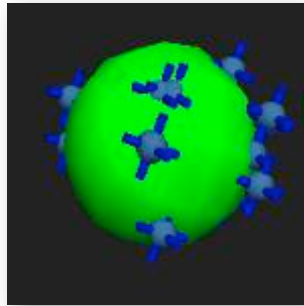
Virus (op)



Virus (ntr)

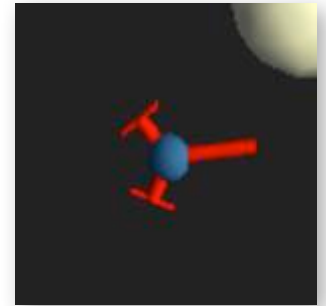


Macrophage

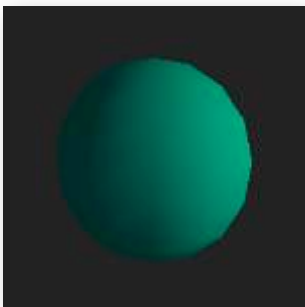


APC Mac

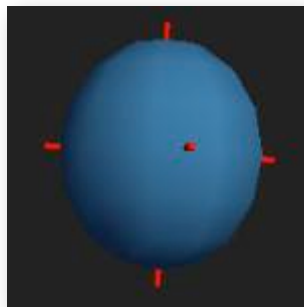
# IS BioAgents



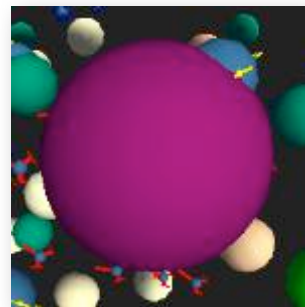
Antibody



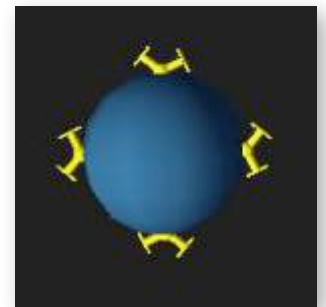
Helper T



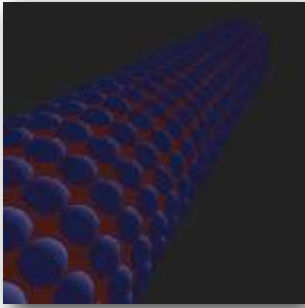
Killer T



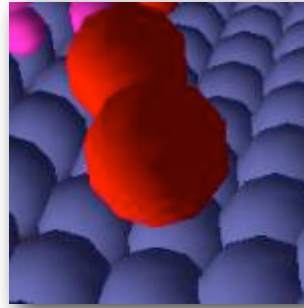
Plasma B



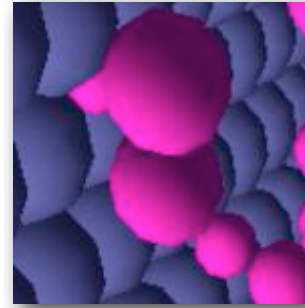
B Cell



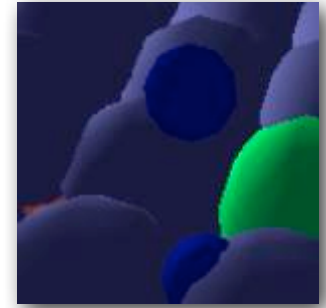
Blood vessel



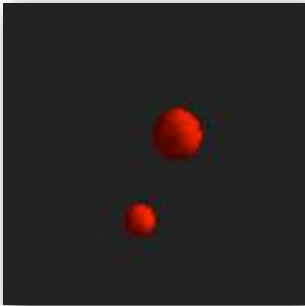
Red blood cells



Neutrophils

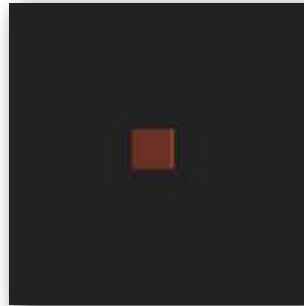


Rolling NΦ



TNF

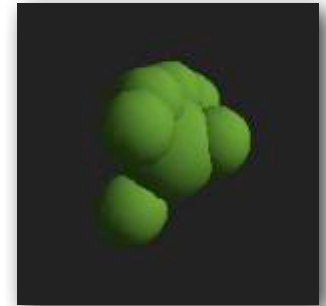
tumor necrosis factor



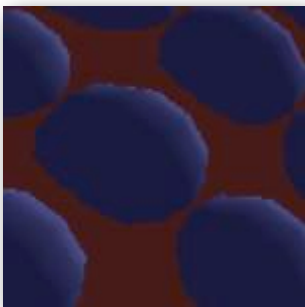
LPS

lipopolysaccharide

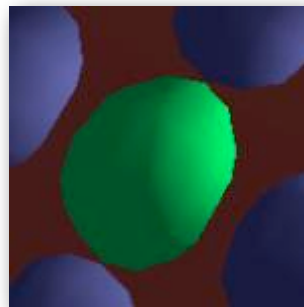
## IS BioAgents (innate)



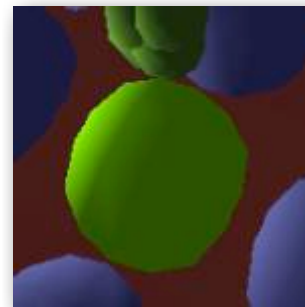
Bacterium



Endothelial cells

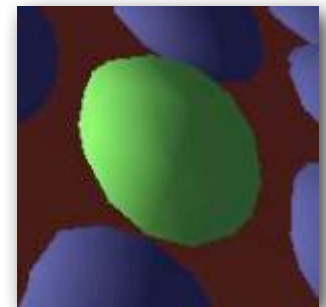


Selectin prod.



ICAM prod.

intercell. adhesion mol.

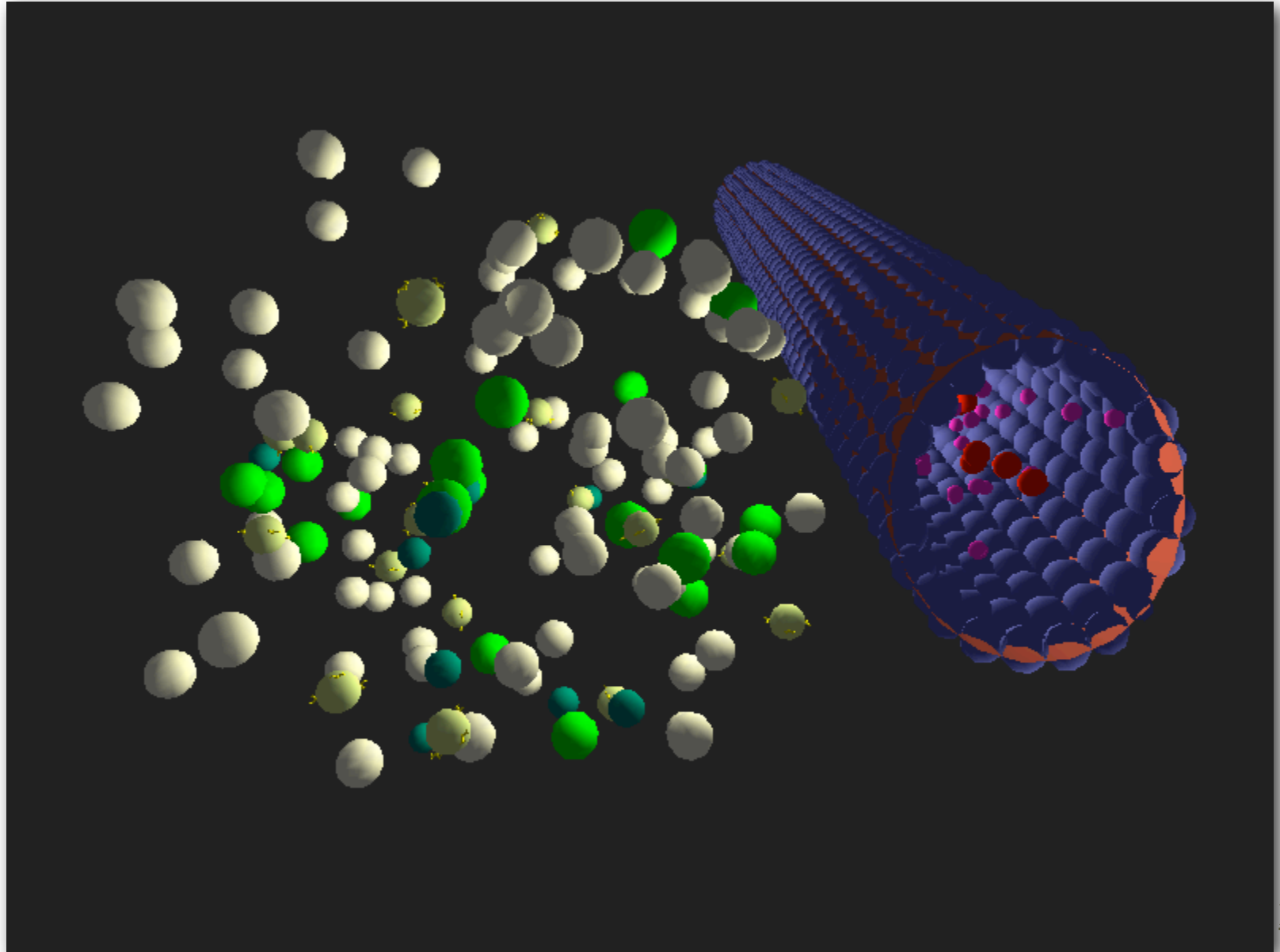


Selectin & ICAM

TNF: secreted by MP & Th; LPS: shed by Gram-negative bacteria from outer cell wall



# Immune System 3D: Animation

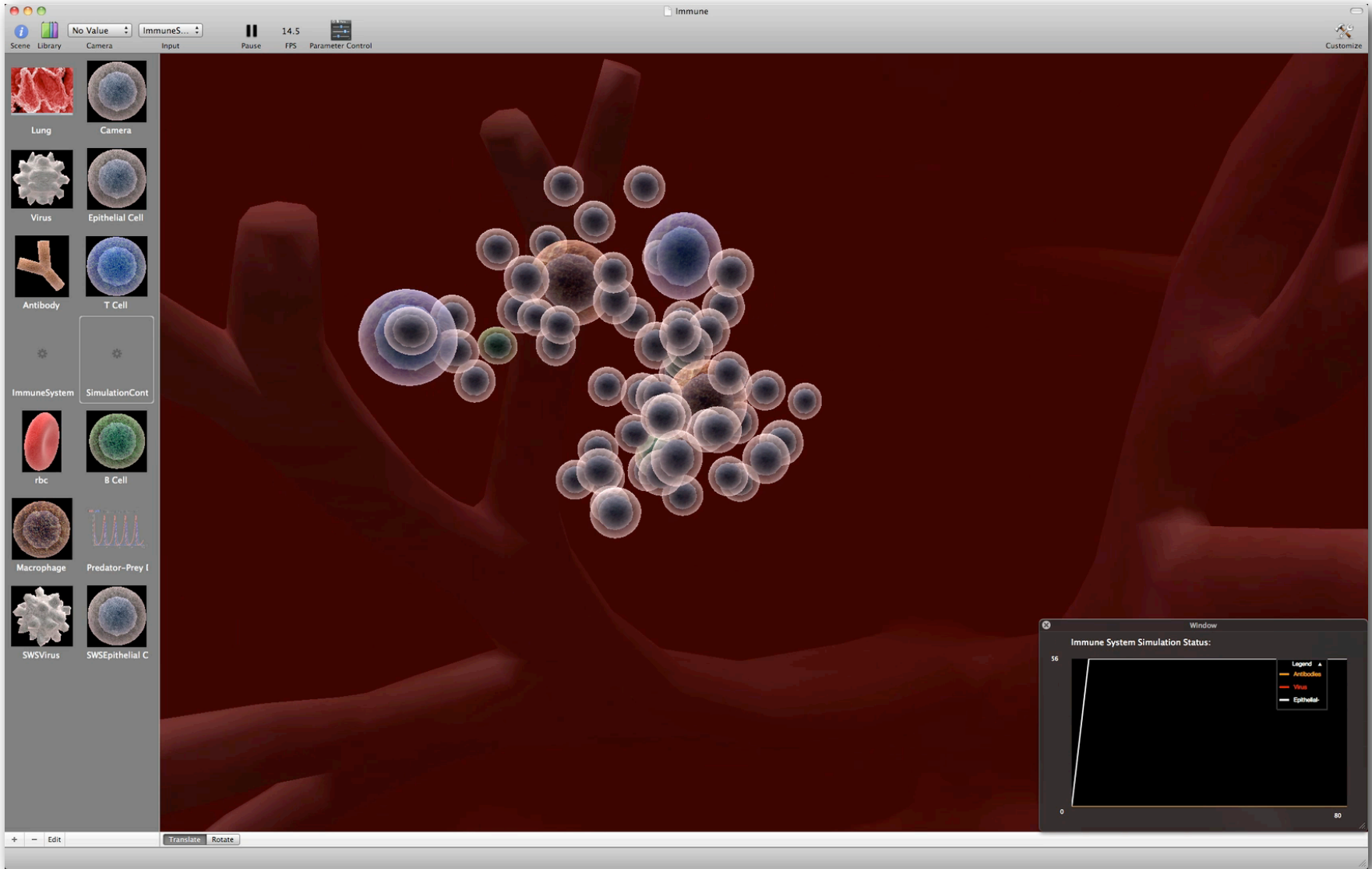


Karel Bergmann, 2005

[Back ...](#)



# Immune System Model 2010

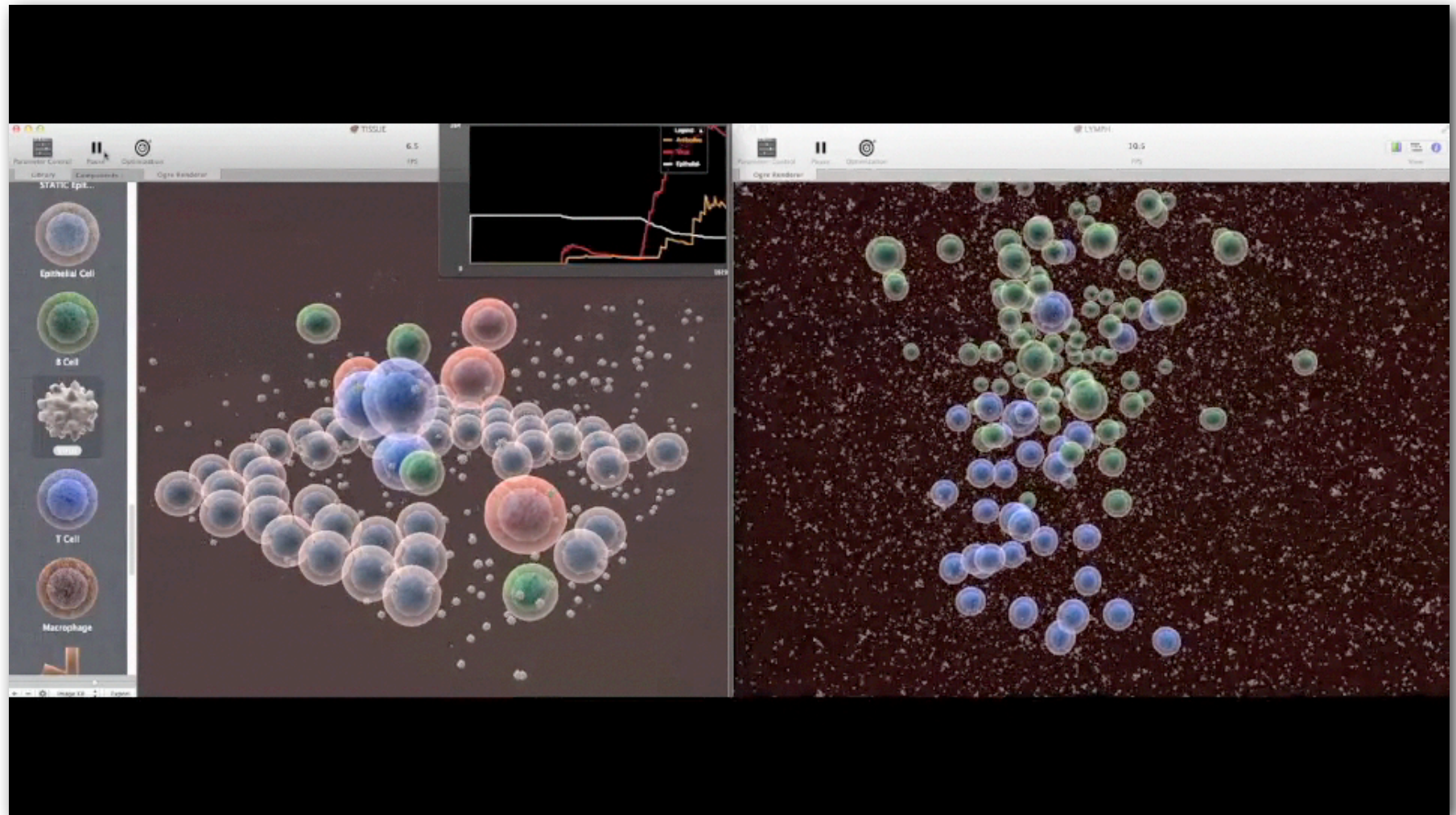


Vladimir Sarpe, 2010

[Back ...](#)

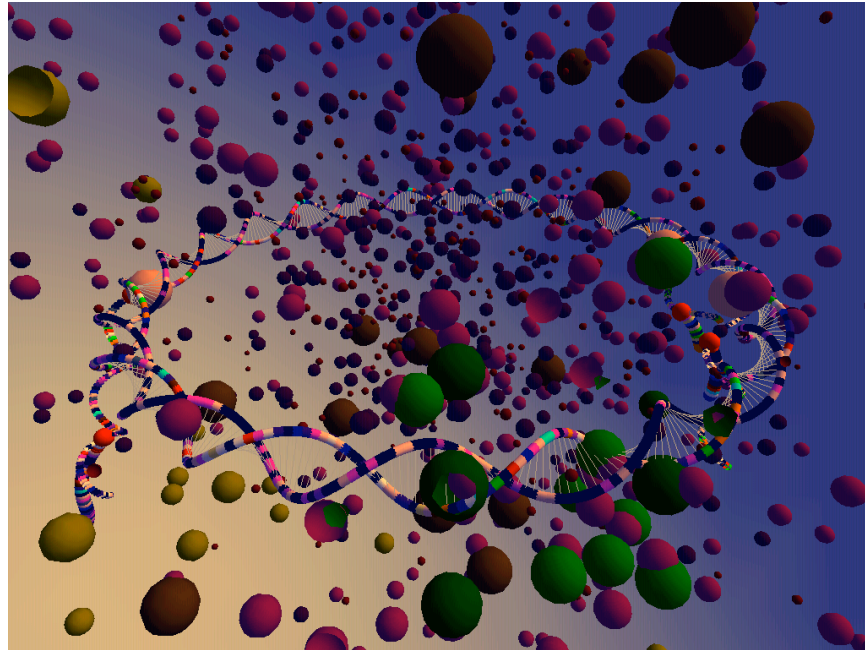


# Distributed Immune System Model 2011

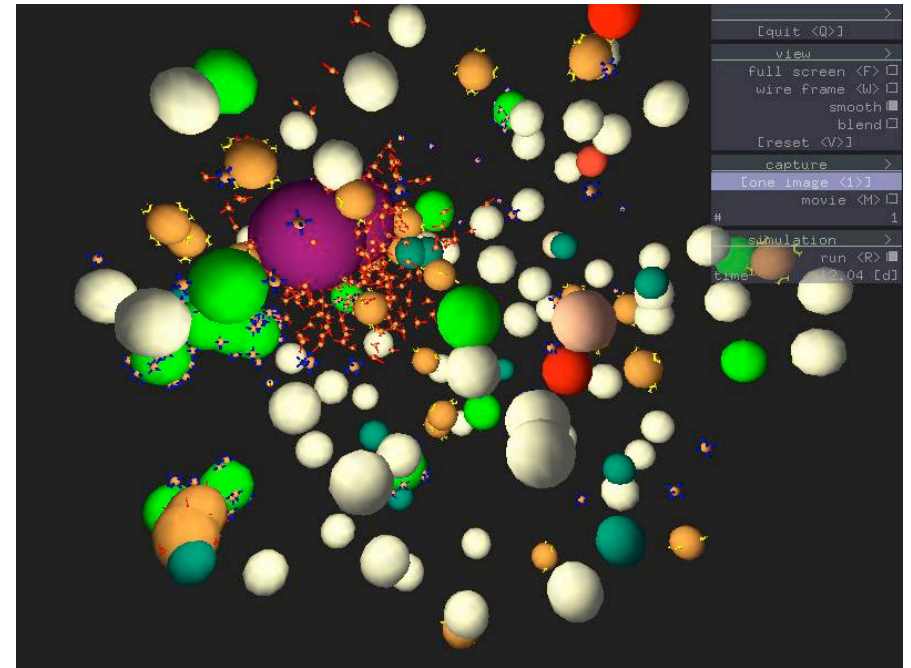
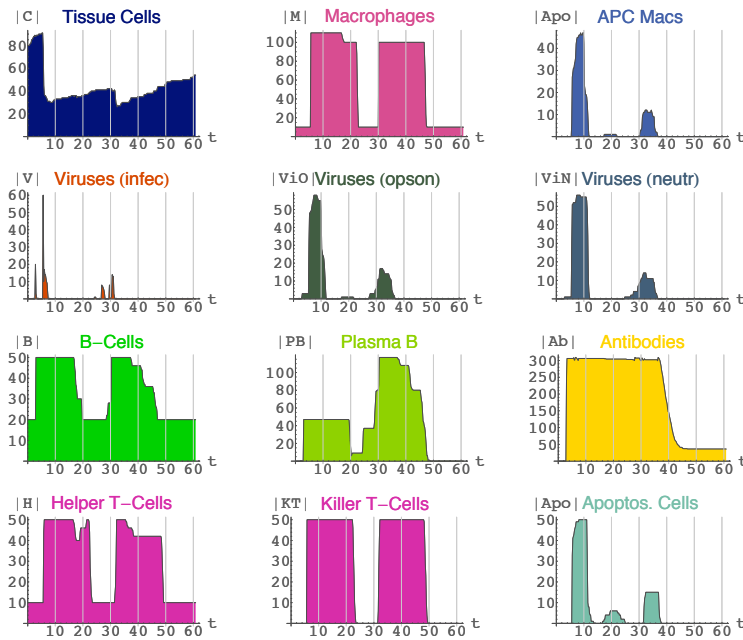


[Back ...](#)



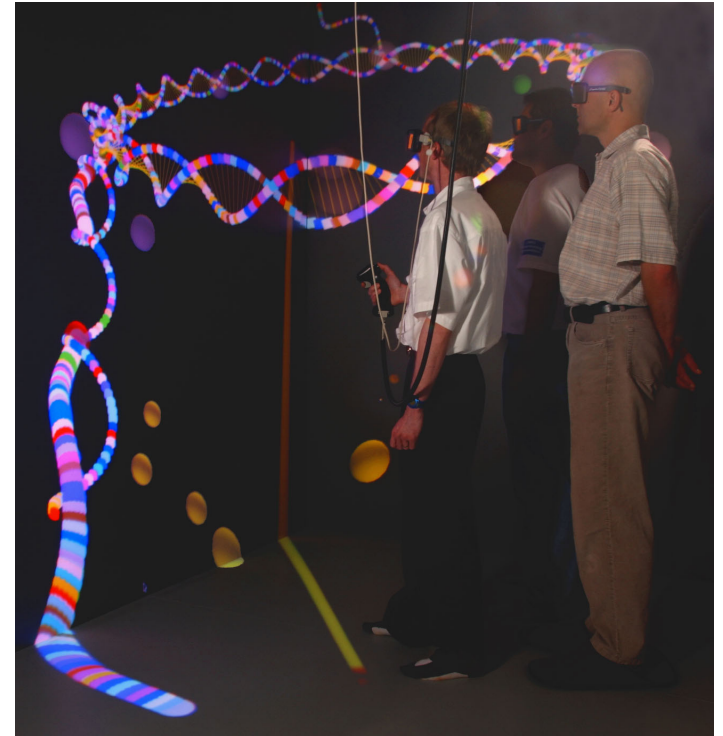


# Grid Swarm Computing

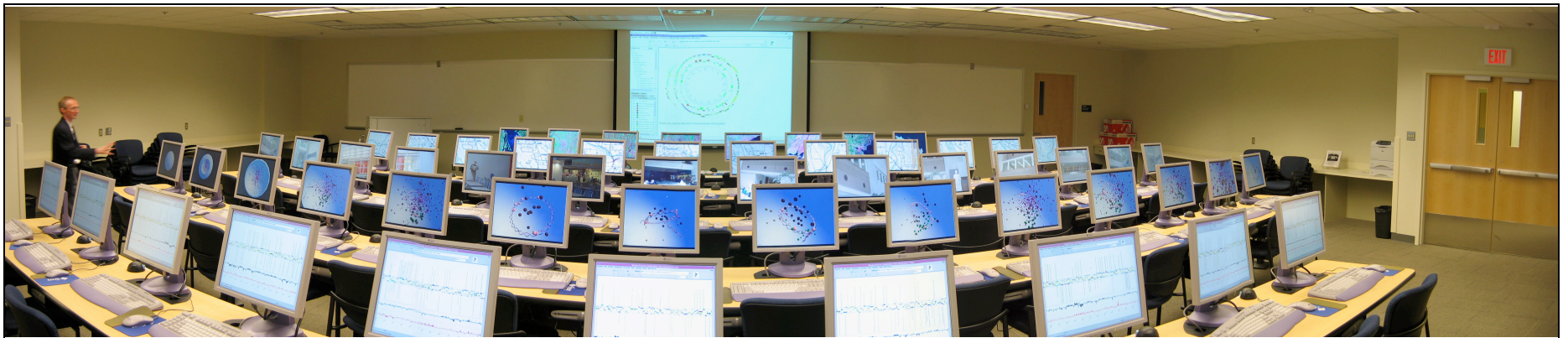




# Visualization Integration

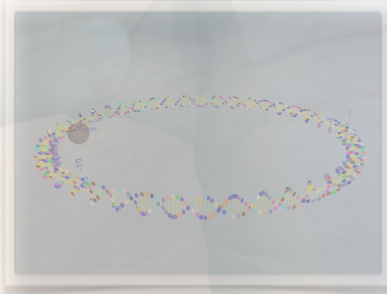


CAVE Immersive Environment at the Sun Centre of Excellence for Visual Genomics, Faculty of Medicine



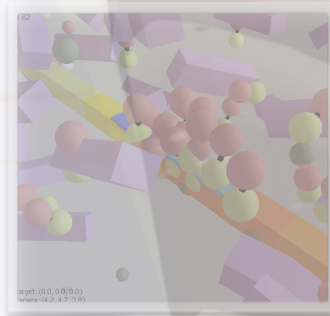
The Bioinformatics Teaching and Computer Lab in the O'Brien Centre for the Bachelor of Health Sciences Faculty of Medicine, University of Calgary

### Lactose Operon



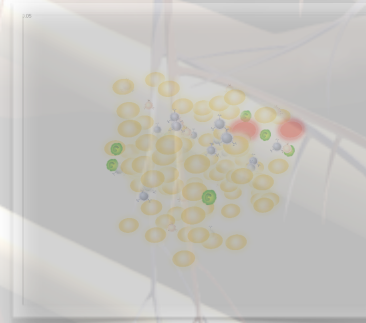
Ian Burleigh

### $\lambda$ Switch



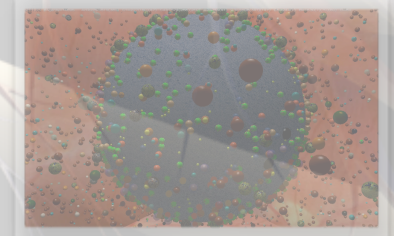
G. Tsui, A. Barbasiewicz

### Immune System



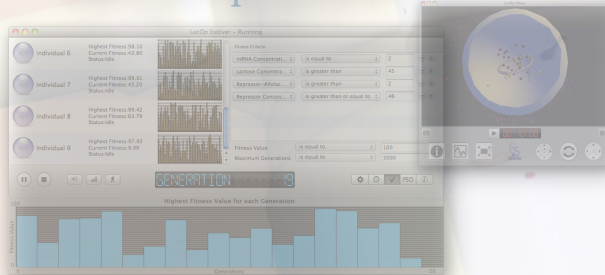
Karel Bergmann, Scott Steil

### Complement System



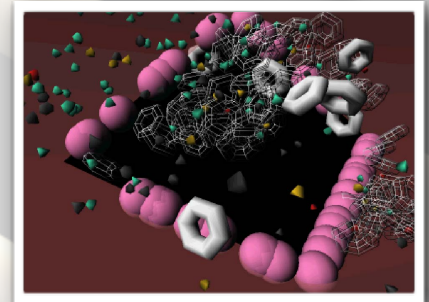
Carey Gingras, Dr. Rolando Feyt

### Lactose Op Evolver

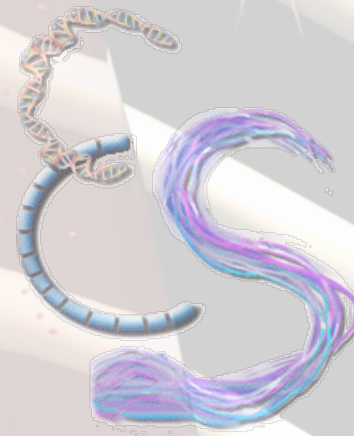


Ryan Moniz

### Blood Clotting



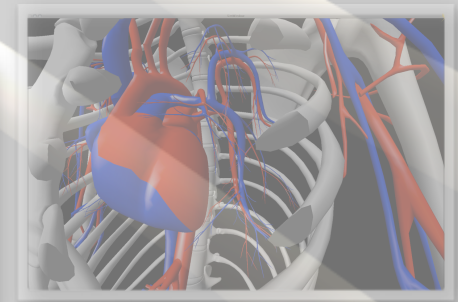
S. Chan, M. Templeton, G. Rowe, R. Degraaf, A. Punj



### LINDSAY



Scott Novakowski

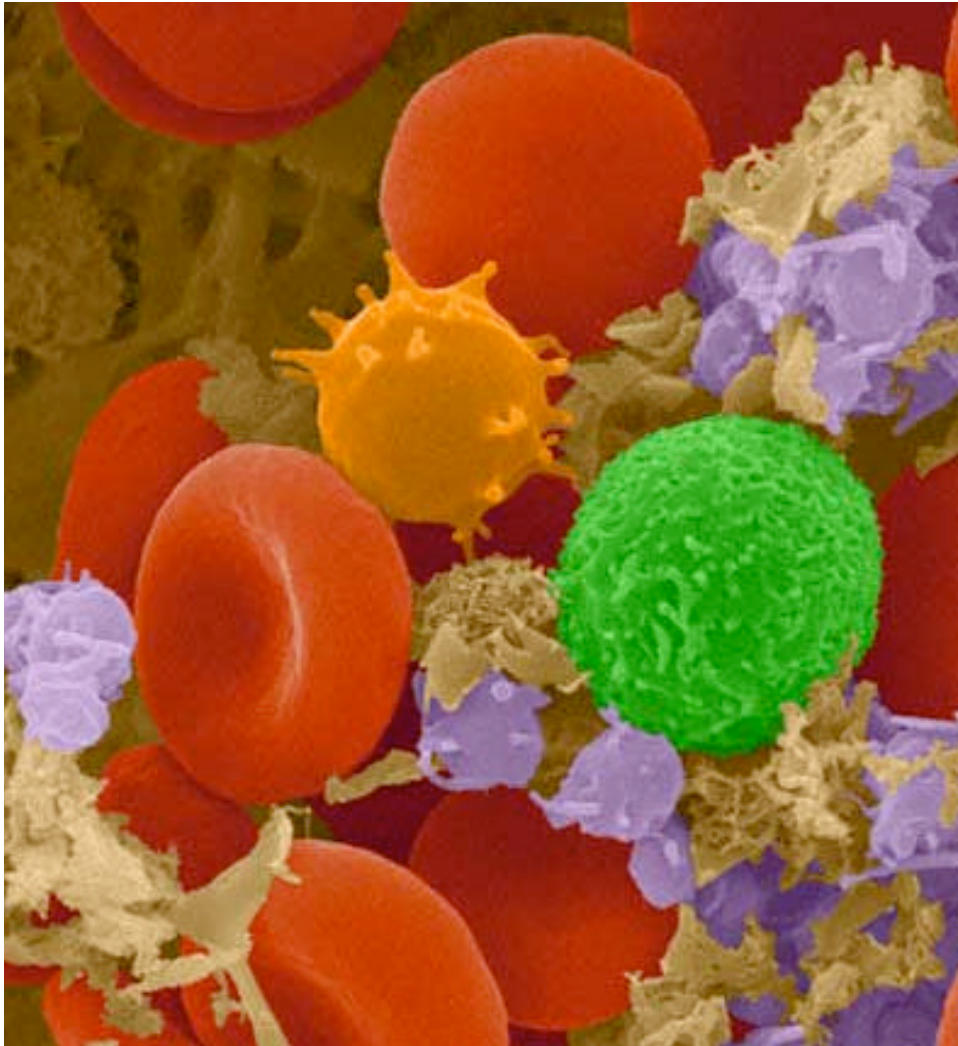


Vlad Sarpe



# Bio-Agents: The Swarming Body

© Dennis Kunkel Microscopy, Inc., [www.DennisKunkel.com](http://www.DennisKunkel.com)



## Human red & white blood cells

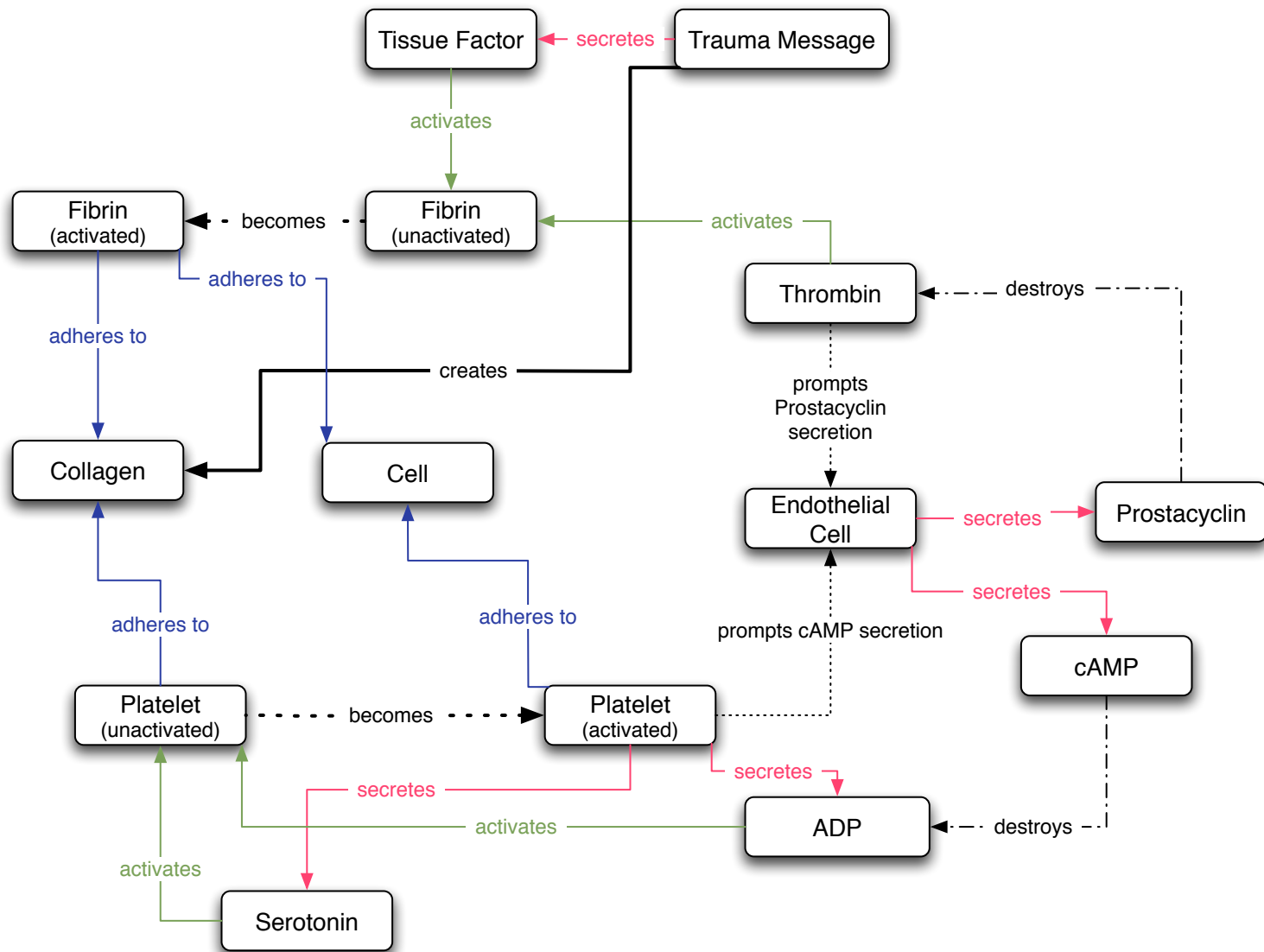
- Red blood cells (red)
- Activ. platelets (purple)
- White blood cells:
  - monocyte (green)
  - T lymphocyte (orange)

Colorized SEM  
(scanning electron  
micrograph)

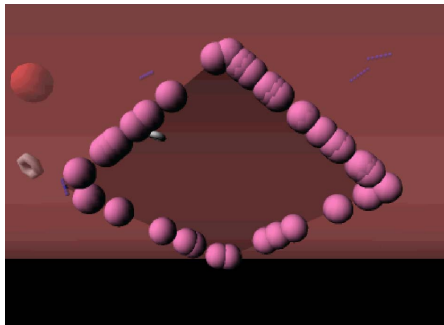
Magnification: 1200X



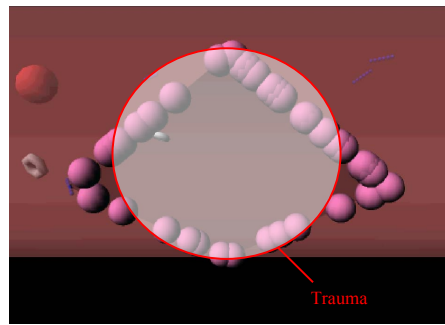
# Blood Clotting: Information Flow



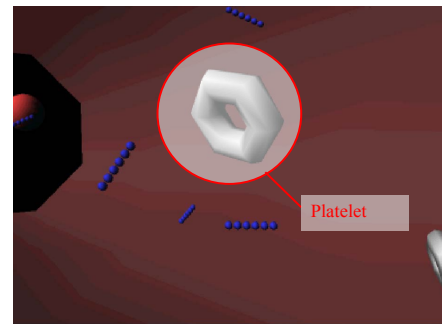
# Blood Clotting



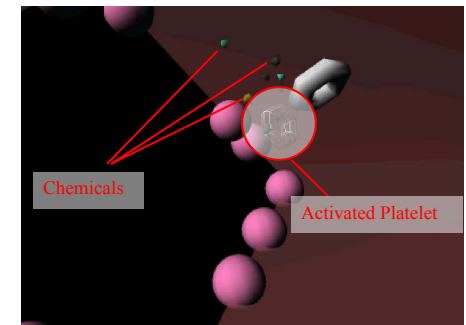
Collagen



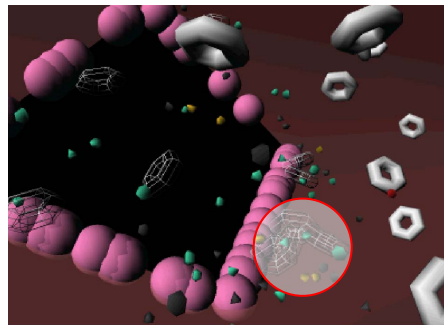
Trauma Site



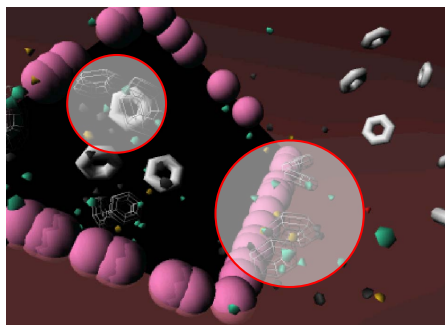
Platelet



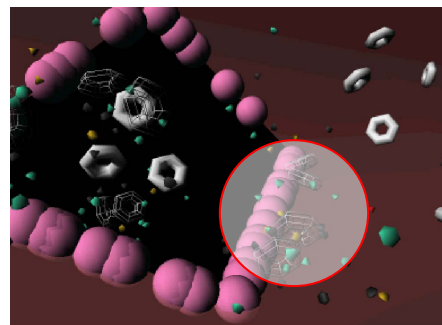
Platelets & Recruitment  
Chemicals



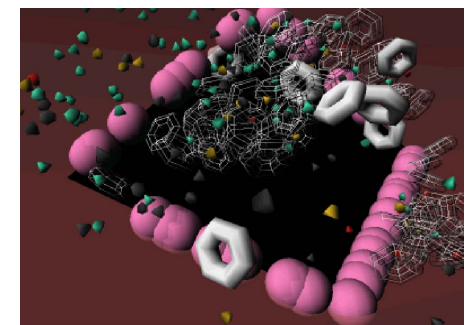
Platelets Layering



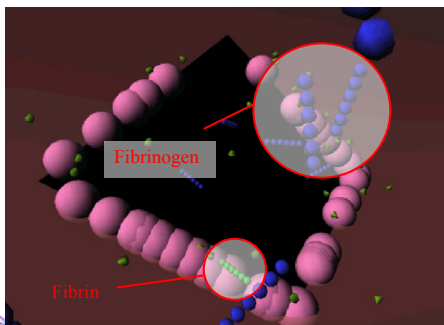
Activated Platelets



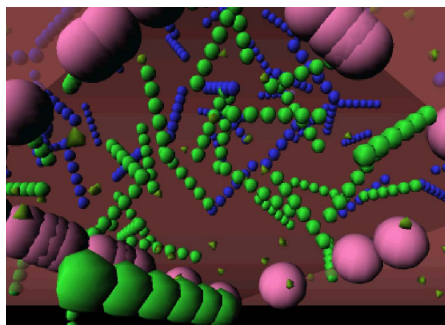
Activated Platelets



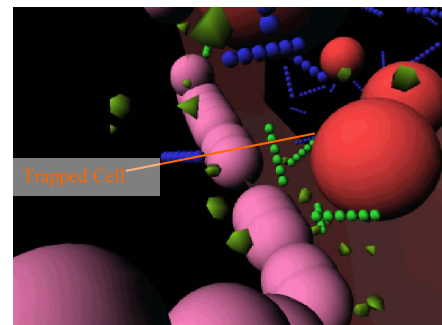
Platelet Plug



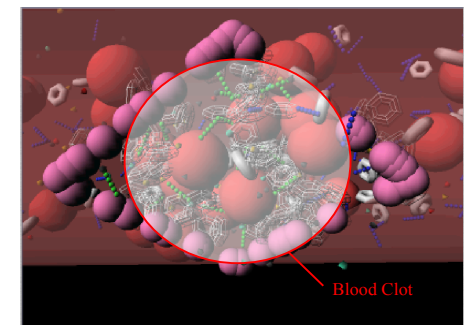
Fibrins & Fibrinogens



Fibrin Network



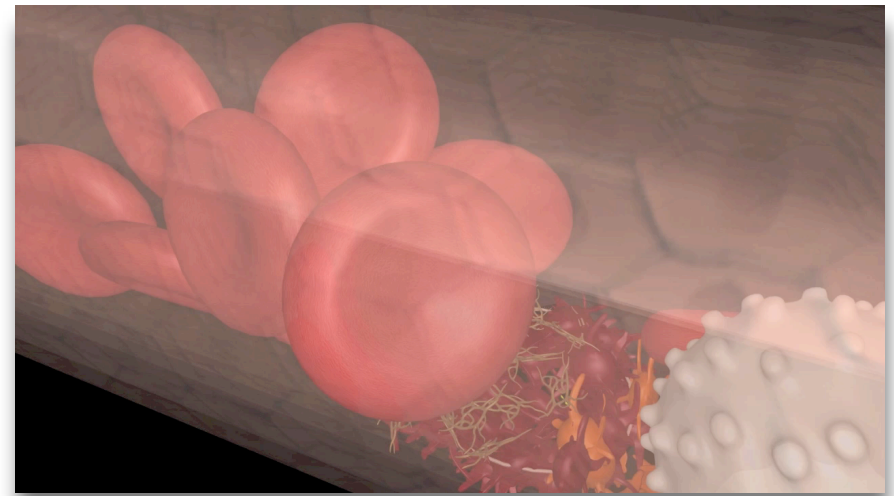
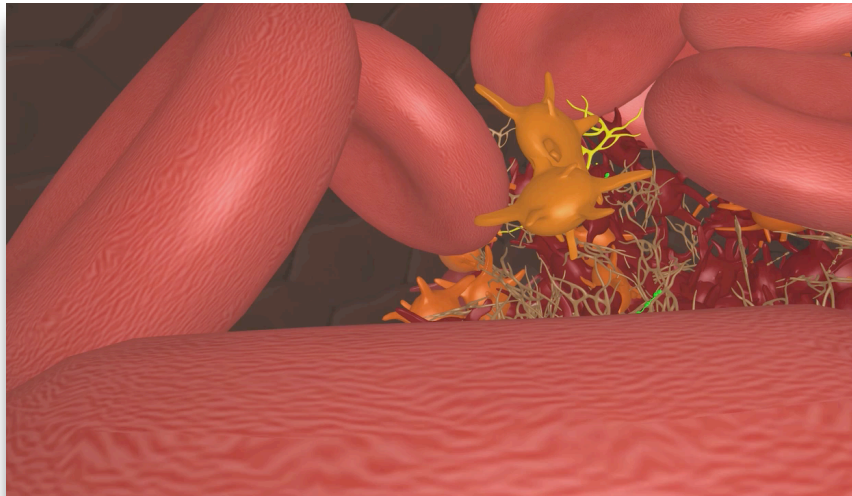
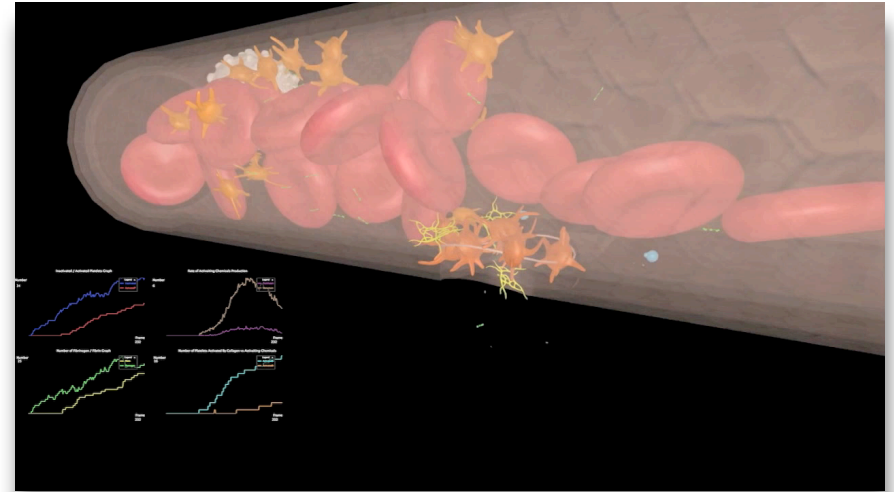
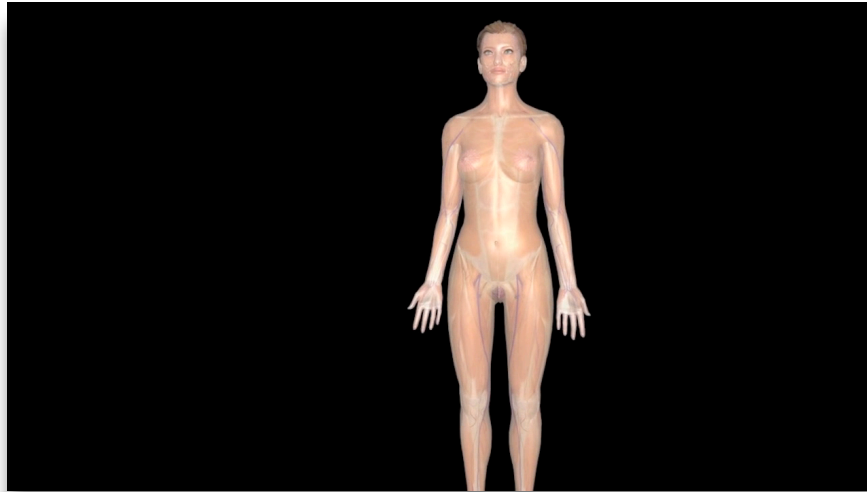
Trapped Red Blood Cell



Blood Clot

S. Chan, M. Templeton, G. Rowe, R. Degraaf, A. Punj

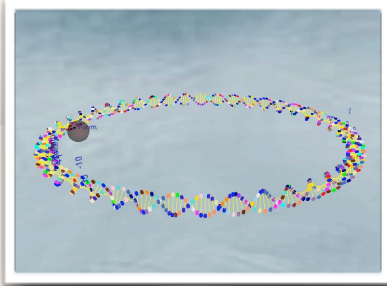
# Blood Coagulation



Iman Yazdanbod, 2010

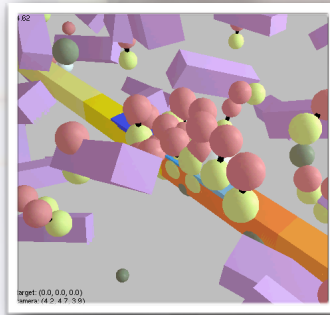


### Lactose Operon



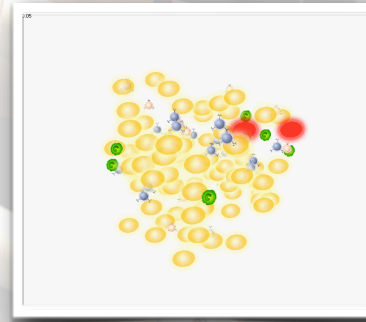
Ian Burleigh

### $\lambda$ Switch



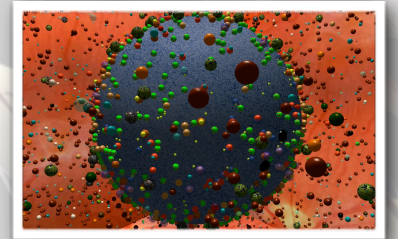
G. Tsui, A. Barbasiewicz

### Immune System



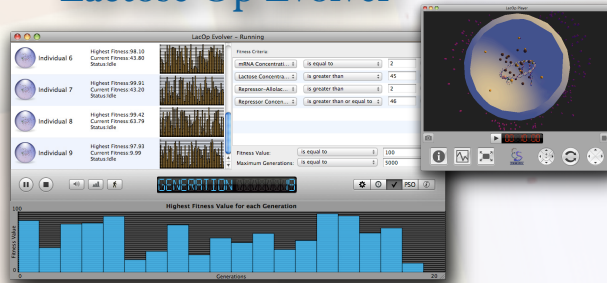
Karel Bergmann, Scott Steil

### Complement System



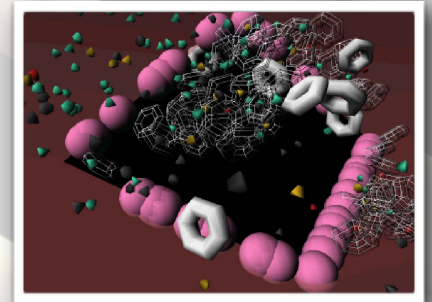
Carey Gingras, Dr. Rolando Feyt

### Lactose Op Evolver

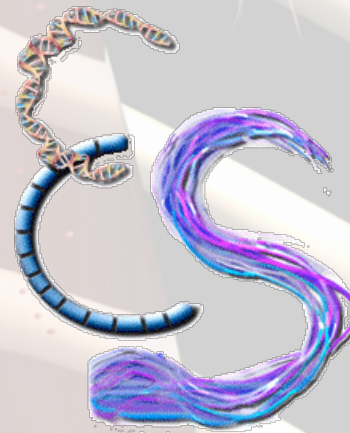


Ryan Moniz

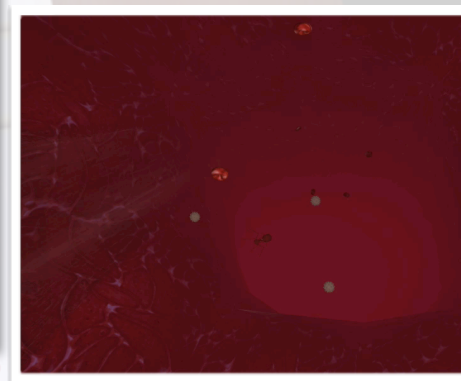
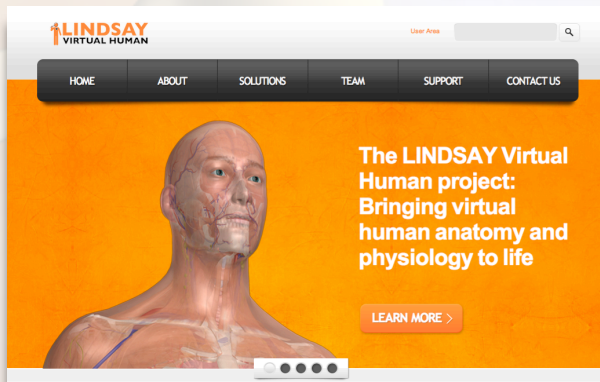
### Blood Clotting



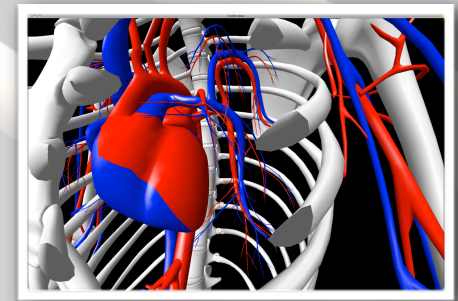
S. Chan, M. Templeton, G. Rowe, R. Degraaf, A. Punj



### LINDSAY



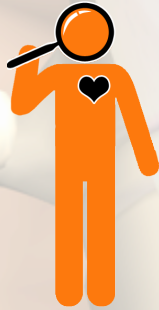
Scott Novakowski



Vlad Sarpe

### Creative Swarms





# LINDSAY

## VIRTUAL HUMAN

**A framework for anatomically embedded  
simulation for medical education**

---

Christian Jacob, Benedikt Hallgrimsson, Bruce Wright

Faculty of Medicine  
University of Calgary

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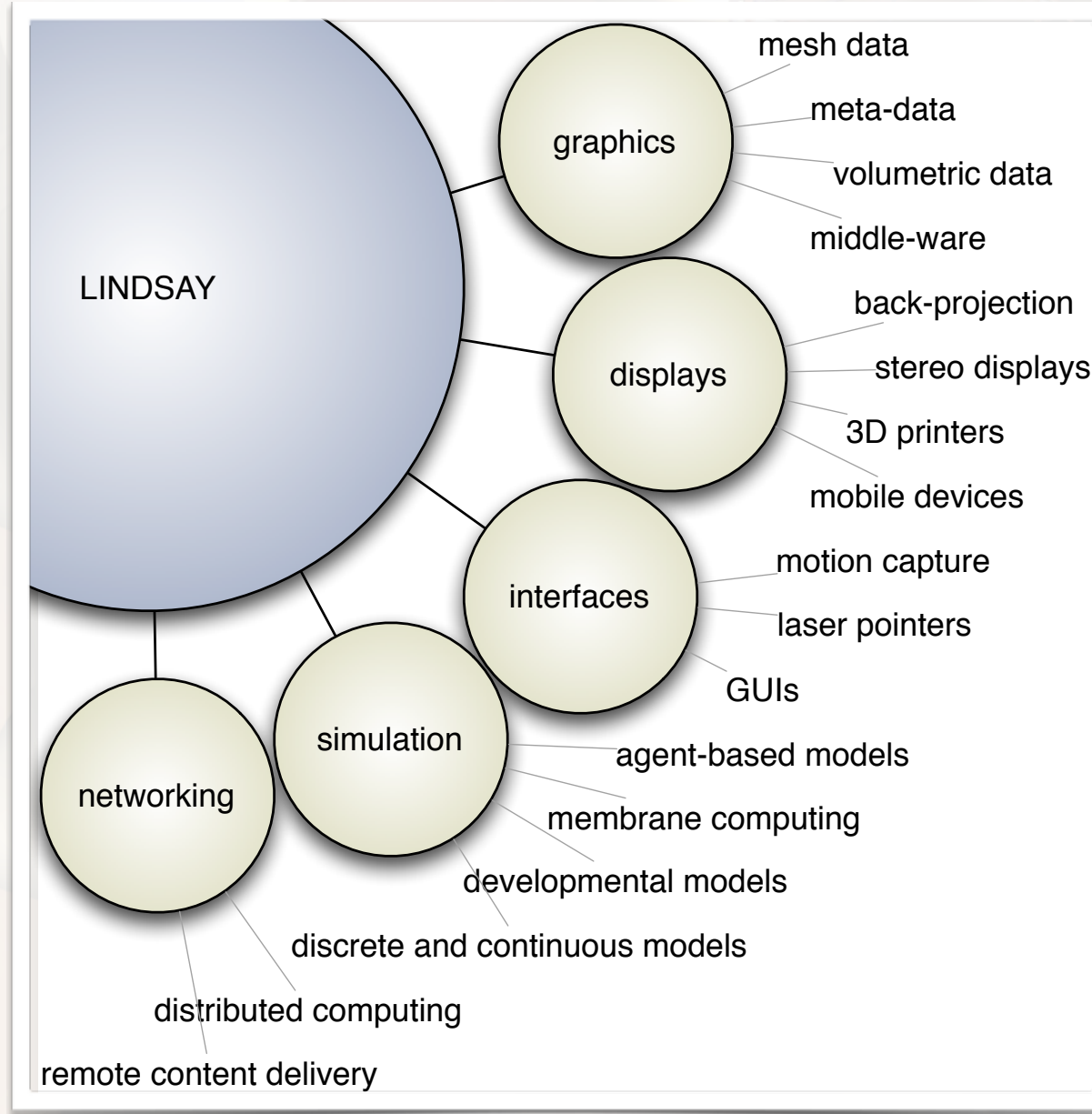
The LINDSAY Virtual Human project:  
Bringing virtual human anatomy and physiology to life

LEARN MORE >



[lindsayvirtualhuman.org](http://lindsayvirtualhuman.org)

# Supporting Technologies



# LINDSAY — Multi-Scale



2009





# LINDSAY Presenter

The screenshot displays the LINDSAY Visualizer application window. The main view shows a 3D anatomical model of a human torso, highlighting the skeletal structure and internal organs. The interface includes several control panels:

- Search Results:** A search bar and a list of search results.
- Category:** A list of categories, currently showing 'Anatomy' and 'Root'.
- Grouping Controls:** Buttons for 'Group', 'Ungroup', 'Save', and 'Open'.
- Table:** A table with columns for 'Name', 'Protocol', and 'Connected'.
- Settings:** Checkboxes for 'Anaglyph' and 'Back Color', along with numerical sliders.
- System Tray:** Displays system information such as 'Sun 2:15 PM' and 'cjacob'.

Atlas

Category	Labels	Label	Labels	Label Color
Female			<input type="checkbox"/>	Color
▶ Lymphatic			<input type="checkbox"/>	Color
▶ Circulatory			<input type="checkbox"/>	Color
▶ Connective			<input type="checkbox"/>	Color
▶ Muscles			<input type="checkbox"/>	Color
▶ Nervous			<input type="checkbox"/>	Color
▶ Organs			<input type="checkbox"/>	Color
▼ Skeleton			<input type="checkbox"/>	Color
▶ Appendicular			<input type="checkbox"/>	Color
▼ Axial			<input type="checkbox"/>	Color
▶ Ribs			<input type="checkbox"/>	Color
▶ Skull			<input type="checkbox"/>	Color
▼ Spine			<input checked="" type="checkbox"/>	Color
▶ Cervical (neck) C1-C7			<input checked="" type="checkbox"/>	Color
▶ Lumbar (lower back) L1-L5			<input checked="" type="checkbox"/>	Color
▶ Thoracic (Chest) T1-T12			<input checked="" type="checkbox"/>	Color
Hyoid			<input checked="" type="checkbox"/>	Color

Heart\_lecture.lintf

Hip\_lecture2.lintf

My-Lecture.lintf

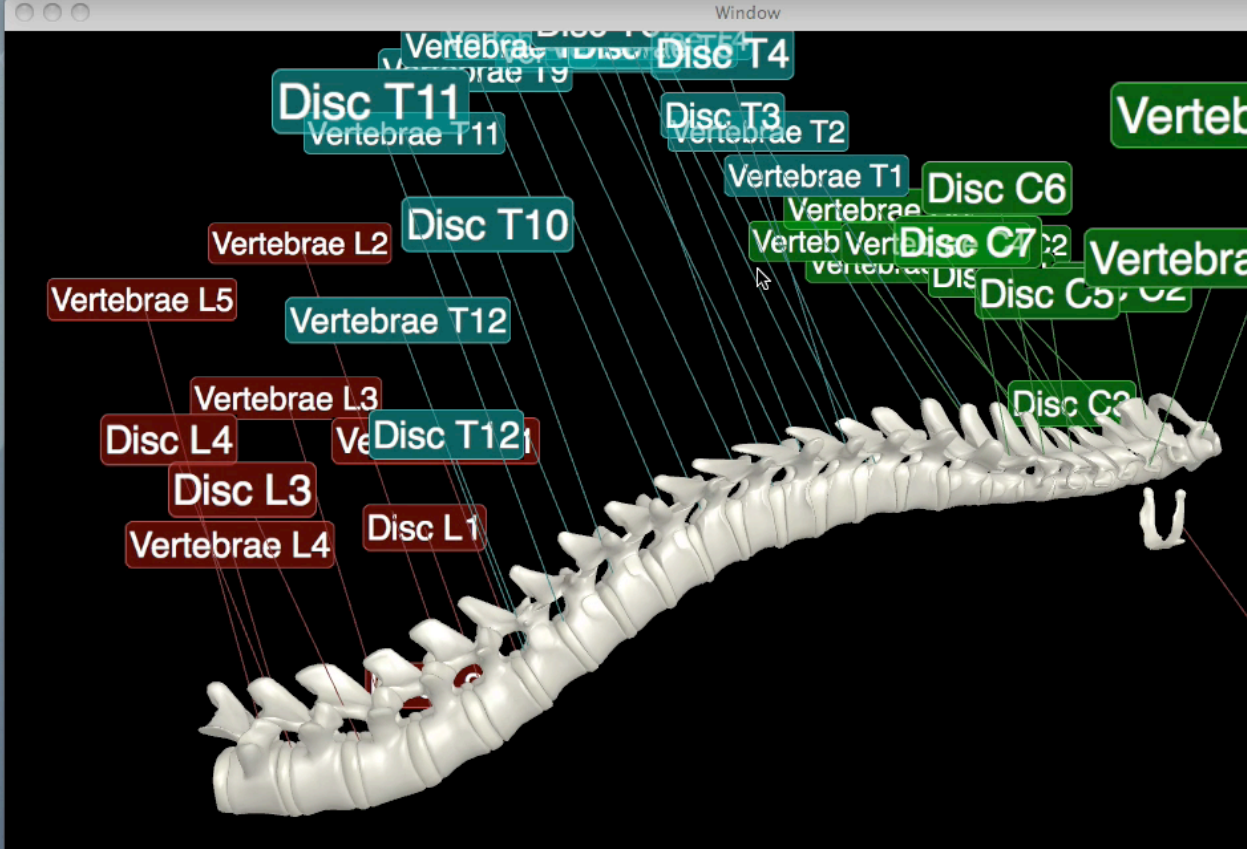
Colors

Palette: Apple

- Brown
- Cyan
- Green
- Magenta
- Orange
- Purple
- Red
- Yellow
- White

Opacity: 100

Window



View 13 <edit>

View 14 <edit>

CAPTURE

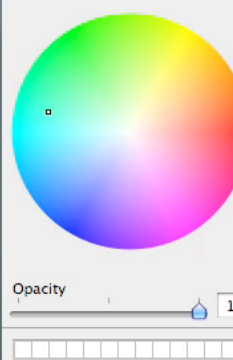
Open Save

Atlas

Category	Labels	Label	Anatomy	Labels	Label Color
			▼ Human Body	<input type="checkbox"/>	Color
			▼ Female	<input type="checkbox"/>	Color
			▶ Lymphatic	<input type="checkbox"/>	Color
			▶ Circulatory	<input type="checkbox"/>	Color
			▶ Connective	<input type="checkbox"/>	Color
			▶ Muscles	<input type="checkbox"/>	Color
			▶ Nervous	<input type="checkbox"/>	Color
			▶ Organs	<input type="checkbox"/>	Color
			▶ Skeleton	<input type="checkbox"/>	Color
			▶ Skin	<input type="checkbox"/>	Color
			▼ Male	<input type="checkbox"/>	Color
			▶ Lymphatic	<input type="checkbox"/>	Color
			▶ Circulatory	<input type="checkbox"/>	Color
			▶ Connective	<input type="checkbox"/>	Color
			▶ Muscles	<input type="checkbox"/>	Color
			▶ Nervous	<input type="checkbox"/>	Color
			▶ Organs	<input type="checkbox"/>	Color

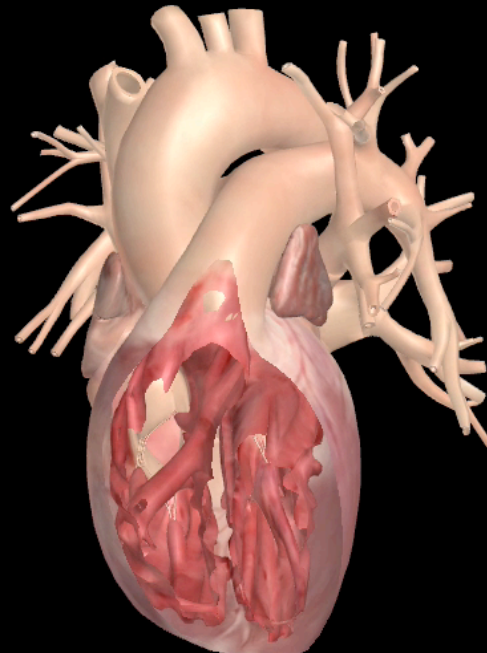


Colors



Opacity: 100

Window

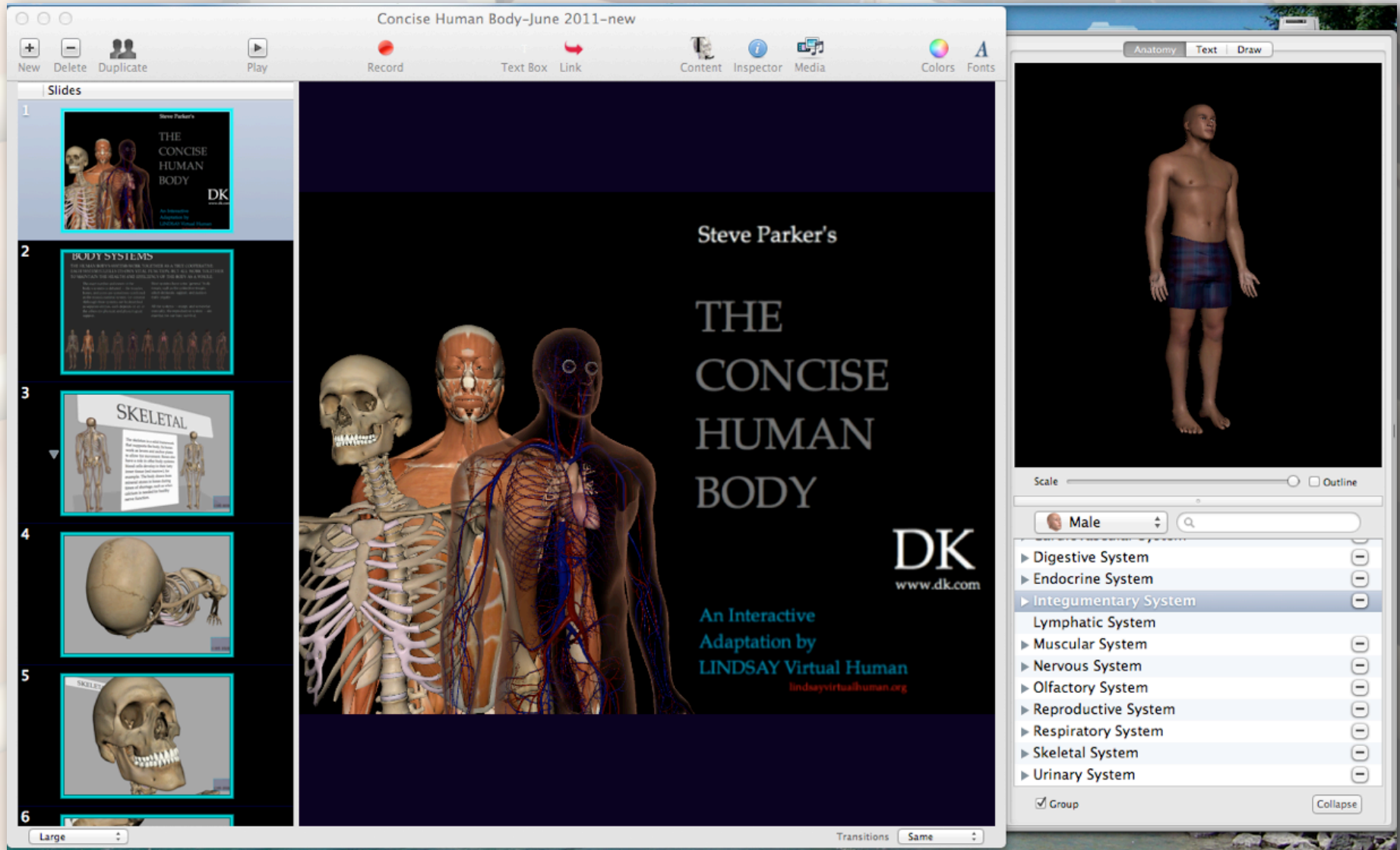


<input type="checkbox"/>	Full male body	×
<input type="checkbox"/>	Circulatory System	×
<input type="checkbox"/>	Heart	×
<input checked="" type="checkbox"/>	Heart Cut	×
<input type="checkbox"/>	Interior of heart	×
<input type="checkbox"/>	Interior of heart labelled	×
<input type="checkbox"/>	Left part of heart	×
<input type="checkbox"/>	Valves of Left Side of Heart	×
<input type="checkbox"/>	Right Side of Heart	×
<input type="checkbox"/>	Tricuspid Vavle	×

CAPTURE

Open Save

# LINDSAY Presenter 2011

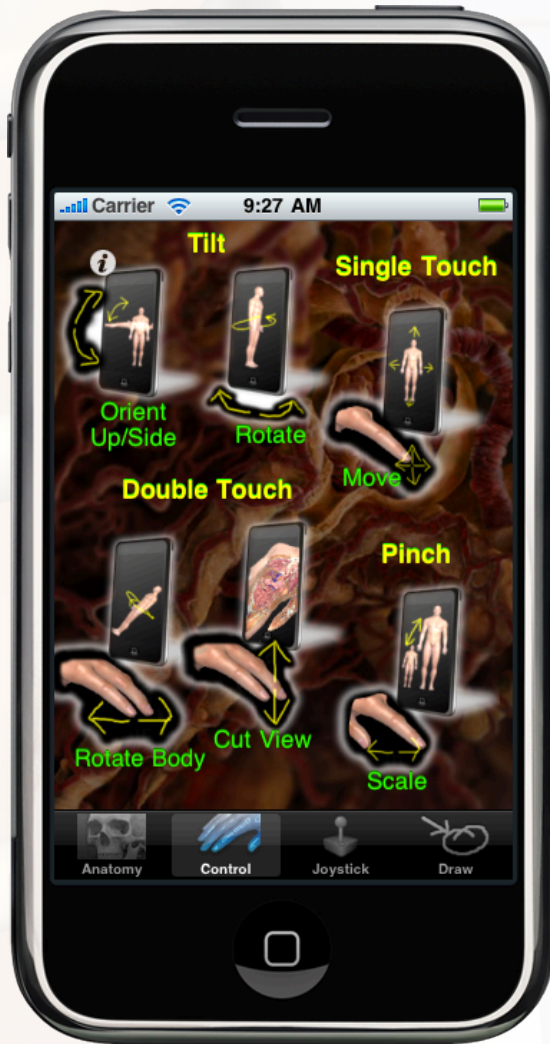


The screenshot displays the LINDSAY Presenter software interface. The main window shows a presentation slide titled "Steve Parker's THE CONCISE HUMAN BODY" by DK. The slide features three 3D anatomical models: a skeleton, a muscular system, and a circulatory system. The text on the slide reads: "An Interactive Adaptation by LINDSAY Virtual Human" with the URL "lindsayvirtualhuman.org".

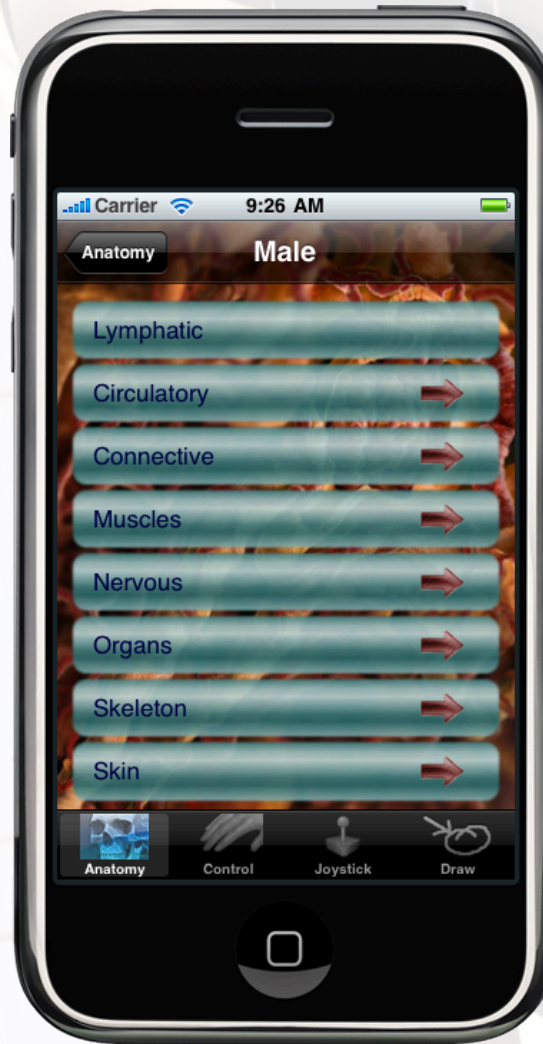
On the left side, there is a "Slides" panel with a list of six slides. Slide 1 is the title slide, slide 2 is "BODY SYSTEMS", slide 3 is "SKELETAL", slide 4 shows a skull, slide 5 shows a skull, and slide 6 is partially visible.

On the right side, there is a 3D model of a male human figure. Below the model is a "Scale" slider and an "Outline" checkbox. A dropdown menu is open, showing a list of body systems: Digestive System, Endocrine System, Integumentary System, Lymphatic System, Muscular System, Nervous System, Olfactory System, Reproductive System, Respiratory System, Skeletal System, and Urinary System. The "Integumentary System" is currently selected. There is also a "Group" checkbox and a "Collapse" button.

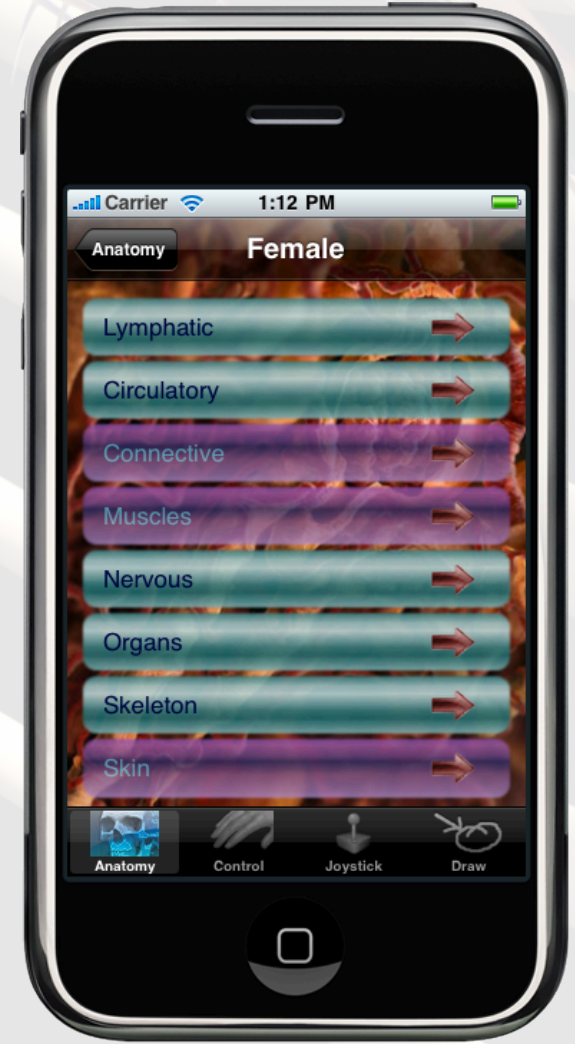
# Remote Control by Touch



Navigation



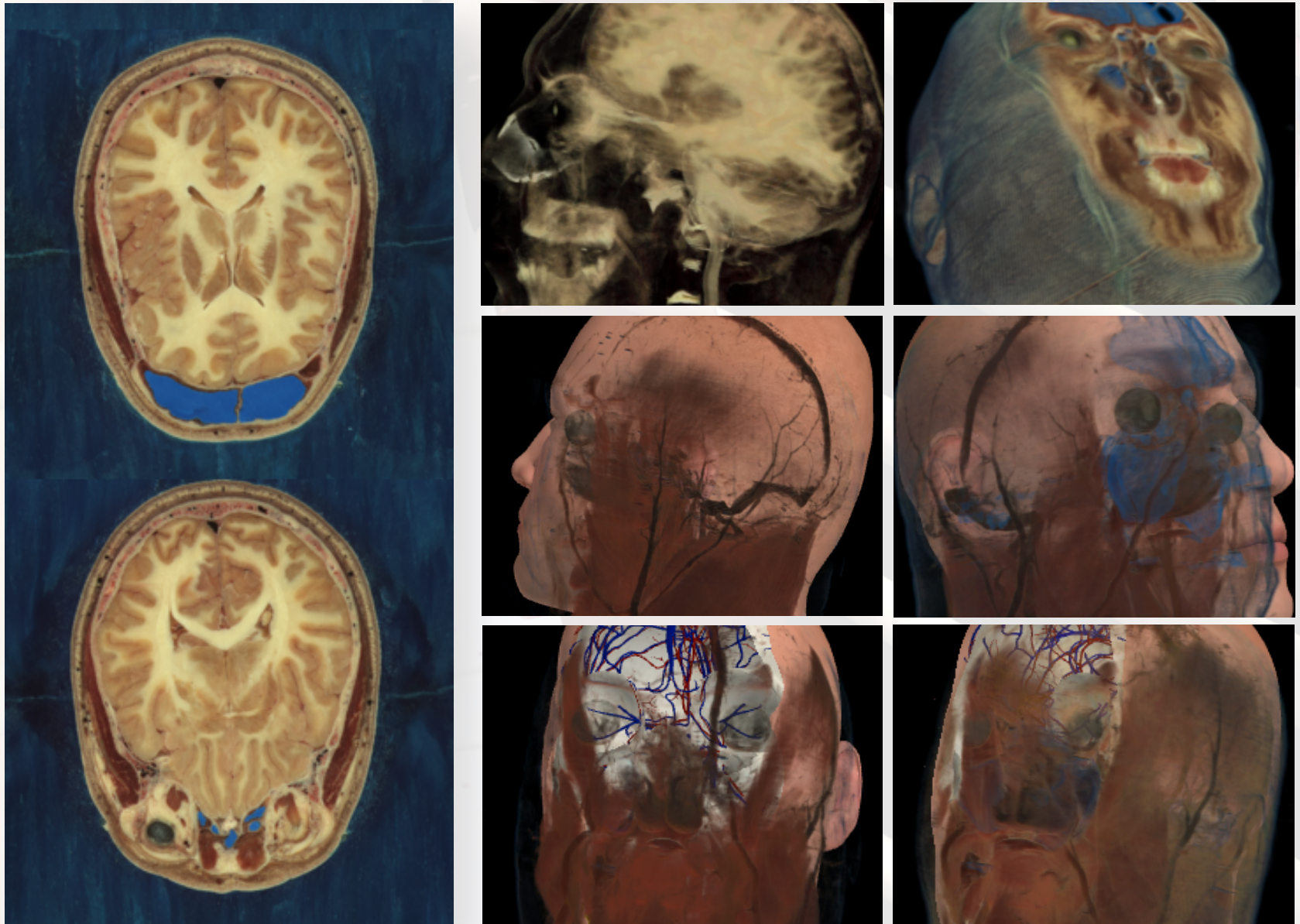
Atlas



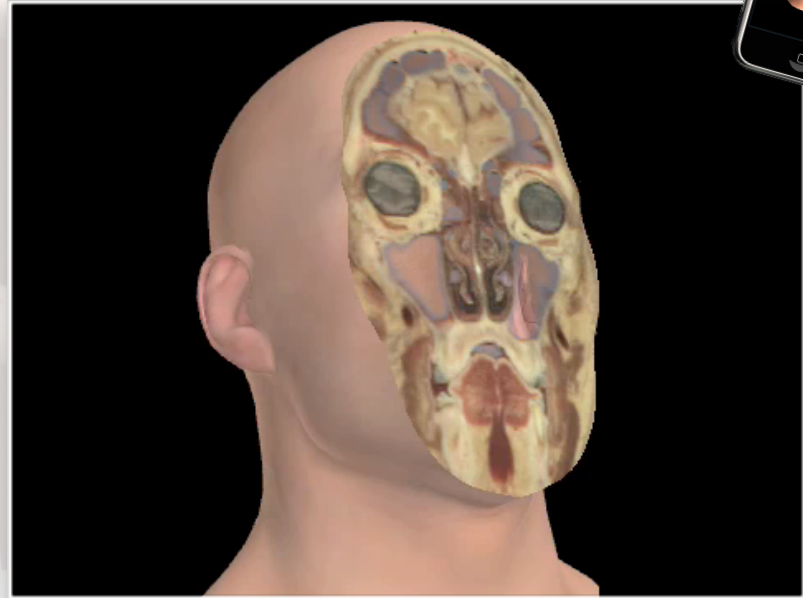
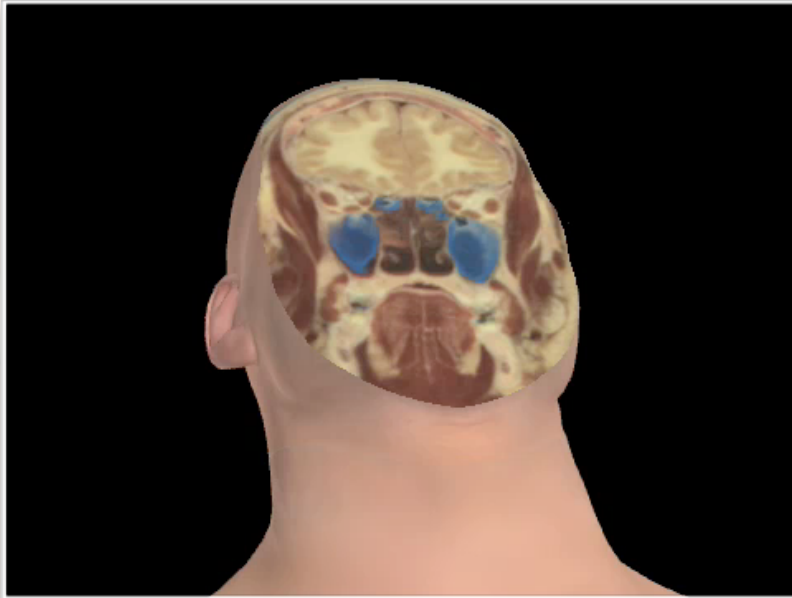
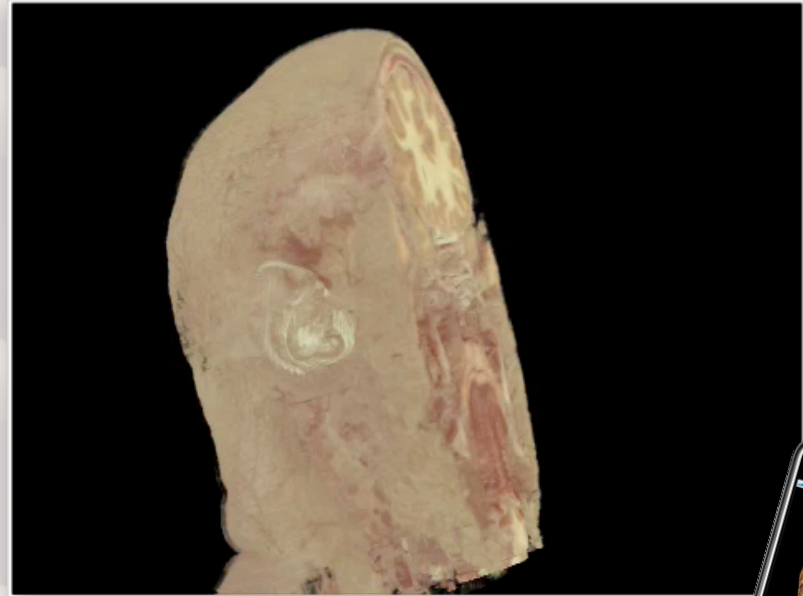
Atlas

# Integrating Volumetric Data: Visible Human

[http://www.nlm.nih.gov/research/visible/visible\\_human.html](http://www.nlm.nih.gov/research/visible/visible_human.html)



# Integrating Volumetric Data: Visible Human



[http://www.nlm.nih.gov/research/visible/visible\\_human.html](http://www.nlm.nih.gov/research/visible/visible_human.html)

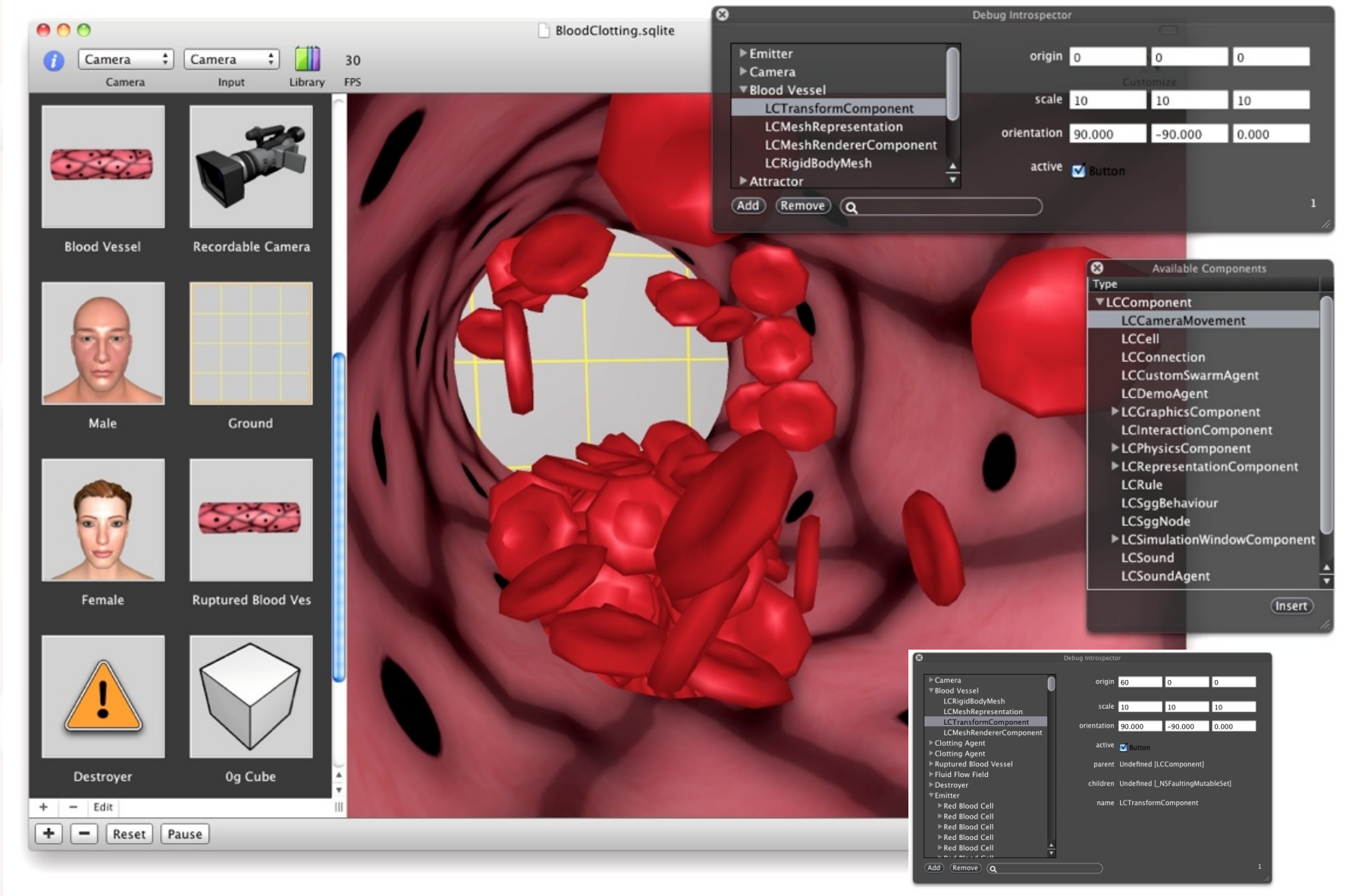
# LINDSAY Composer



Timothy Davison, Ivan Kruykov, 2010



# LINDSAY Composer



The screenshot displays the LINDSAY Composer interface for a simulation titled "BloodClotting.sqlite". The main window shows a 3D view of a blood vessel with red blood cells and a central clot. On the left, a library contains components like "Blood Vessel", "Recordable Camera", "Male", "Ground", "Female", "Ruptured Blood Ves", "Destroyer", and "Og Cube".

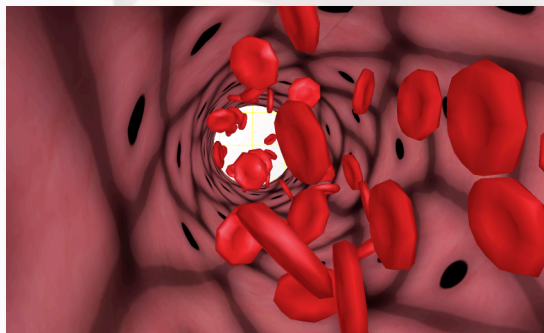
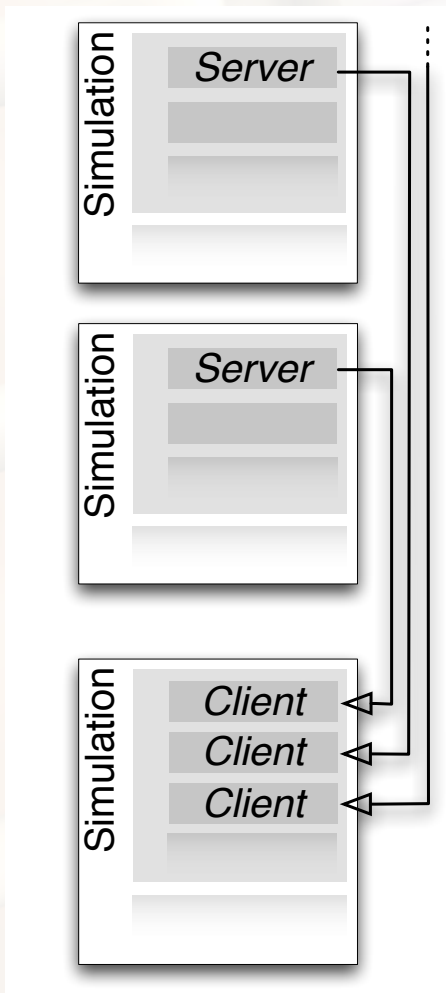
Two "Debug Introspector" panels are visible:

- Top Panel:** Shows the hierarchy for a selected "Blood Vessel" component, including "LCTransformComponent", "LCMeshRepresentation", "LCMeshRenderComponent", and "LCRigidBodyMesh". Properties include origin (0, 0, 0), scale (10, 10, 10), orientation (90.000, -90.000, 0.000), and an active checkbox.
- Bottom Panel:** Shows the hierarchy for a selected "Camera" component, including "LCRigidBodyMesh", "LCMeshRepresentation", "LCTransformComponent", "LCMeshRenderComponent", "Clotting Agent", "Clotting Agent", "Ruptured Blood Vessel", "Fluid Flow Field", "Destroyer", and "Emitter". Properties include origin (60, 0, 0), scale (10, 10, 10), orientation (90.000, -90.000, 0.000), and an active checkbox.

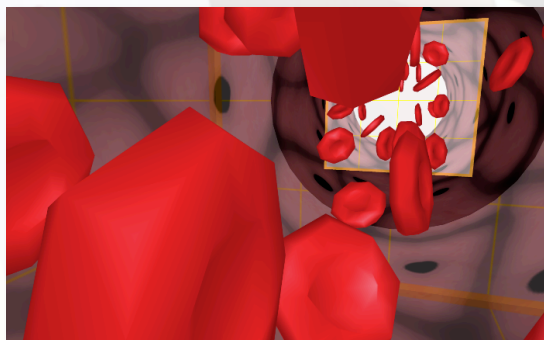
An "Available Components" panel on the right lists various component types such as "LCCameraMovement", "LCCell", "LCCustomSwarmAgent", "LCDemoAgent", "LCGraphicsComponent", "LCInteractionComponent", "LCPhysicsComponent", "LCRepresentationComponent", "LCRule", "LCSggBehaviour", "LCSggNode", "LCSimulationWindowComponent", "LCSound", and "LCSoundAgent".

Timothy Davison, 2010

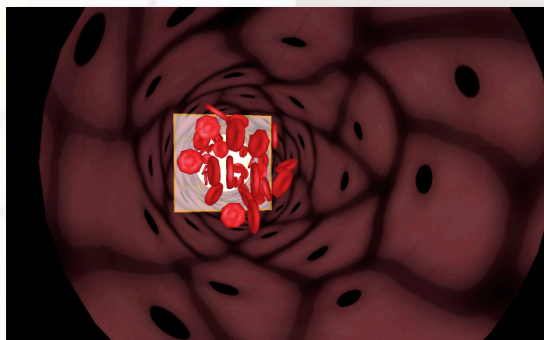
# LINDSAY Client/Server



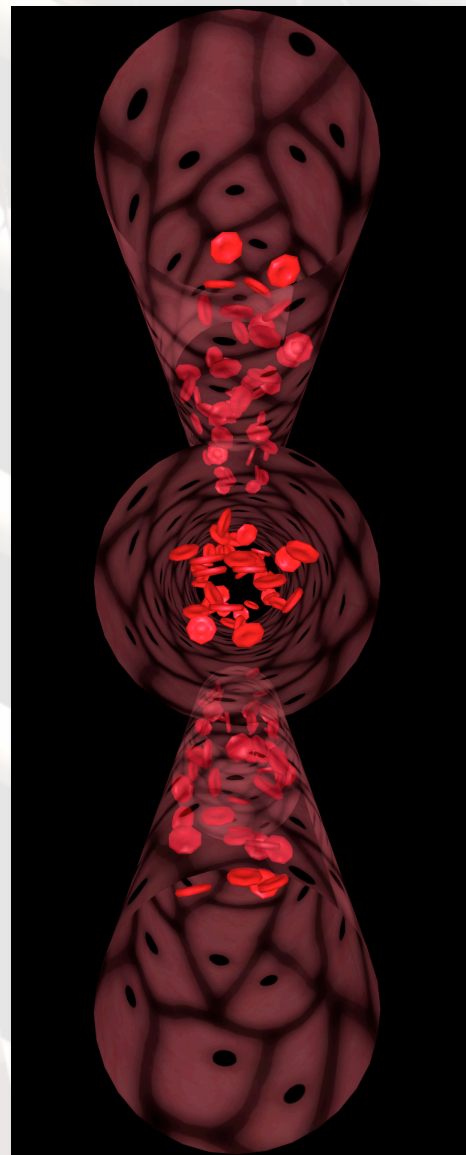
View 1



View 2

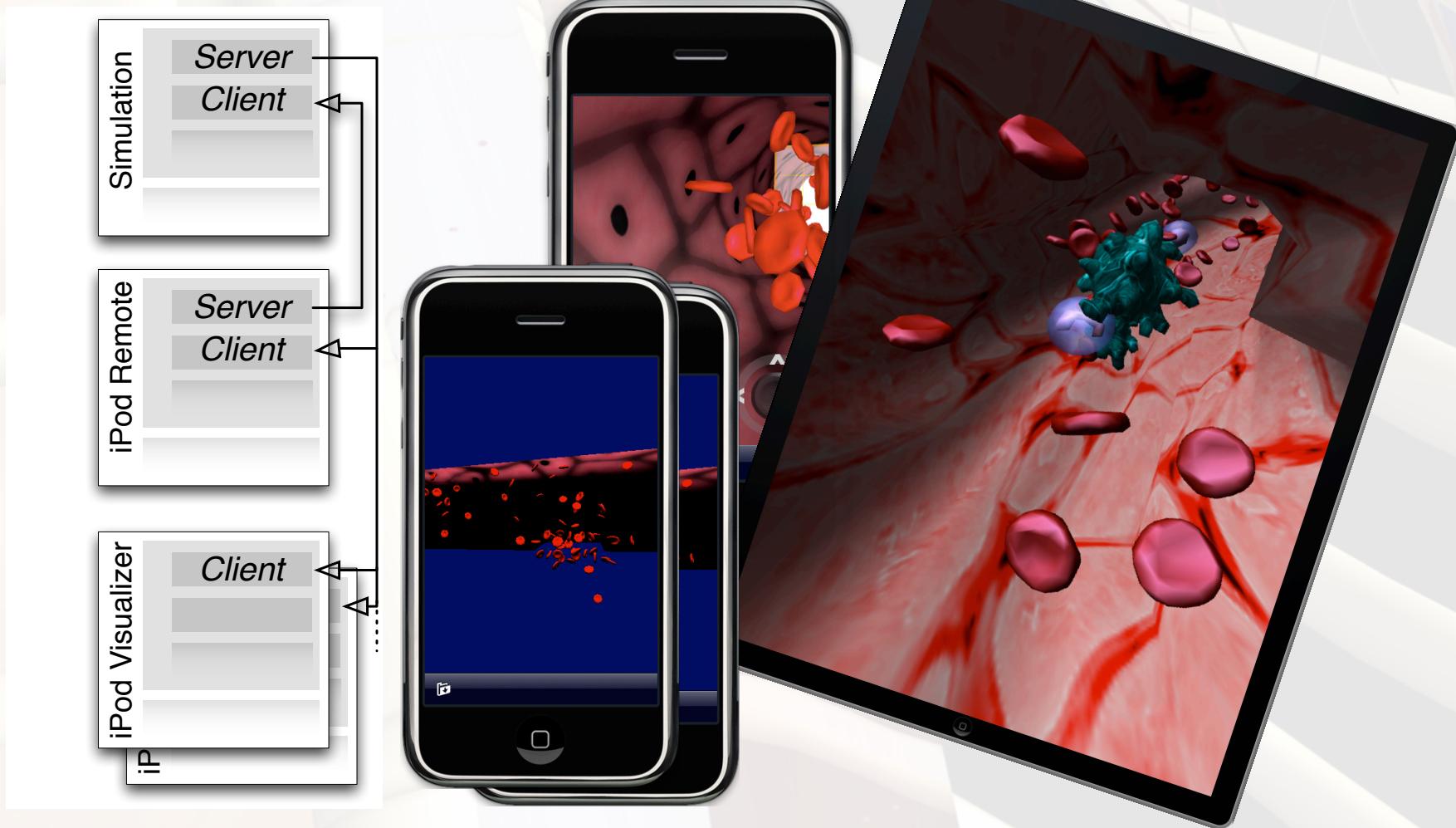


View 3



Timothy Davison, Hamid Baghi, 2010

# LINDSAY Interactive Classroom



*iPhone & iPad -  
LINDSAY Navigators*

## Visualization

## Navigation

Timothy Davison, Hamid Baghi, 2010

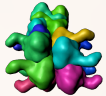
# LINDSAY Multi-Scale Example



RNA Poly



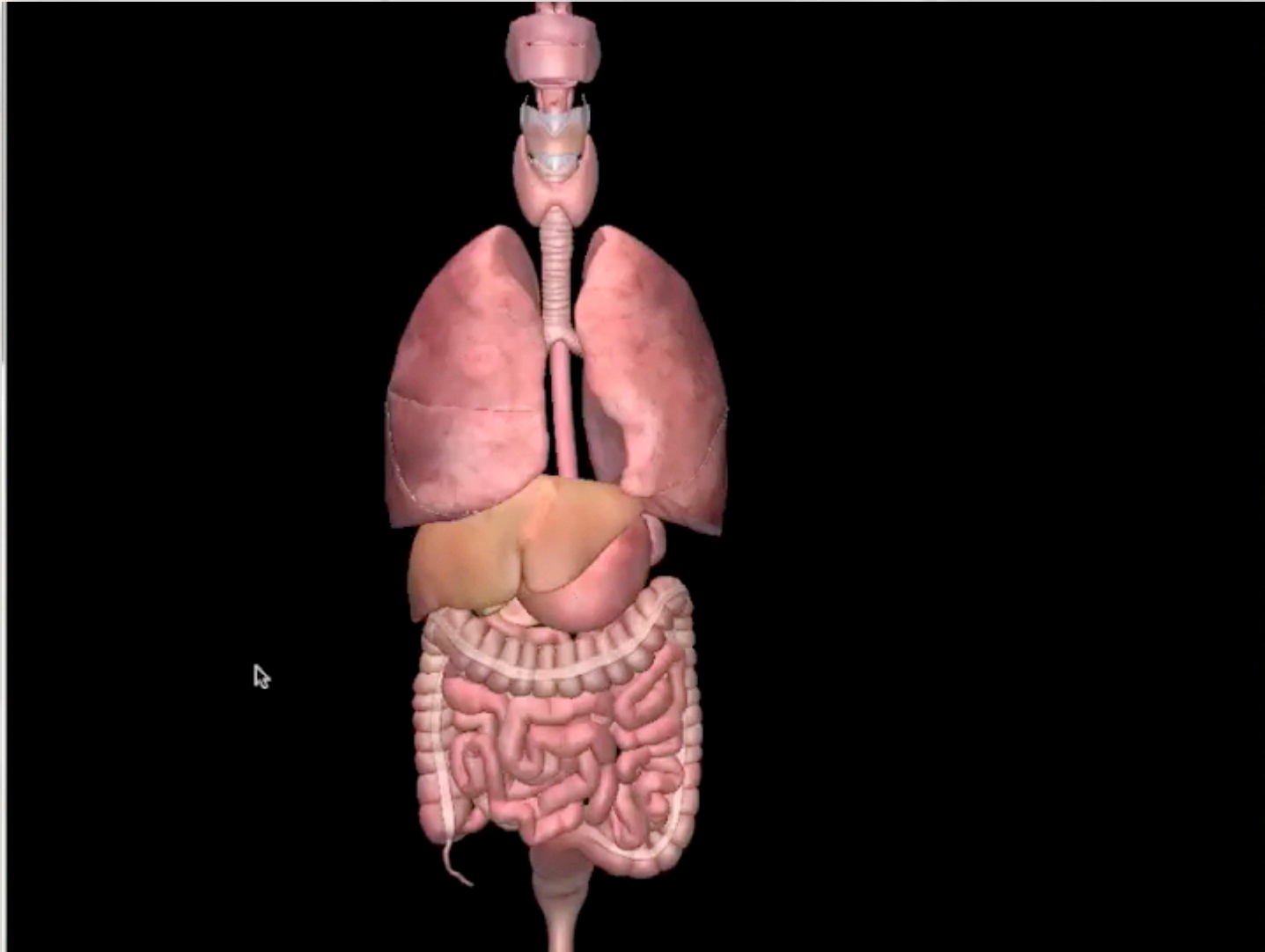
Ribosome



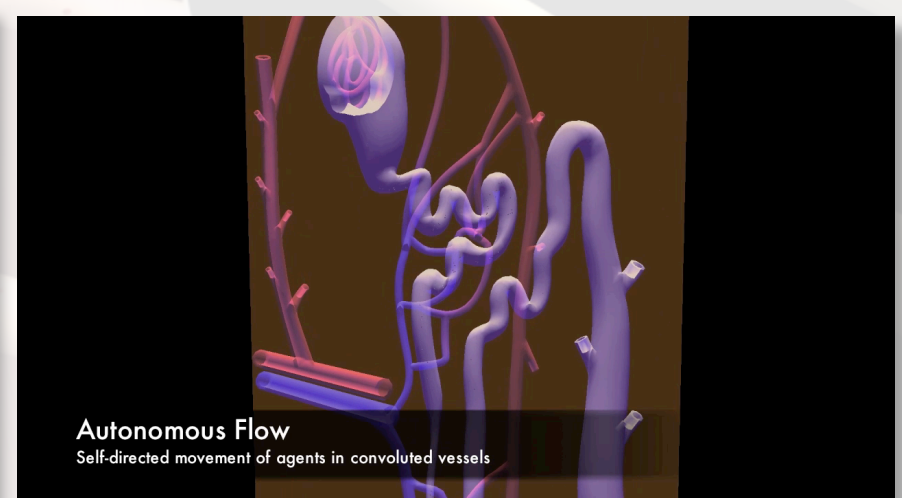
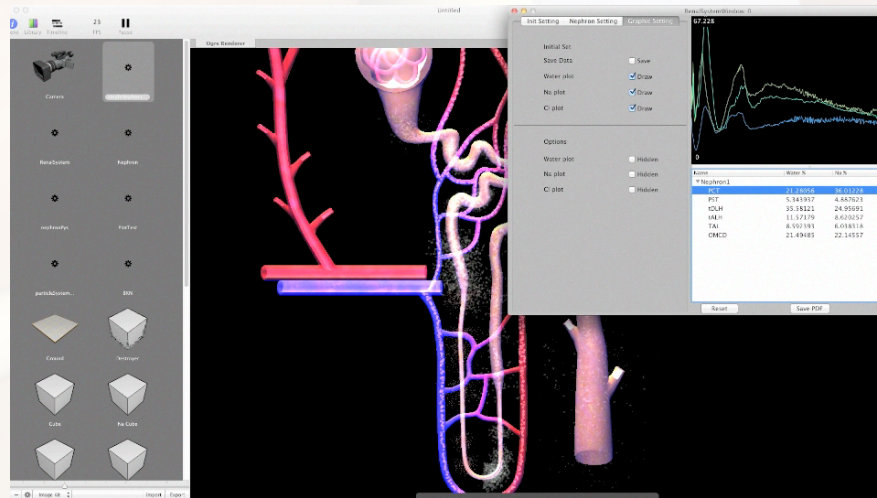
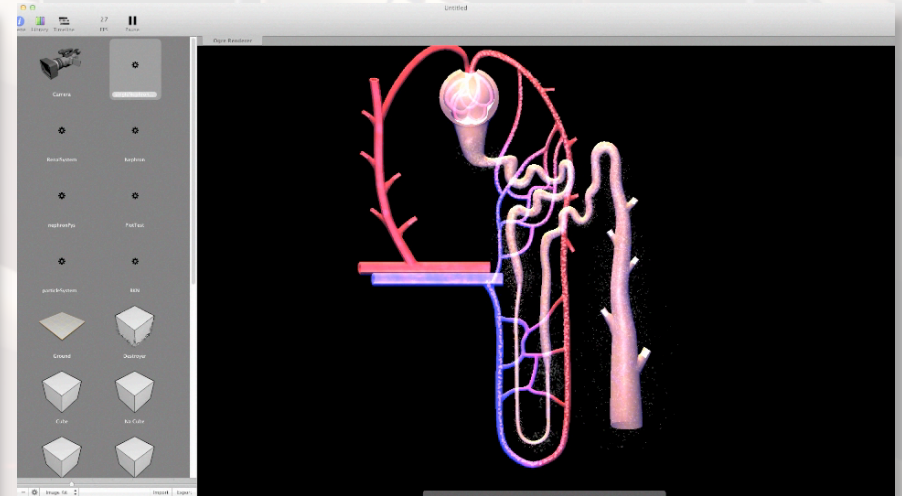
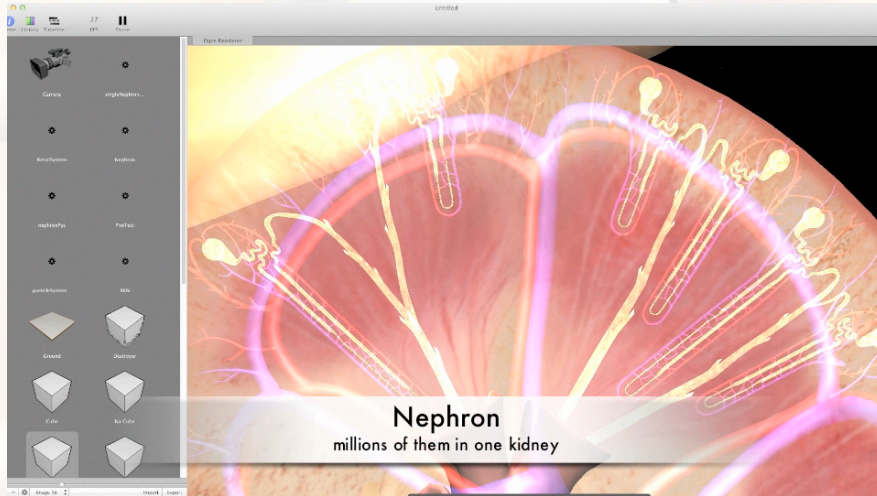
Al<sub>2</sub>



H<sub>2</sub>O



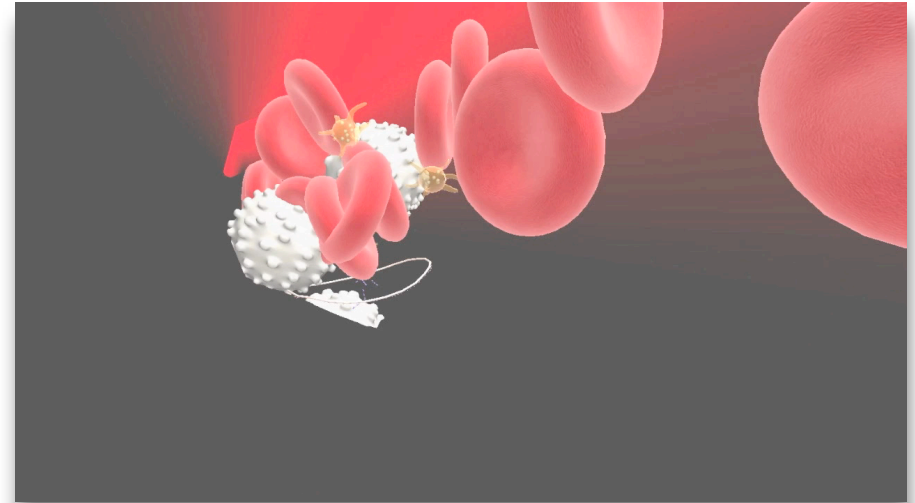
# Multi-scale Renal System Models



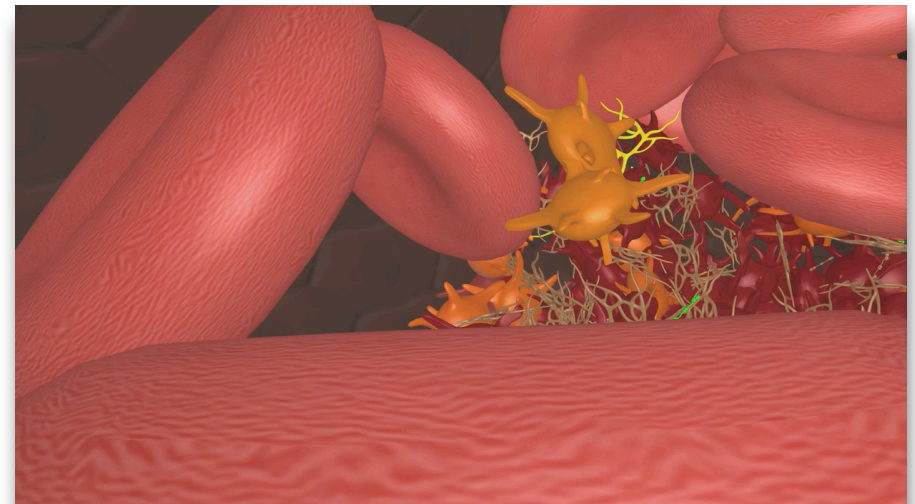
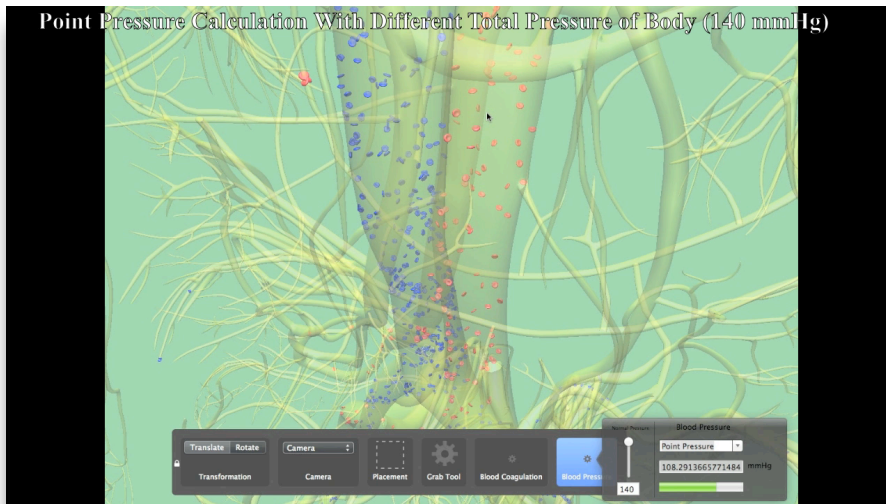
Chenzhe Qian, Douglas Yuen, 2011

# Circulatory System

Circulatory System  
in the context of  
Lindsay Virtual Human

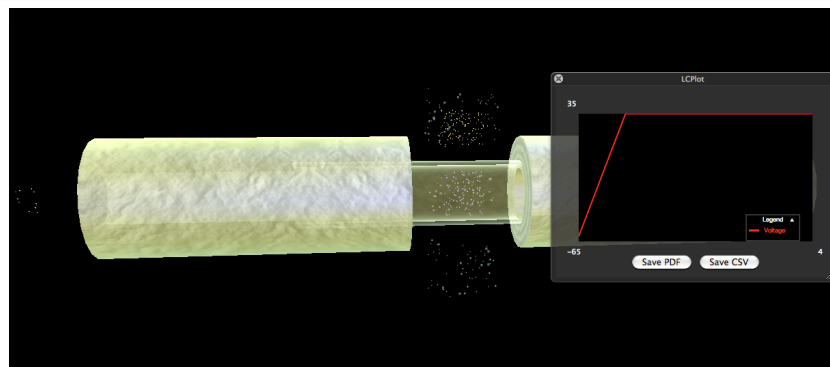
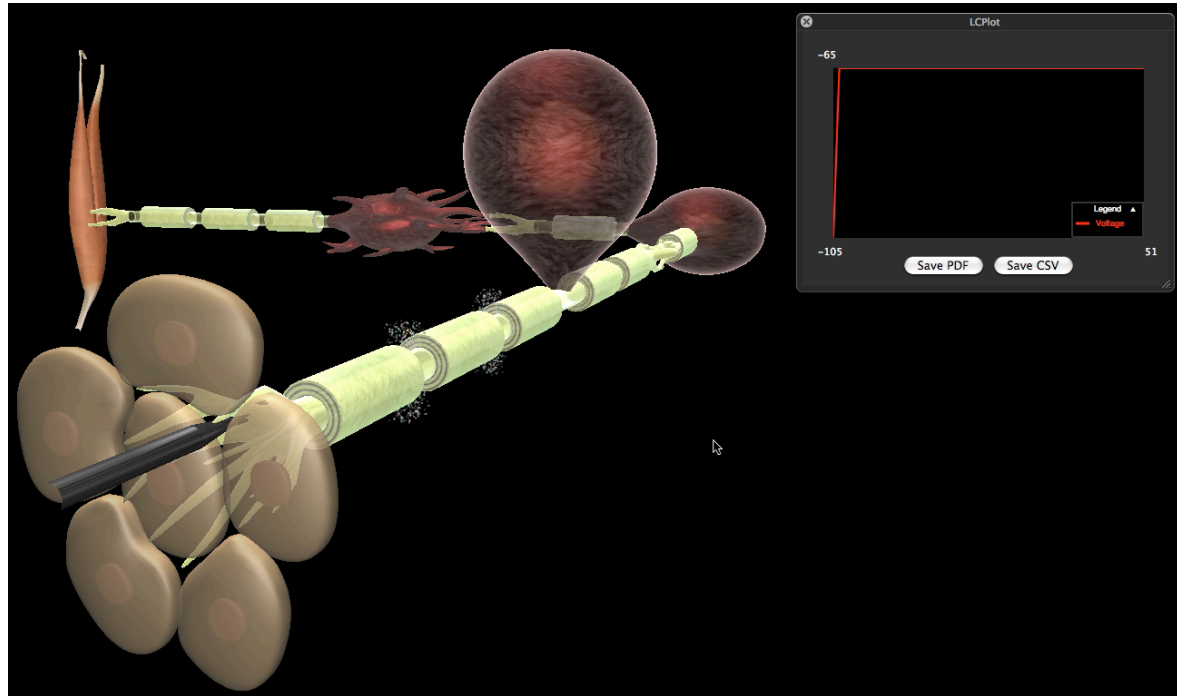


Point Pressure Calculation With Different Total Pressure of Body (140 mmHg)



Iman Yazdanbod, Summer 2011

# Reflex Arc



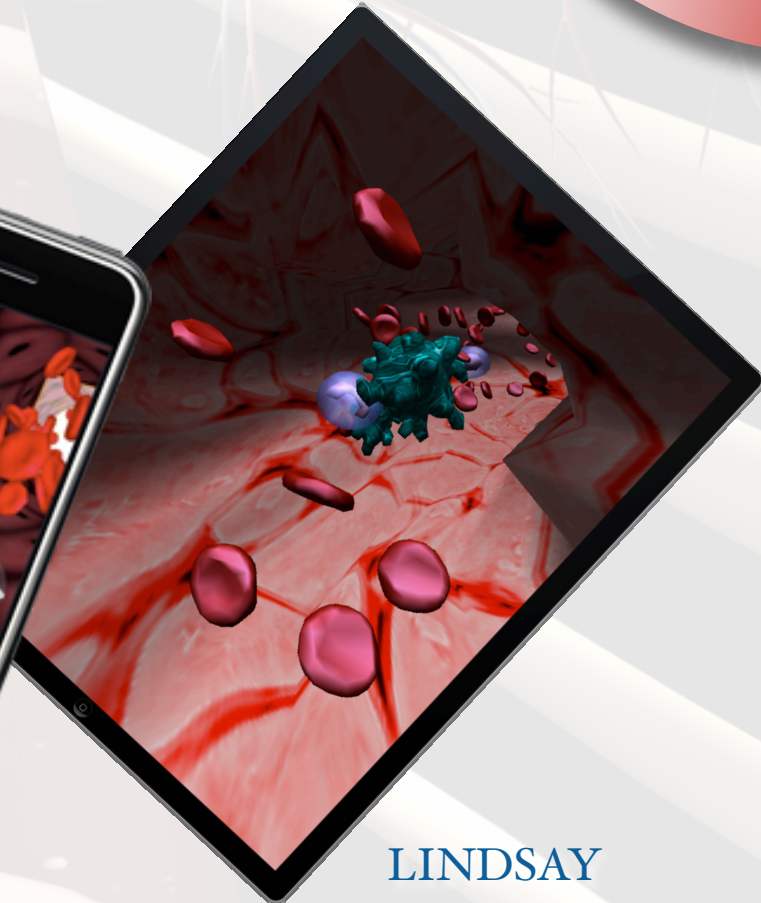
Tatiana Karaman, Summer 2011

# iLINDSAY Mobile

iPad Demo



LINDSAY  
BodyBrowser



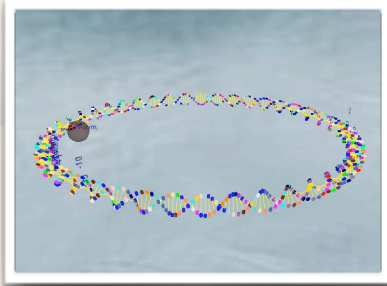
LINDSAY  
FlyThroughs

Afshin Esmaeili, 2011



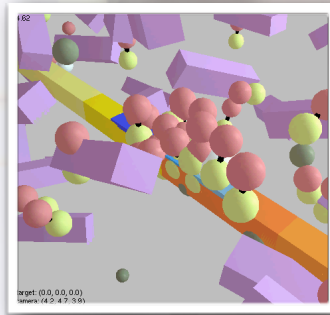


### Lactose Operon



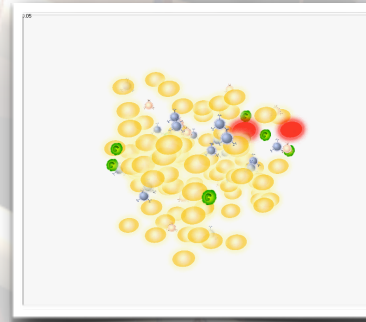
Ian Burleigh

### $\lambda$ Switch



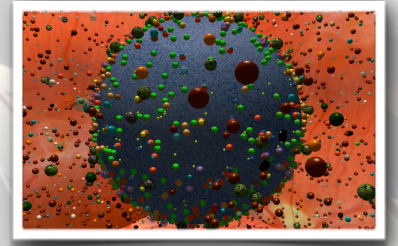
G. Tsui, A. Barbasiewicz

### Immune System



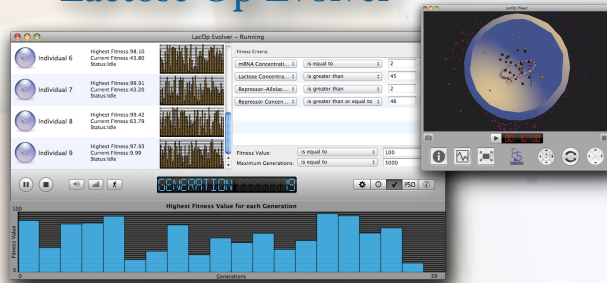
Karel Bergmann, Scott Steil

### Complement System



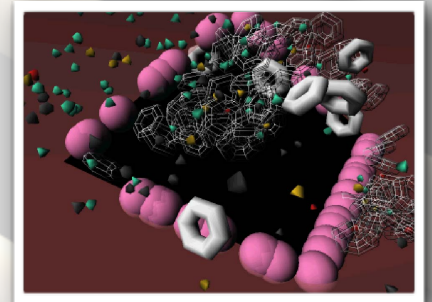
Carey Gingras, Dr. Rolando Feyt

### Lactose Op Evolver



Ryan Moniz

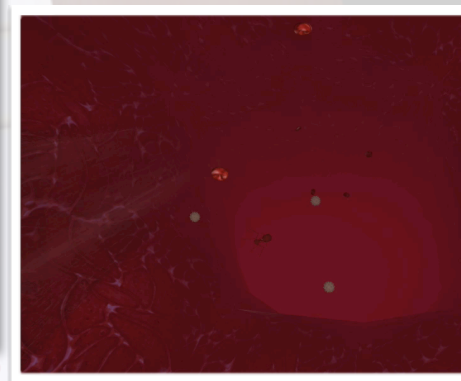
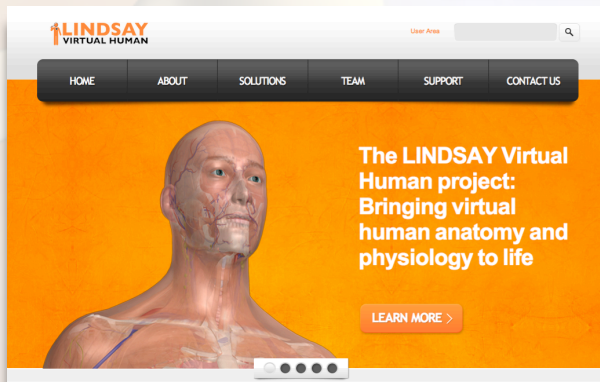
### Blood Clotting



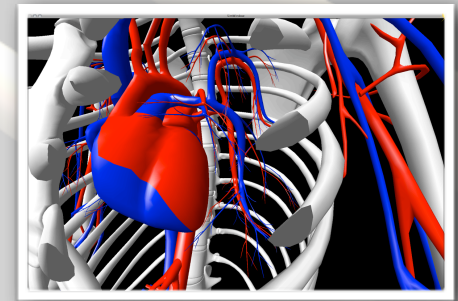
S. Chan, M. Templeton, G. Rowe, R. Degraaf, A. Punj



### LINDSAY



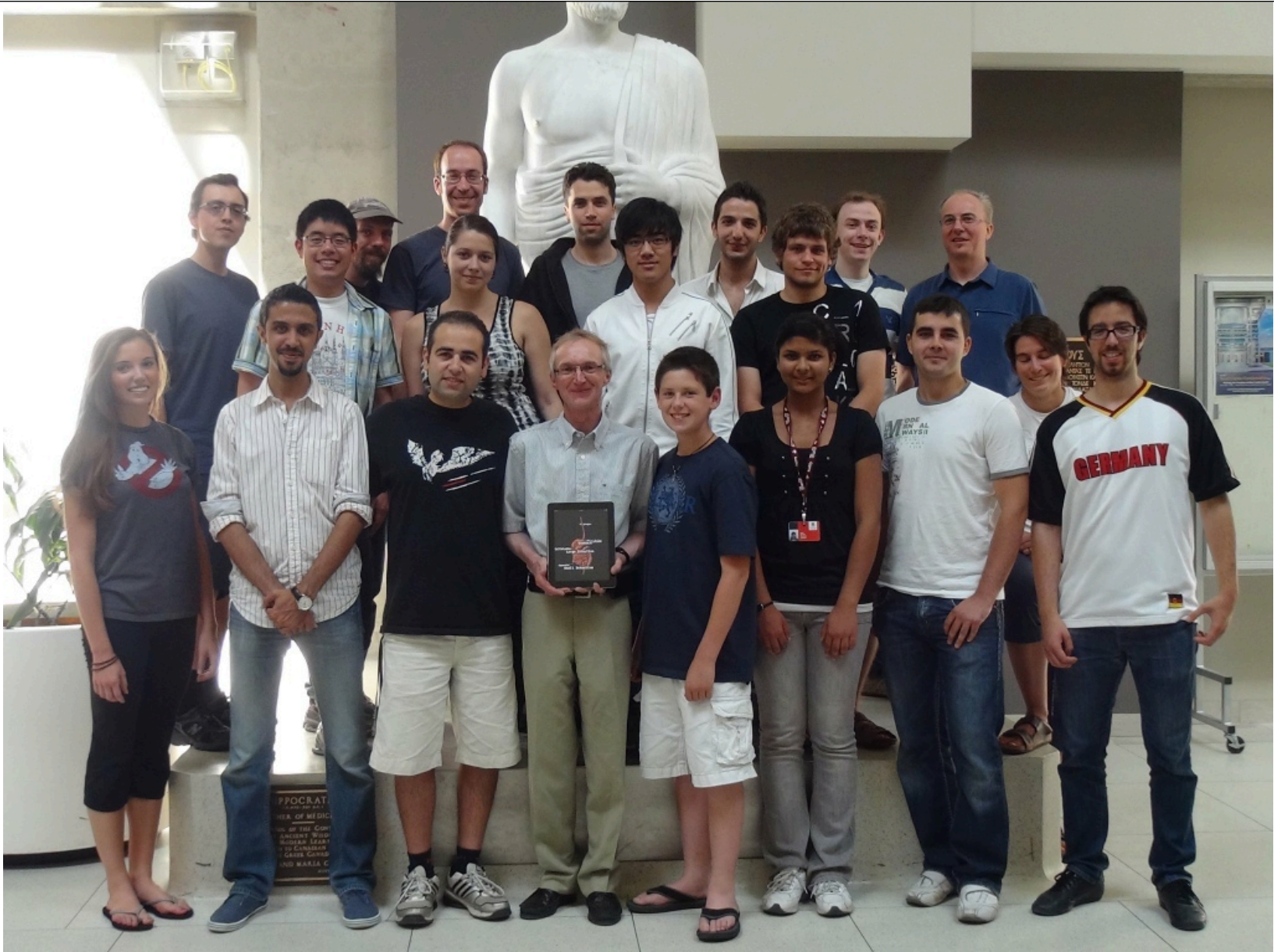
Scott Novakowski



Vlad Sarpe

### Creative Swarms





Back row: Jeff Wintersinger, Douglas Yuen, Scott Novakowski, Scott Steil, Tatiana Karaman, David Phillips, Isaac Lin, Iman Yazdanbod, Ivan Kryukov, Timothy Davison, Carey Gingras

Front row: Jessica Pow, Abbas Sarraf Shirazi, Afshin Esmaeili, Christian Jacob, Dennis Brown, Ayushi Gupta, Vladimir Sarpe, Heather Jamniczki, Stefan Marcus

Missing on photo: Sebastian von Mammen, Chenzhe Qian, Benedikt Hallgrimsson, Bruce Wright

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The LINDSAY Virtual Human project:  
Bringing virtual human anatomy and physiology to life

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