Digital Human: Simulation of the Heart and other Organs

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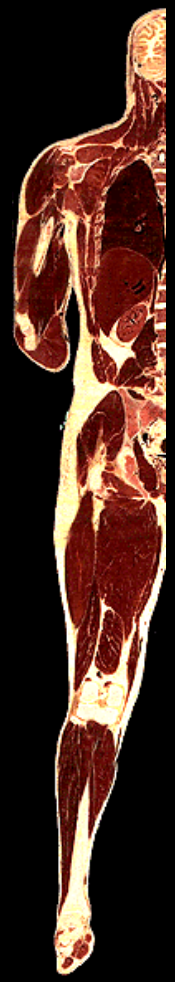
The 20+ Year Vision

- Imagine a “digital body double”
  - 3D image-based medical record
  - Includes diagnostic, pathologic, and other information
- Used for:
  - Diagnosis
  - Less invasive surgery-by-robot
  - Experimental treatments

- Digital Human Effort
  - Lead by the Federation of American Scientists

Digital Human Today: Imaging



- The Visible Human Project
  - 18,000 digitized sections of the body
    - Male: 1mm sections, released in 1994
    - Female: .33mm sections, released in 1995
  - Goals
    - study of human anatomy
    - testing medical imaging algorithms
  - Current applications:
    - educational, diagnostic, treatment planning, virtual reality, artistic, mathematical and industrial
    - Used by > 1,400 licensees in 42 countries

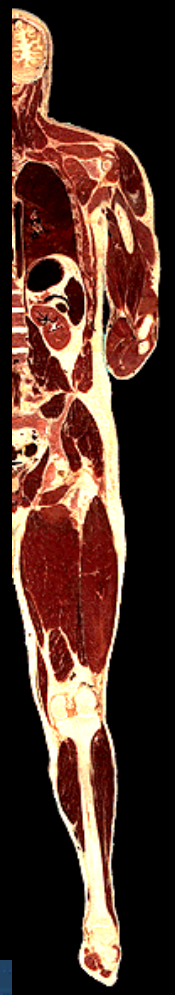
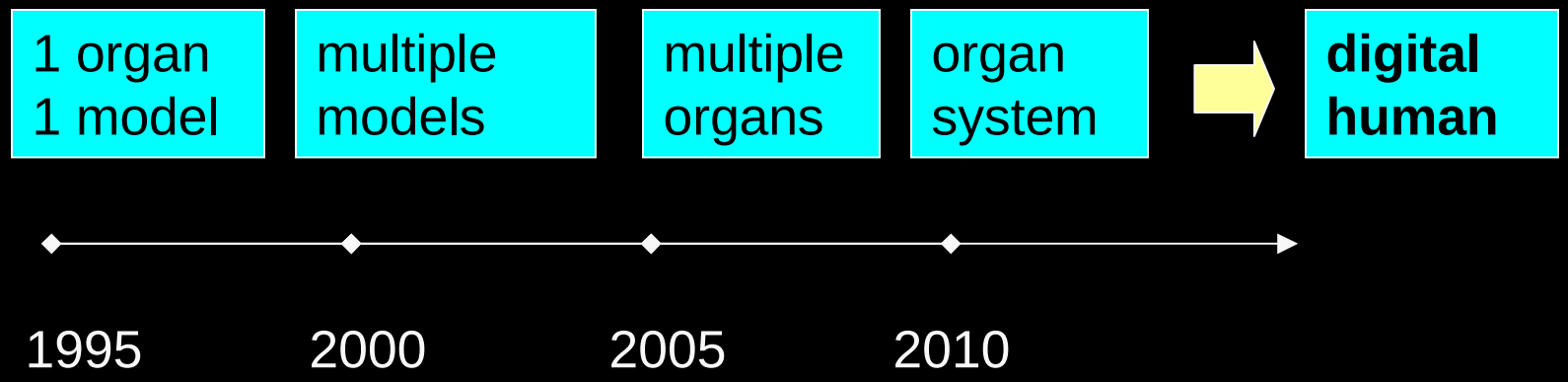


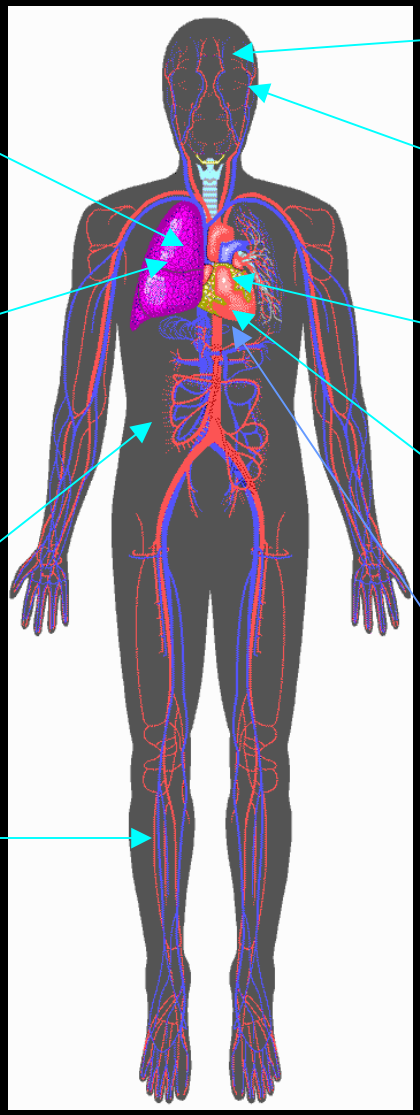
Image Source: www.madsci.org

Digital Human Roadmap



algorithms & mathematics	3D model construction	faster algorithms	coupled models
computer systems	scalable parallel implementations	faster computers	improved programmability

Organ Simulation



Brain
- Ellisman

Lung transport
- Vanderbilt

Cochlea
- Caltech, UM, UCB

Lung flow
- ORNL

Cardiac flow
- NYU,…

Kidney mesh generation
- Dartmouth

Cardiac cells/muscles
- SDSC, Auckland, UW, Utah,

Skeletal mesh generation

Electrocardiography
- Johns Hopkins,…

Just a few of the efforts at understanding and simulating parts of the human body

Immersed Boundaries within the Body

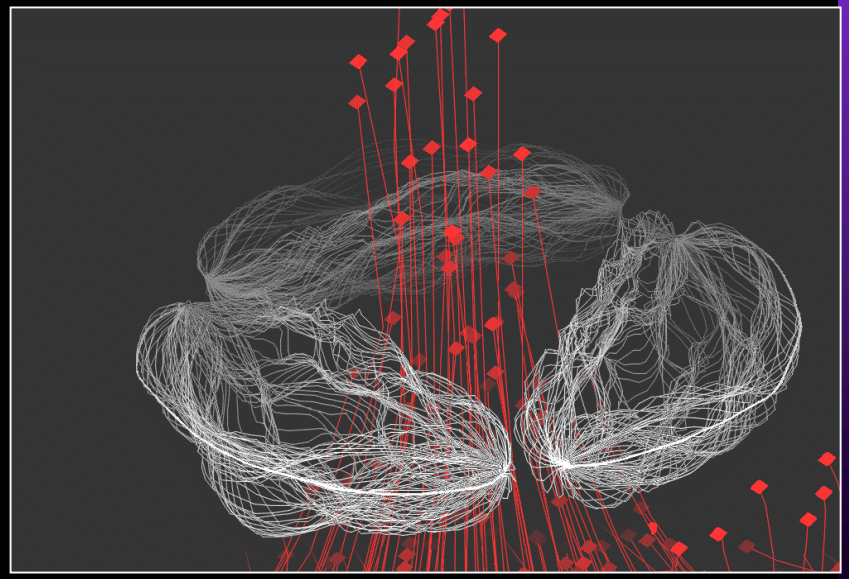
- Fluid flow within the body is one of the major challenges, e.g.,
  - Blood through the heart
  - Coagulation of platelets in clots
  - Effect of sounds waves on the inner ear
  - Movement of bacteria
- A key problem is modeling an elastic structure immersed in a fluid
  - Irregular moving boundaries
  - Wide range of scales
  - Vary by structure, connectivity, viscosity, external forced, internally-generated forces, etc.

Heart Simulation

Developed by Peskin and McQueen at NYU

- Ran on vector and shared memory machines
- 100 CPU hours on a Cray C90
- Models blood flow in the heart
- Immersed boundaries are individual muscle fibers

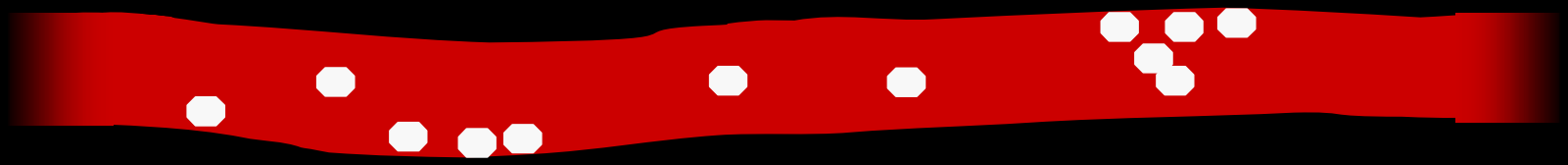
- Rules for contraction, valves, etc. included
- Applications:
  - Understanding structural abnormalities
  - Evaluating artificial heart valves
  - Eventually, artificial hearts



Source: www.psc.org

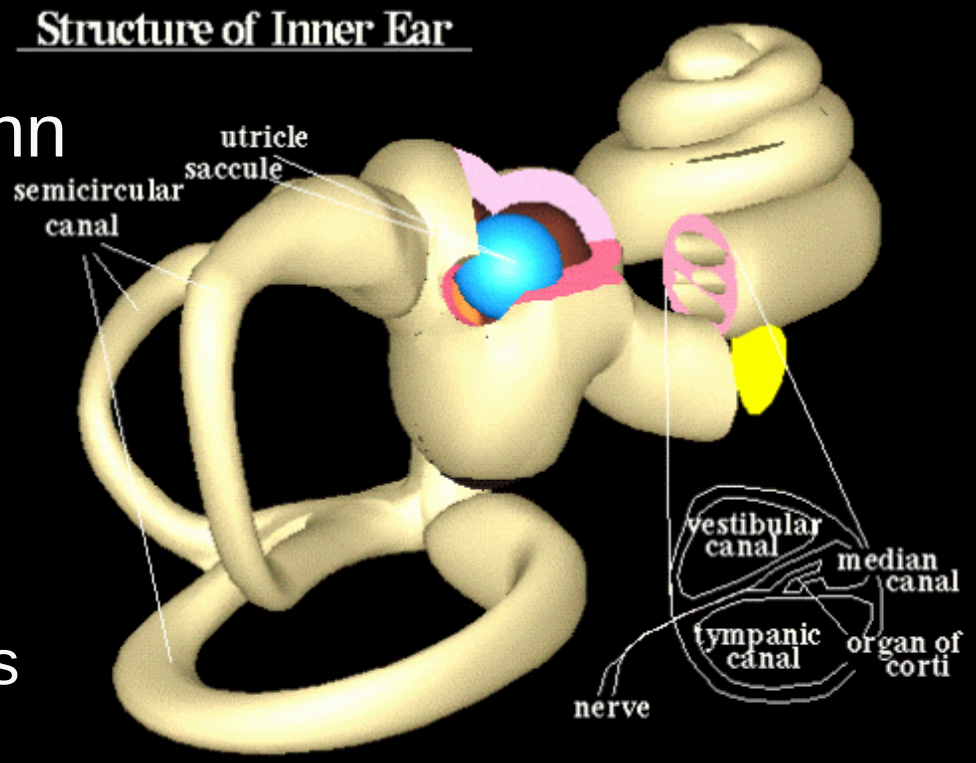
Platelet Coagulation

- Developed by Fogelson and Peskin
  - Simulation of blood clotting in 2D
  - Immersed boundaries are
    - Cell walls, represented by polygons
    - Artery walls
  - Rules added to simulate adhesion
  - For vector and shared memory machines
  - We did earlier work on this 2D problem in Split-C



Cochlea Simulation

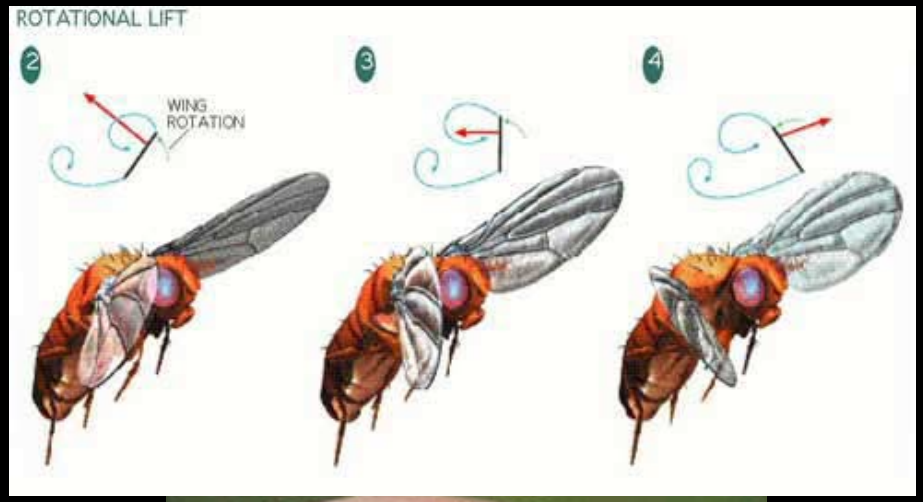
- Simulation by Givelberg and Bunn
  - In OpenMP
  - 18 hours on HP Superdome
- Embedded 2D structures are
  - Elastic membranes and shells



  - Simulates fluid-structure interactions due to incoming sound waves
  - Potential applications: design of cochlear implants

Insect Flight Simulation

- Work by on insect flight
  - Wings are immersed 2D structure
- Under development
  - UW (Wang) and NYU (Miller)
- Applications to
  - Insect robot design



Source: Dickenson, UCB

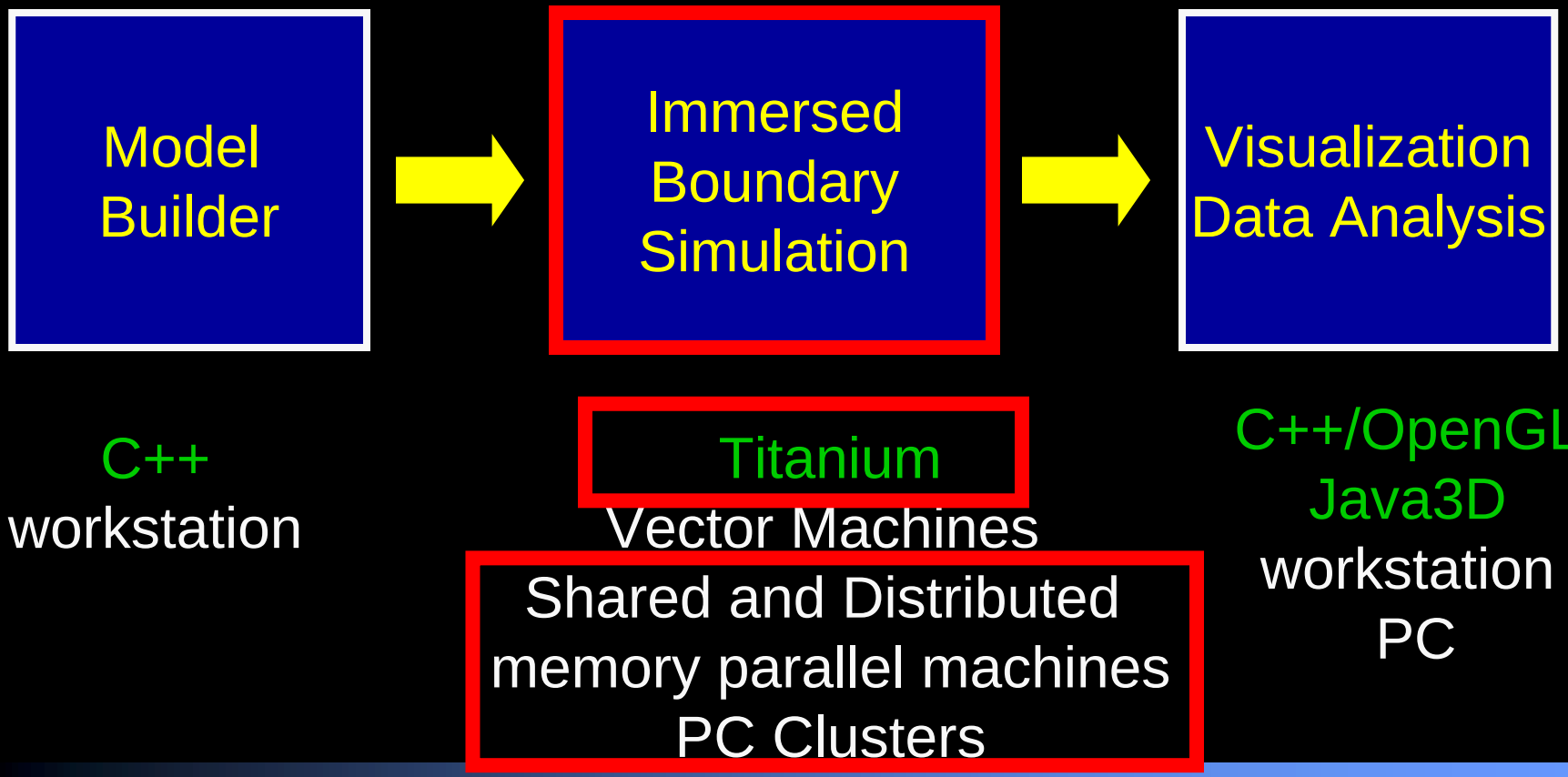
Small Animal Motion

- Simulation of small animal motion by Fauci, Dillon and other
  - Swimming of eels, sperm, and bacteria
  - Crawling motion of amoeba
  - Biofilms, such as plaque, with multiple micro-organisms
- Applications at a smaller scale
  - Molecular motors, fluctuations in DNA
  - Thermal properties may become important
    - Brownian motion extension by Kramer, RPI

Other Applications

- The immersed boundary method has also been used, or is being applied to
  - Flags and parachutes
  - Flagella
  - Embryo growth
  - Valveless pumping (E. Jung)
  - Paper making
  - Whirling instability of an elastic filament (S. Lim)
  - Flow in collapsible tubes (M. Rozar)
  - Flapping of a flexible filament in a flowing soap film (L. Zhu)
  - Deformation of red blood cells in shear flow (Eggleon and Popel)

Immersed Boundary Simulation Framework



Building 3D Models from Images

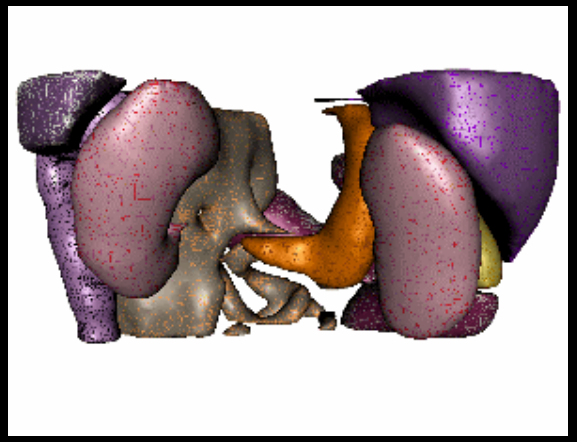
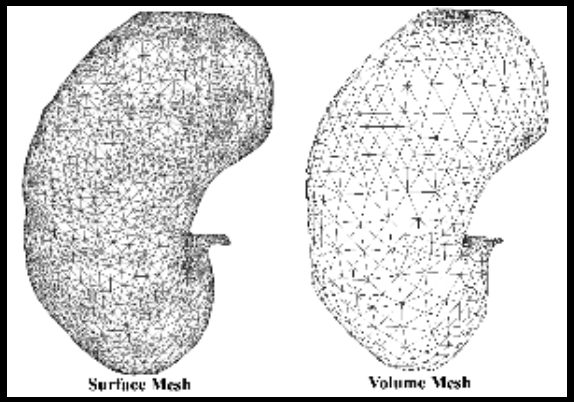


Image data from
- visible human
- MRI
- Laboratory experiments

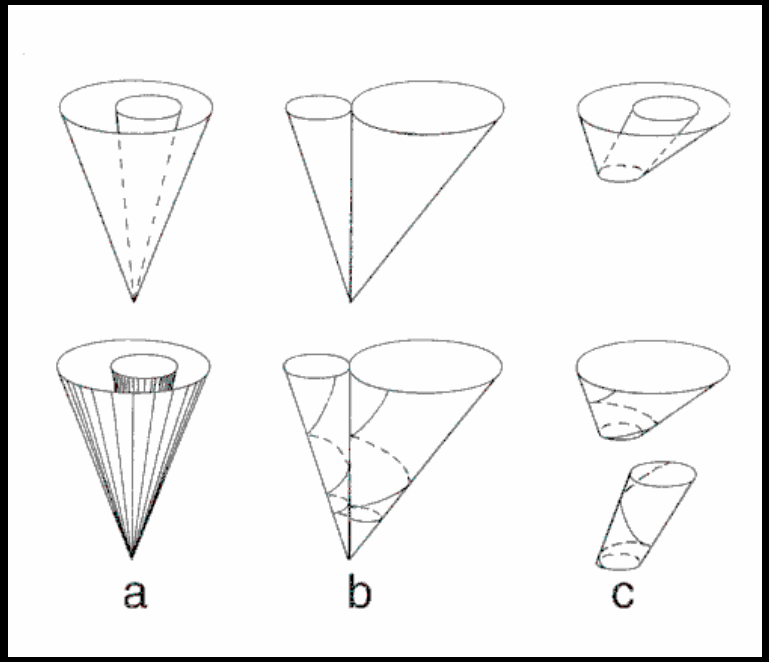


Automatic construction
- Surface mesh
- Volume mesh
- John Sullivan et al, WPI

Image source: John Sullivan et al, WPI

Heart Structure Model

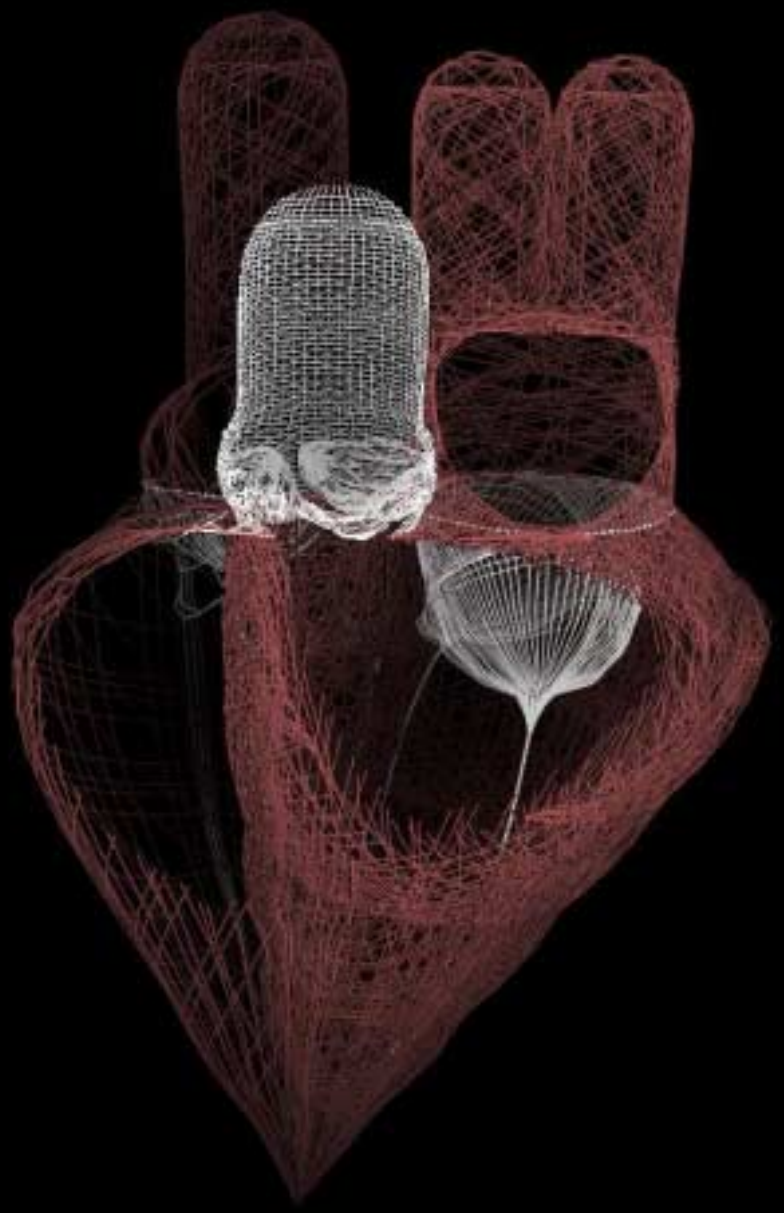
- Current model is based on three types of cones to construct ventricals
  - Outer/Inner layer
  - Right-Inner/Left-Outer
  - Left Cylinder layer



- Advantages: simple model
- Disadvantages: unrealistic and time-consuming to compute

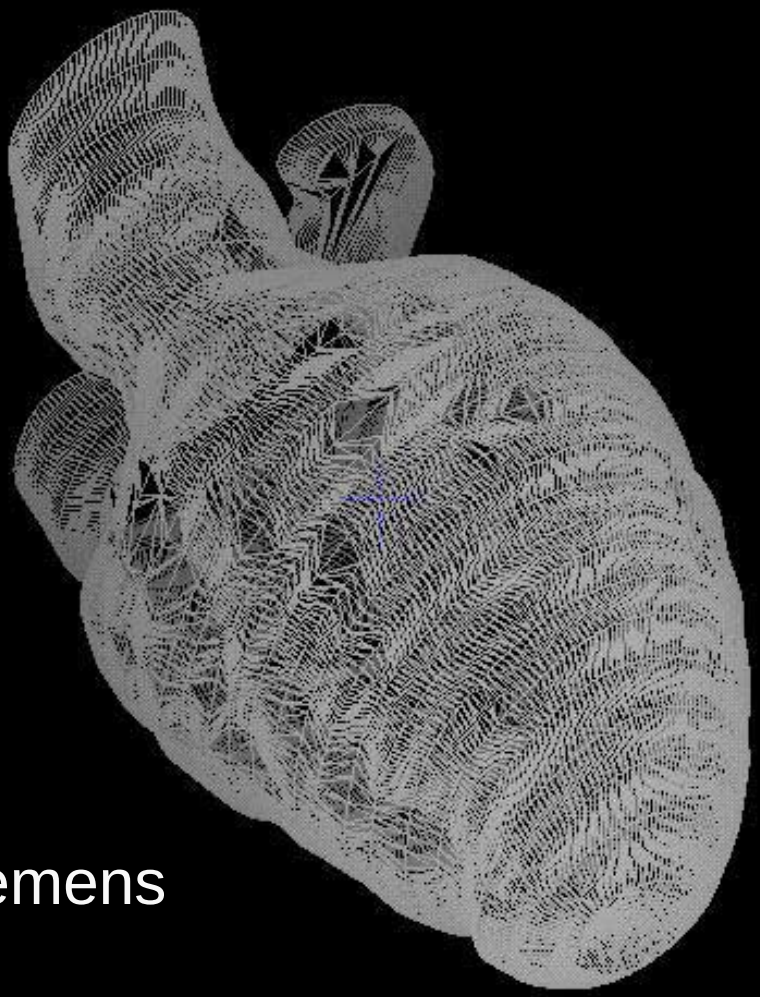
Old Heart Model

- Full structure shows cone shape
- Includes atria, ventricles, valves, and some arteries
- The rest of the circulatory system is modeled by sources and sinks



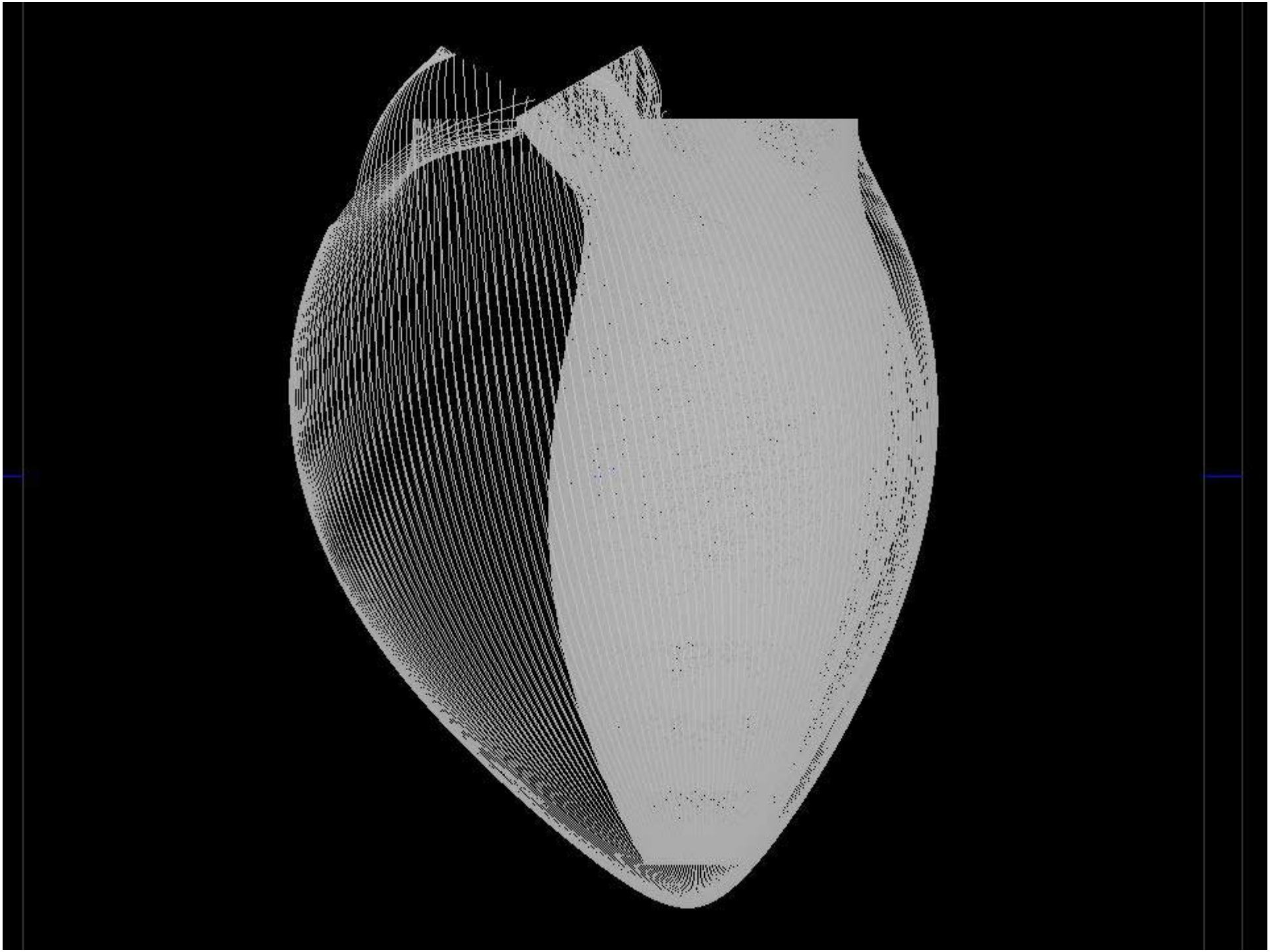
New Heart Model

- New model replaces the geodesics with triangulated surfaces
  - Based on CT scans from a healthy human.
  - Triangulated surface o left ventricle is shown



Work by:

- Peskin & McQueen, NYU
- Paragios & O'Donnell, Siemens
- Setserr, Cleveland Clinic

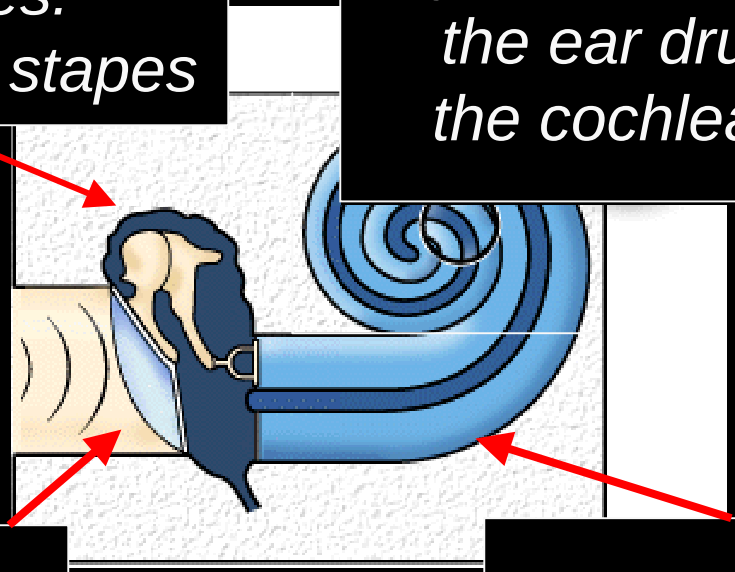


Structure of the Middle Ear

Sound Energy ➔ Cochlear Waves

Transmission of sound wave energy by the ossicles from the ear drum into the cochlear canal

The ossicles: malleus, incus, stapes

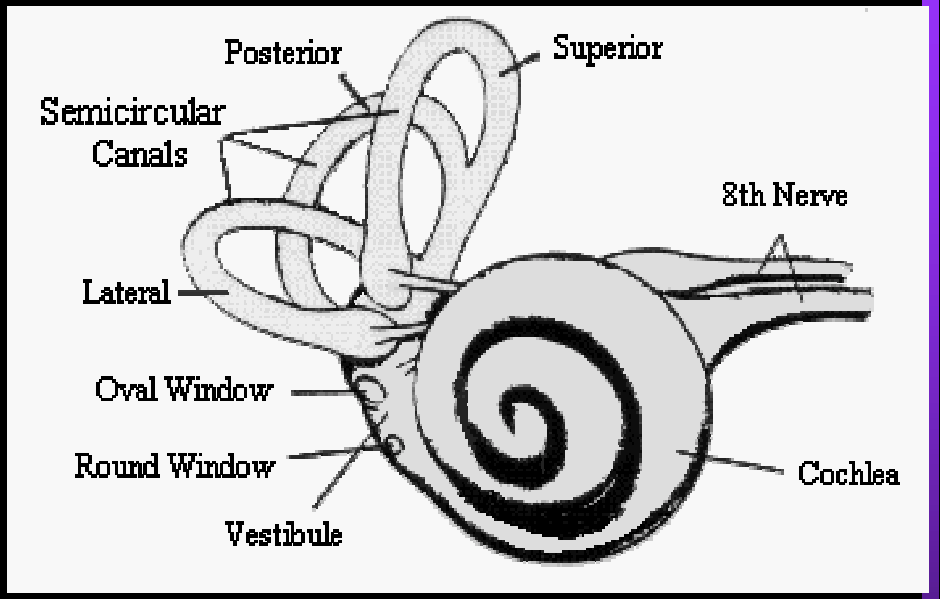


Ear drum

Cochlear canal

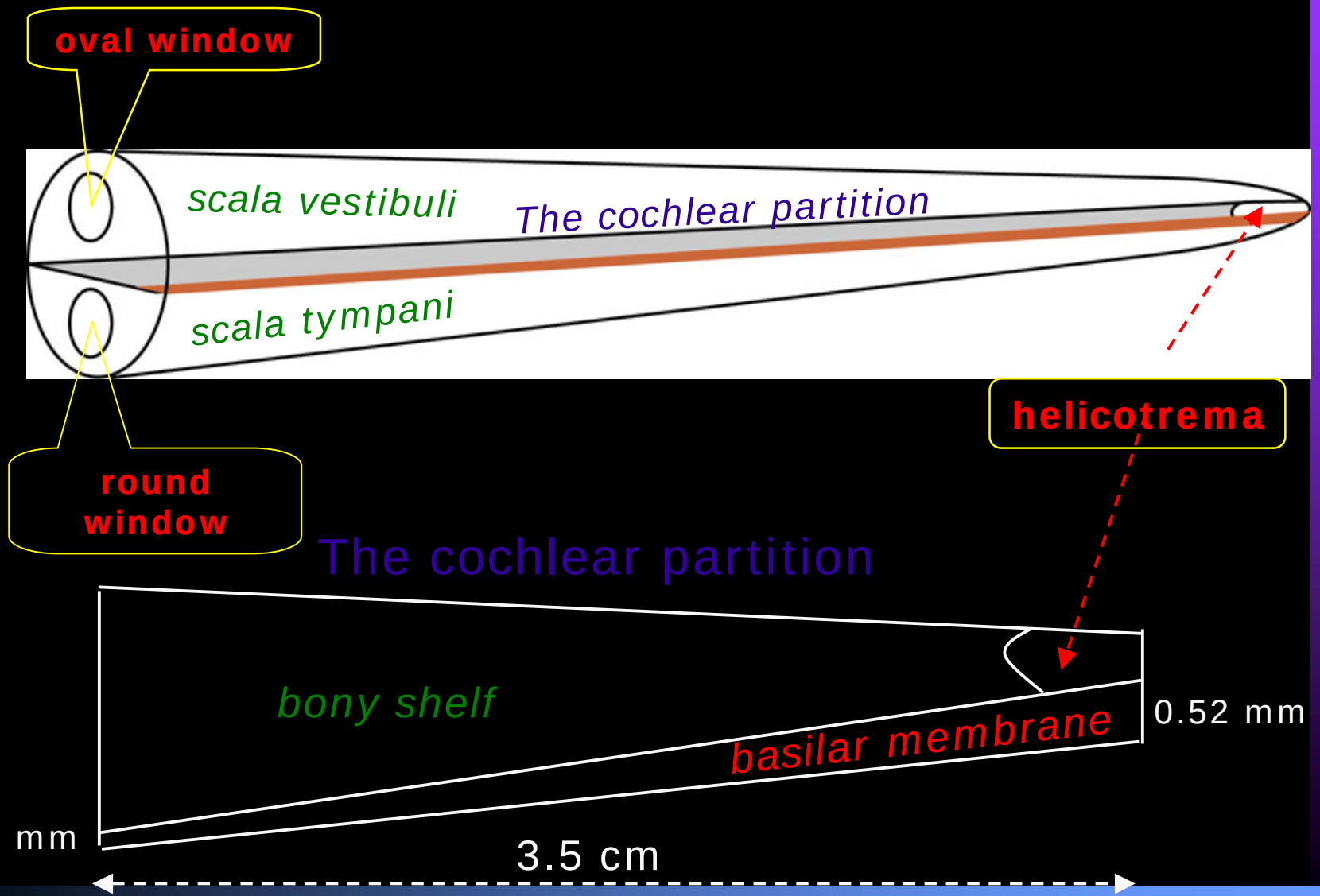
Cochlea and Semi-circular Canals

- The inner ear is a fluid-filled cavity containing the cochlea and the semi-circular canals
- Semi-circular canals responsible for balance
- The fluid is *incompressible* and *viscous*
- Input is from the stapes knocking on the oval window; the round window is covered by a membrane to conserve volume



1 cm

Schematic Description of the Cochlea



Apical Turn of the Cochlea

Immersed Boundary Equations

$$\begin{cases} \rho\left(\frac{\partial \mathbf{u}}{\partial t} + \mathbf{u}\cdot\nabla\mathbf{u}\right) = -\nabla p + \mu\nabla^2\mathbf{u} + \mathbf{F} \\ \nabla\cdot\mathbf{u} = 0 \end{cases}$$

$$\mathbf{F}(\mathbf{x},t) = \int \mathbf{f}(\mathbf{q},t)\,\delta(\mathbf{x}-\mathbf{X}(\mathbf{q},t))\,d\mathbf{q}$$

$$\begin{aligned} \frac{\partial \mathbf{X}}{\partial t} &= \mathbf{u}(\mathbf{X}(\mathbf{q},t),t) \\ &= \int \mathbf{u}(\mathbf{x},t)\,\delta(\mathbf{x}-\mathbf{X}(\mathbf{q},t))\,d\mathbf{x} \end{aligned}$$

$\mathbf{u}$, p, $\mathbf{F}$	fluid velocity, pressure, force
ρ, μ	fluid density, fluid viscosity
$\mathbf{f}$	the force applied by the immersed matter
$\mathbf{x}$	position of the fluid particle
$\mathbf{X}$	position of the immersed matter particle

First Order Immersed Boundary Method

Compute the force **f** the immersed material applies to the fluid.

Compute the force applied to the fluid grid:

$$\mathbf{F^n(x)} = \sum_{\mathbf{q}} \mathbf{f^n(q)} \delta_{\mathbf{h}}(\mathbf{x} - \mathbf{X^n(q)}) \Delta \mathbf{q}$$

Solve the Navier-Stokes equations:

$$\rho \left(\frac{\mathbf{u^{n+1}} - \mathbf{u^n}}{\Delta t} + \sum_{\alpha=1}^{3} u_\alpha^n D_\alpha^{\pm} \mathbf{u^n} \right) = -\mathbf{D}^0 p^{n+1} + \mu \sum_{\alpha=1}^{3} D_\alpha^+ D_\alpha^- \mathbf{u^{n+1}} + \mathbf{f^n}$$

$$\mathbf{D}^0 \cdot \mathbf{u^{n+1}} = 0$$

Move the material:

$$\mathbf{X^{n+1}(q)} = \mathbf{X^n(q)} + \Delta \mathbf{t} \sum_{\mathbf{x}} \mathbf{u^{n+1}(x)} \delta_{\mathbf{h}}(\mathbf{x} - \mathbf{X(q)}) \mathbf{h^3}$$

Immersed Boundary Method

Combines Lagrangean and Eulerian Components

Navier-Stokes equations discretized on a periodic rectangular 3-d grid

viscous in-compressible fluid

Hooke's spring law Discretized on a 1-d grid

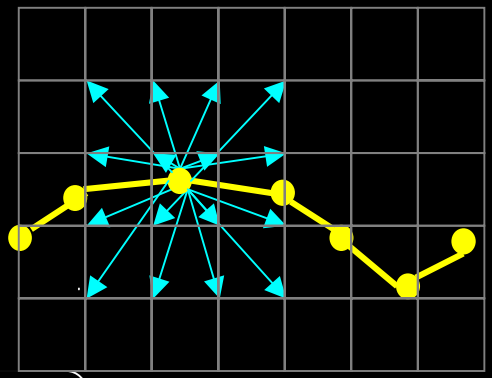
elastic shell

Fourth order PDE discretized on a 2-d grid

Immersed Boundary Method Structure

4 steps in each timestep

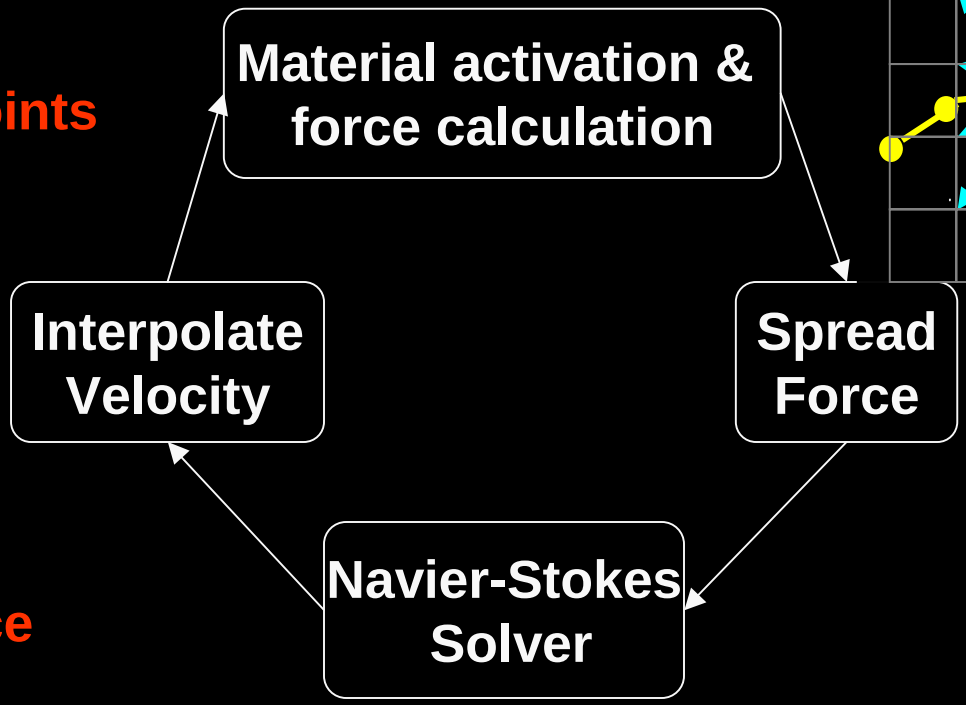
2D Dirac Delta Function



Material Points

Interaction

Fluid Lattice



Challenges to Parallelization

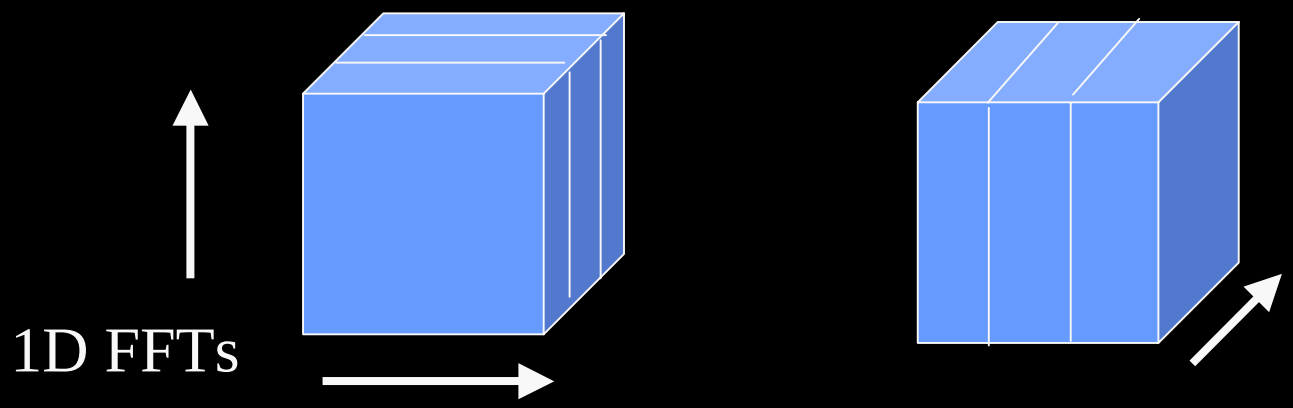
- Irregular material points need to interact with regular fluid lattice.
  - Trade-off between load balancing of material and minimizing communication
    - Efficient “scatter-gather” across processors
- Need a scalable fluid solver
  - Currently based on 3D FFT
    - Requires an all-to-all “transpose”
  - May try to use multigrid in the future
    - Adaptive Mesh Refinement would help

Parallel Algorithm

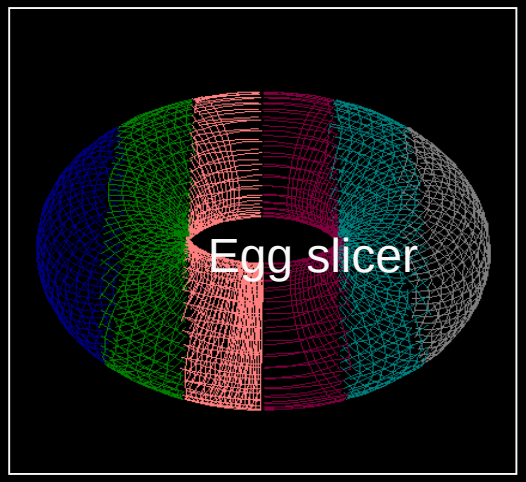
- Immersed materials are described by a hierarchy of 1d or 2d arrays
- Grids in current code
  - Reside on a single processor
  - Previous (and possibly future) versions may split them
- The 3D fluid grid uses a 1D distribution (slabs)
- Interactions between the fluid and material structures requires inter-processor communication.
- Special data structures are maintained for efficient communication.

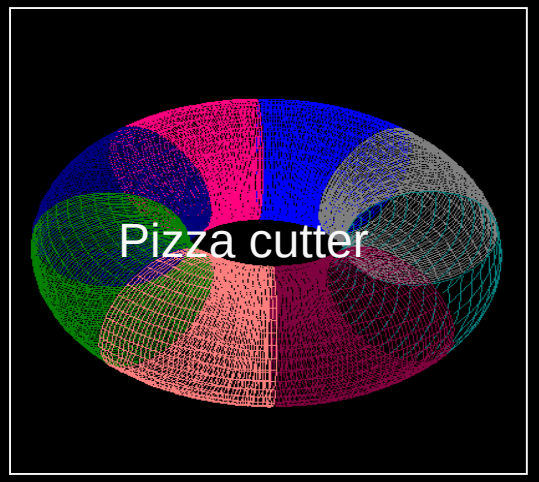
Fluid Solver

- The incompressible requires an elliptic solver
  - High communication demand
  - Information propagates across domain
- FFT-based solver divides domain into slabs
  - Transposes before last direction of FFT
  - Would like to use finer decomposition

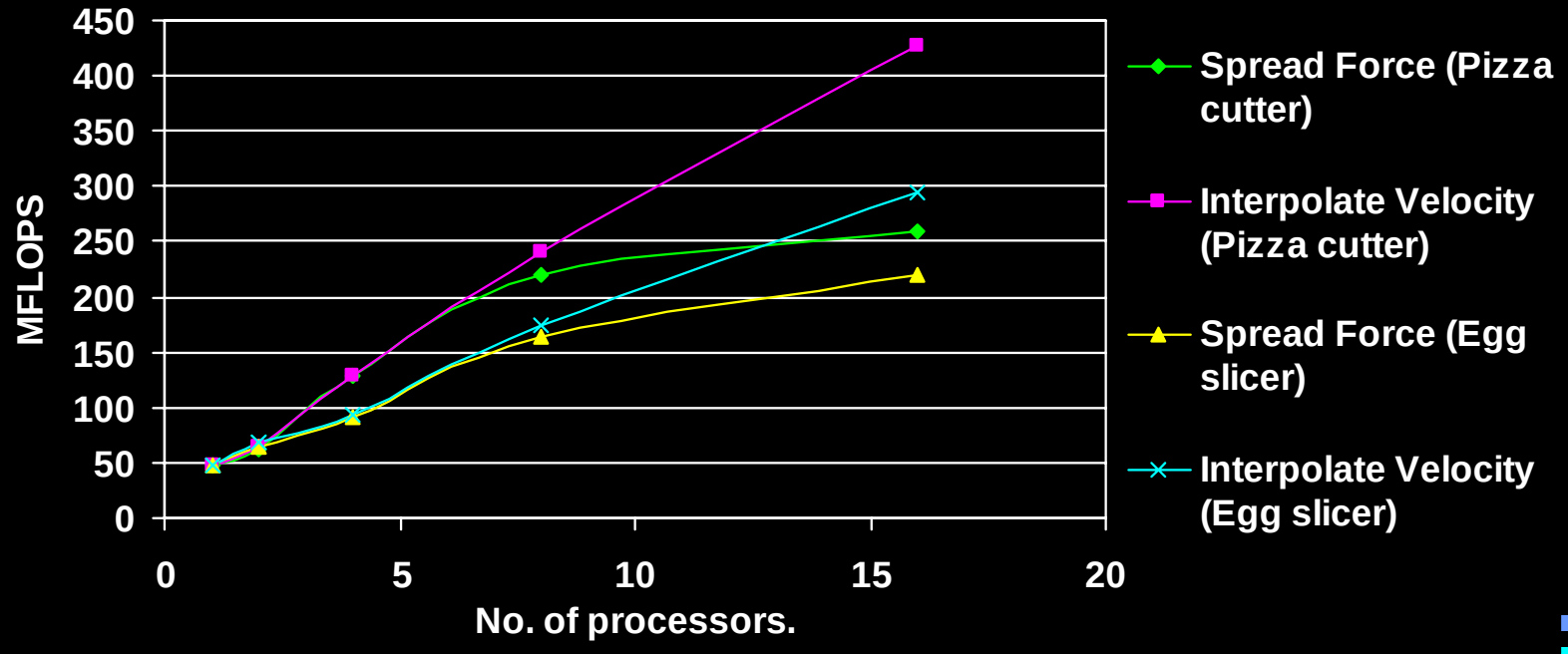


Load Balancing



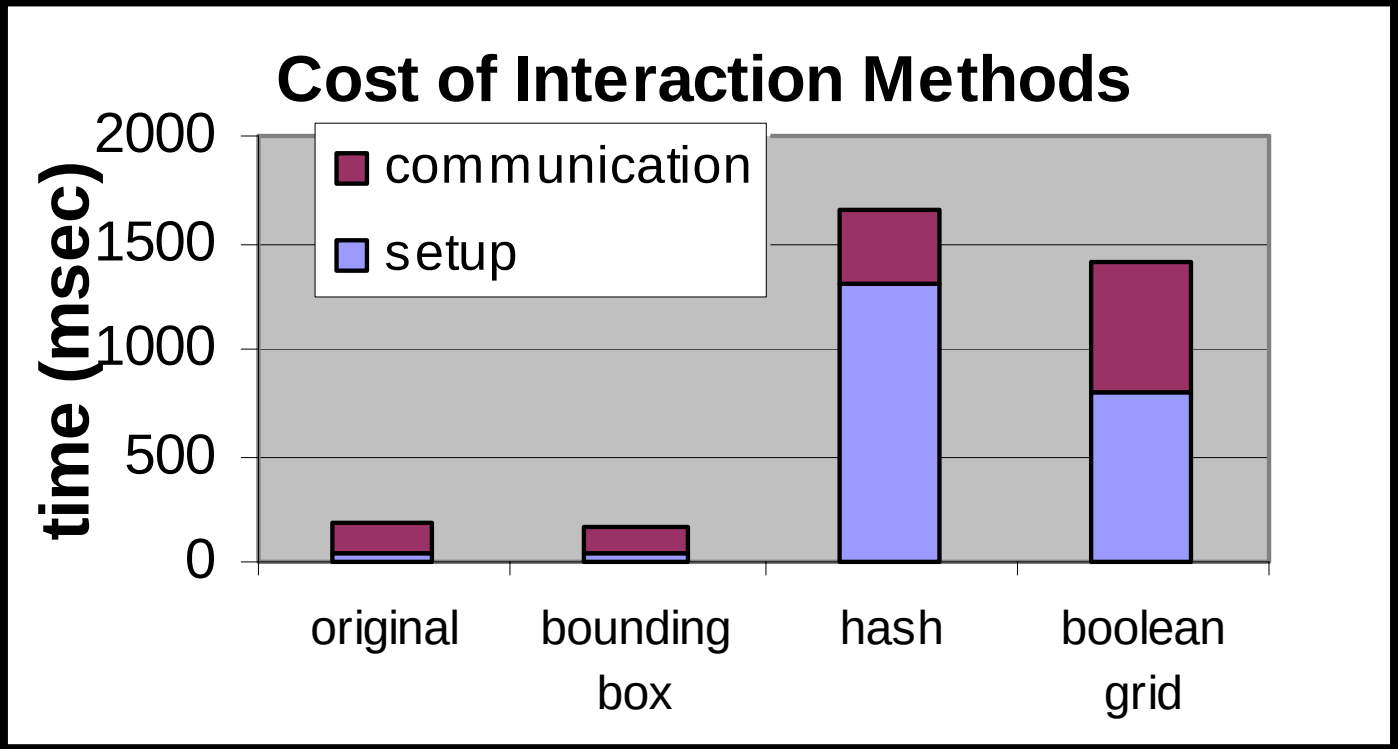


Fluid grid is divided in slabs for 3D FFT

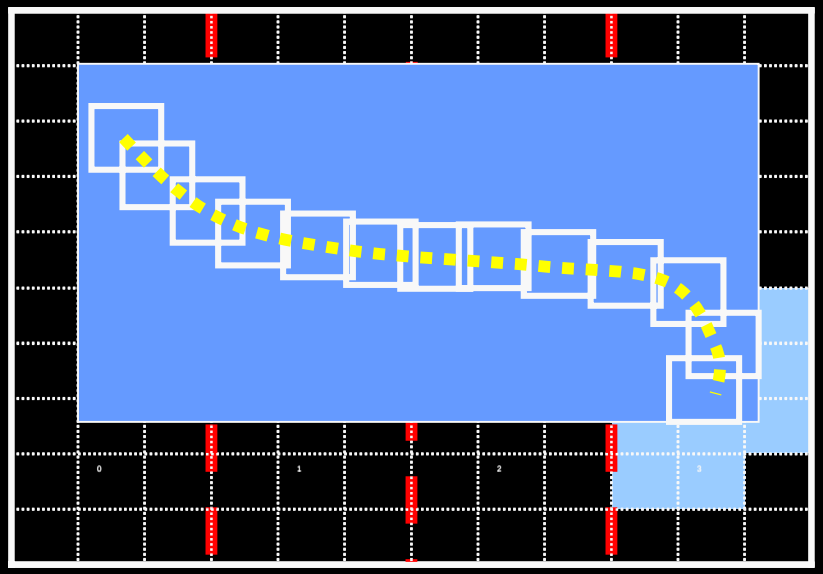


Data Structures for Interaction

- Experimented with several method
- Bounding box is the best (although it sends significantly more data than necessary)

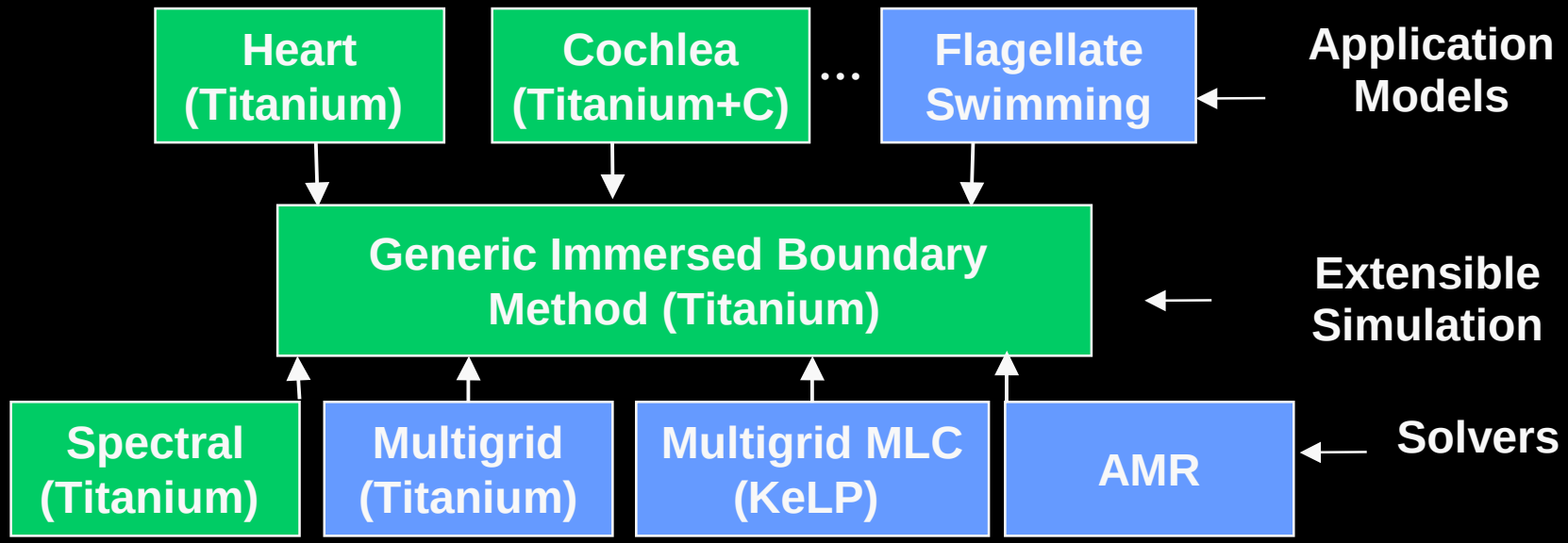


Data Structures for Interaction



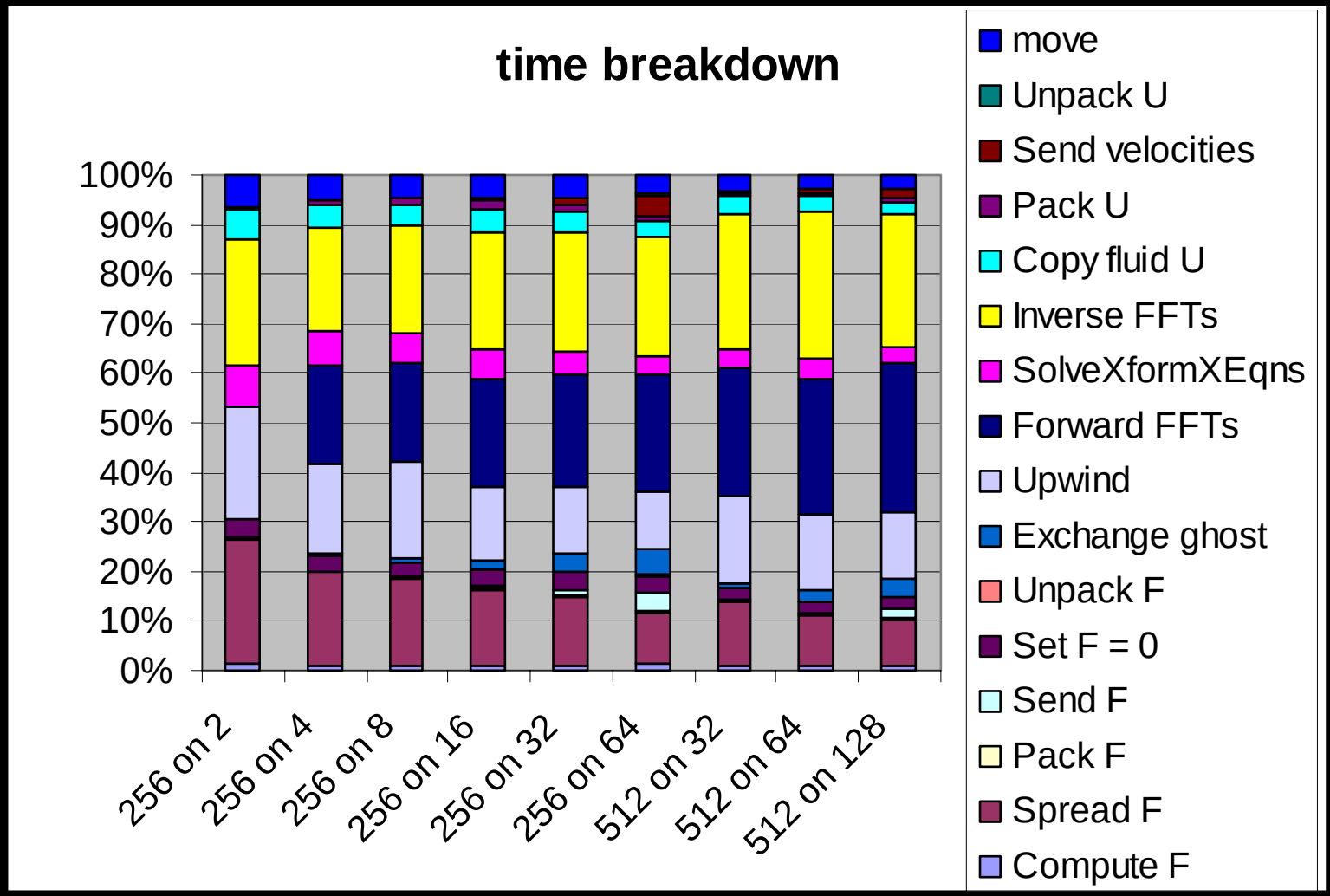
- Bounding box computes only low/high
- Logical grid of 4x4x4 cubes used to balance cost of communication and setup
- Communication aggregation also done

Software Architecture



- Can add new models by extending material points
- Uses Java inheritance for simplicity

Performance Analysis



Tools for High Performance

Challenges to parallel simulation of a digital human are generic

- Parallel machines are too hard to program
  - Users “left behind” with each new major generation
- Efficiency is too low
  - Even after a large programming effort
  - Single digit efficiency numbers are common
- Approach
  - Titanium: A modern (Java-based) language that provides performance transparency
  - BeBOP: Self-tuning scientific kernels
  - GASNet: Portable fast communication

Titanium Overview

Object-oriented language based on Java with:

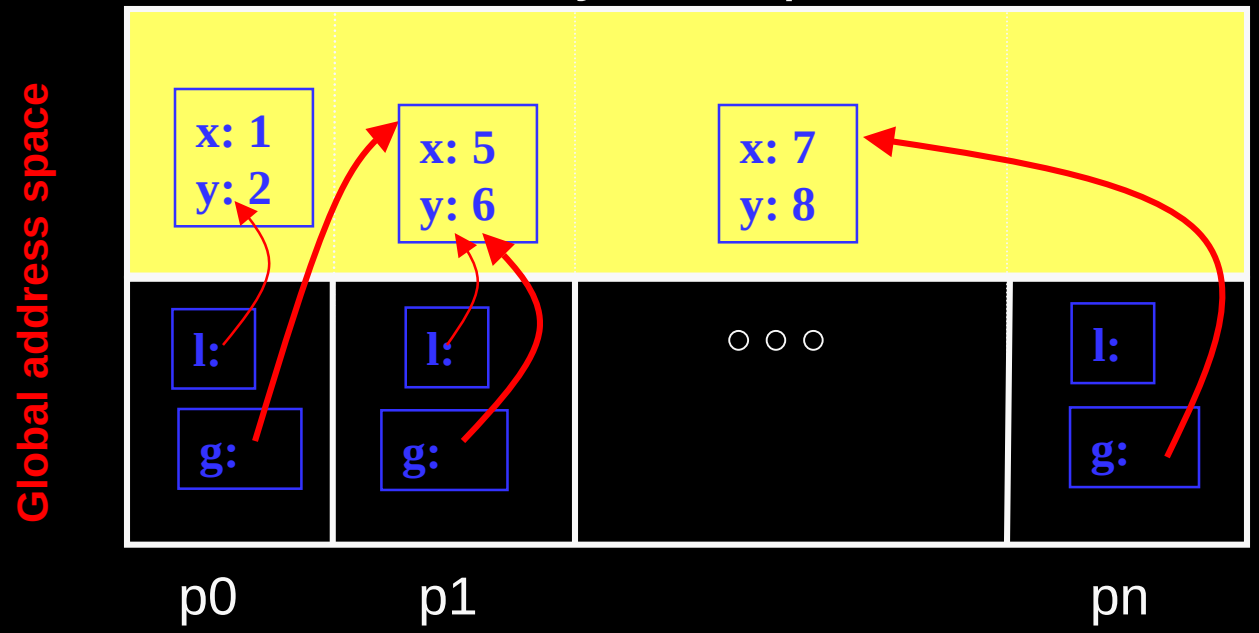
- Scalable parallelism
  - Single Program Multiple Data (SPMD) model of parallelism, 1 thread per processor
- Global address space
  - Processors can read/write memory on other processor
  - Pointer dereference can cause communication
- Intermediate point between message passing and shared memory

Language Support for Performance

- Multidimensional arrays
  - Contiguous storage
  - Support for sub-array operations without copying
- Support for small objects
  - E.g., complex numbers
  - Called “immutables” in Titanium
  - Sometimes called “value” classes
- Semi-automatic memory management
  - Create named “regions” for new and delete
  - Avoids distributed garbage collection
- Optimizations on parallel code
  - Communication and memory hierarchies

Global Address Space Languages

- Titanium is similar to UPC and Co-Array Fortran
- Globally shared address space is partitioned
- References (pointers) are either local or global (meaning possibly remote)
- Distributed arrays and pointer-based structures

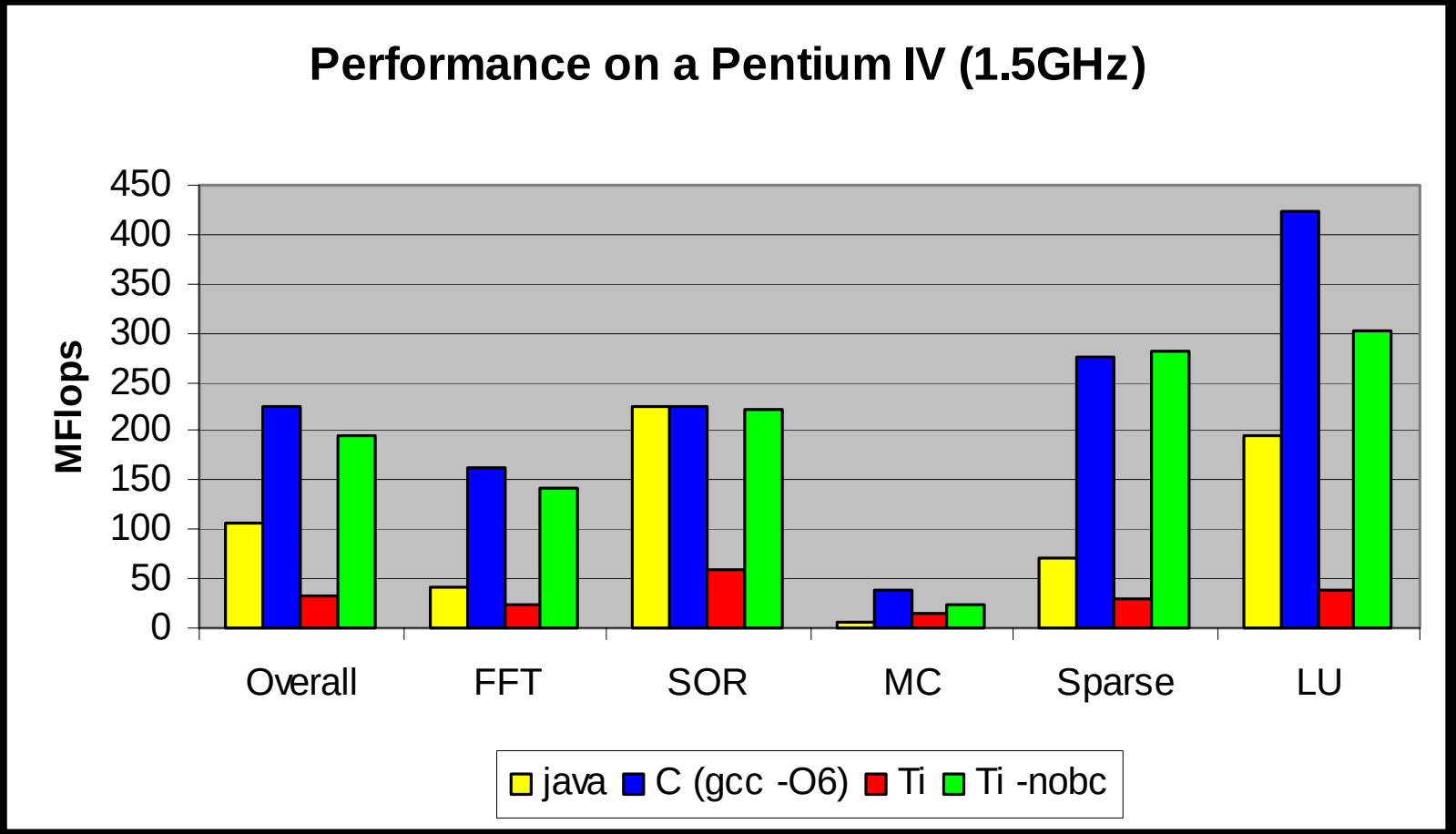


Object heaps are shared

Program stacks are private

- Static parallelism (like MPI)

Performance of Titanium Compiler



Titanium Research Problems

- Analysis of explicitly parallel code
- Optimizations for
  - Memory hierarchies
  - Communication (overlap and aggregation)
  - Synchronization
- Dynamic as well as static optimizations
  - For sparse and unstructured data
  - Extensible language (compiler support for scientific data structures)
- Lightweight one-sided communication
  - Joint with UPC group
  - GASNet layer

Semantics: Sequential Consistency

- When compiling sequential programs:

```
x = expr1;
y = expr2;
```

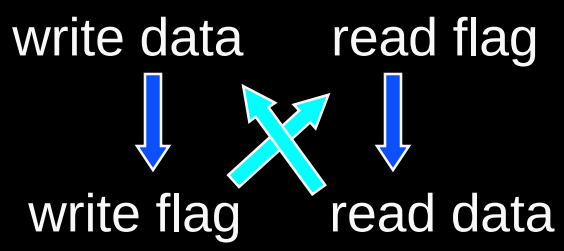
```
y = expr2;
x = expr1;
```

  Valid if y not in expr1 and x not in expr2 (roughly)
- When compiling parallel code, not sufficient test.

```
Initially flag = data = 0
Proc A          Proc B
data = 1;       while (flag!=1);
flag = 1;       ... = ...data...;
```

Cycle Detection: Analysis Problem

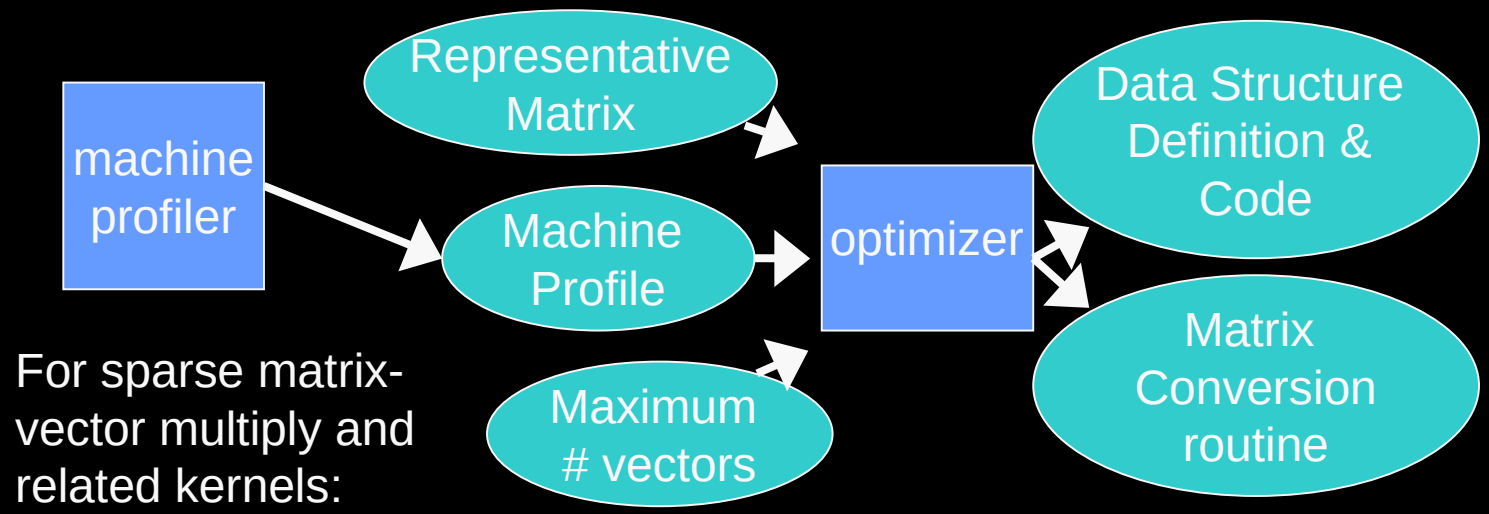
- Processors define a “program order” on accesses from the same thread
  - ⟶ P is the union of these total orders
- Memory system define an “access order” on accesses to the same variable
  - ⟶ A is access order (read/write & write/write pairs)



- A violation of sequential consistency is cycle in P U A.
- Intuition: time cannot flow backwards.

Automatic Performance Tuning

- Problem: low single-processor performance
  - 100s of arithmetic operations per memory operation
  - Complex processors and memory systems are challenging
  - Techniques like tiling help, but parameters are hard to find
- Solution: let computers do automatic tuning
  - FFTW, Atlas (dense linear algebra), Titanium for multigrid
  - BeBOP: sparse matrix kernels, optimizations depend on matrix

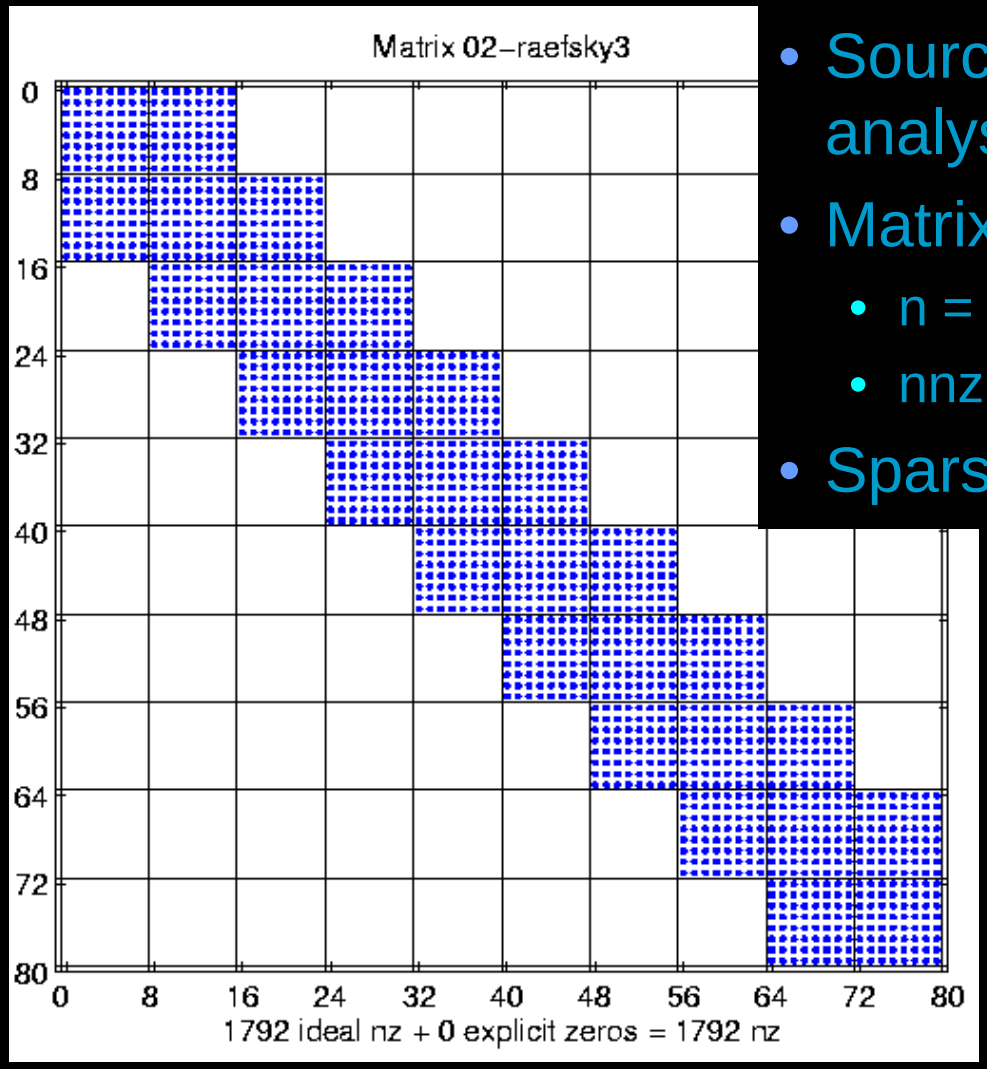


For sparse matrix-vector multiply and related kernels:

Summary of Optimizations

- Optimizations for sparse matrix-vector multiply
  - **Register blocking**: up to **4x**
  - **Variable block splitting**: **2.1x**
  - **Diagonals**: **2x**
  - **Reordering** to create dense structure + **splitting**: **2x**
  - **Symmetry**: **2.8x**
  - **Cache blocking**: **2.2x**
  - **Multiple vectors (SpMM)**: **7x**
  - And combinations…
- Sparse triangular solve
  - Hybrid sparse/dense data structure: **1.8x**
- Higher-level kernels
  - **AA^T*x**, A^TA*x: **4x**
  - **A^2*x**: **2x**

Example: The Difficulty of Tuning

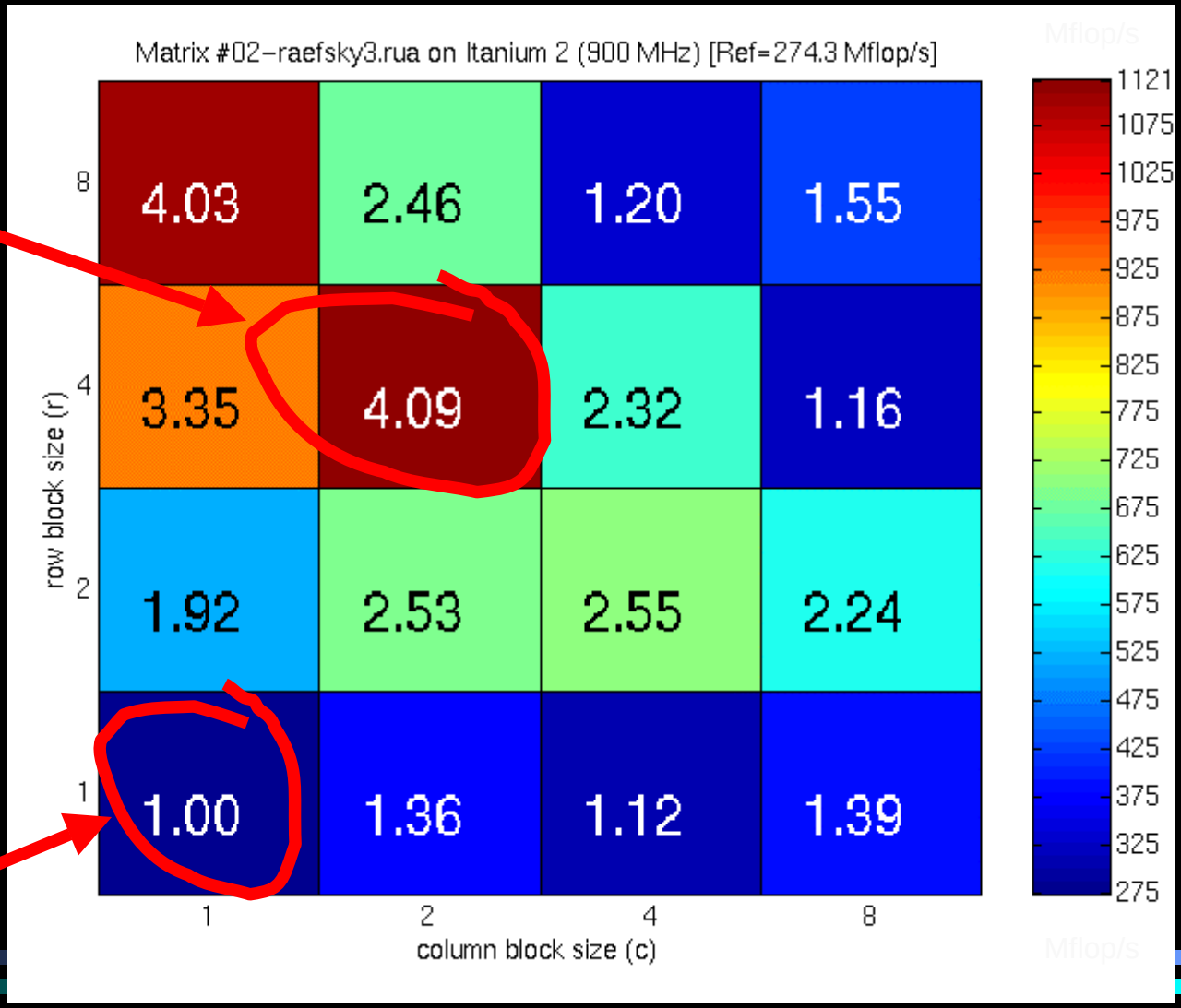


- Source: NASA structural analysis problem
- Matrix:
  - n = 21216
  - nnz = 1.5 M
- Sparse matrix-vector multiply

- Register blocking: store each block contiguously with a single index
- Use 8x8 blocks to math structure, right?

Speedups from Blocking on Itanium 2

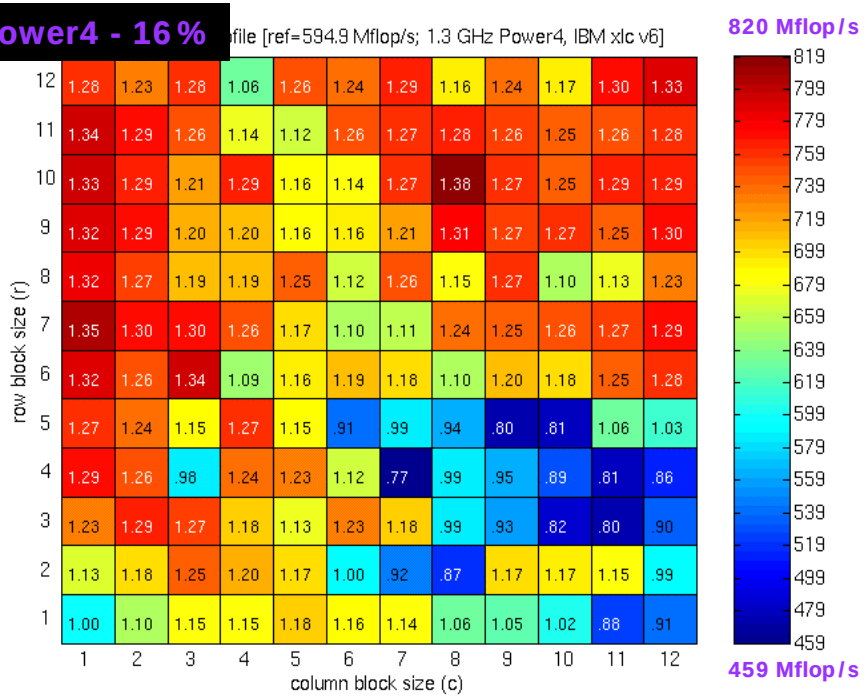
The “natural” block size is far from optimal: search for best.



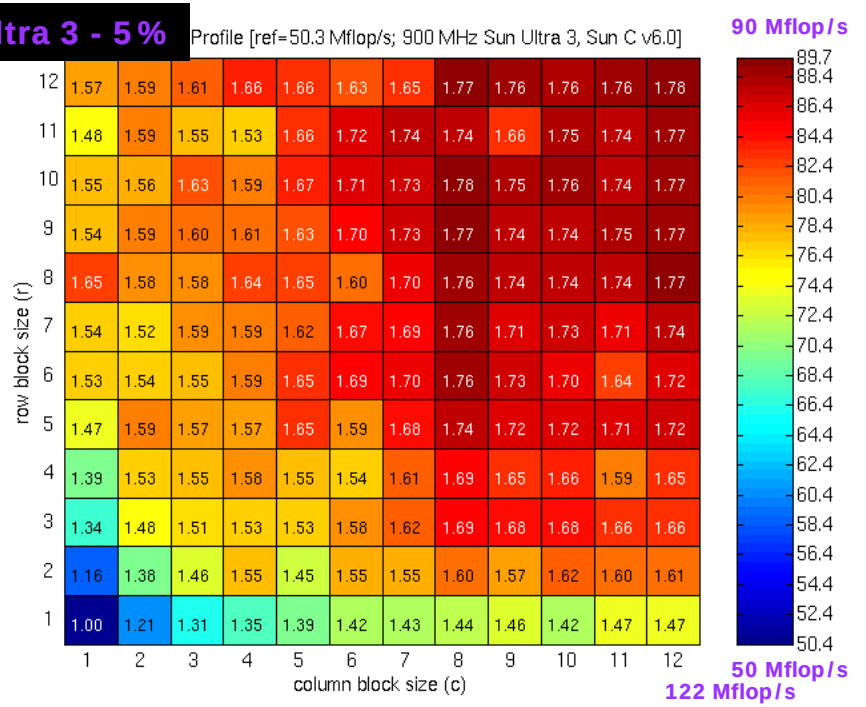
Best: 4x2

Reference

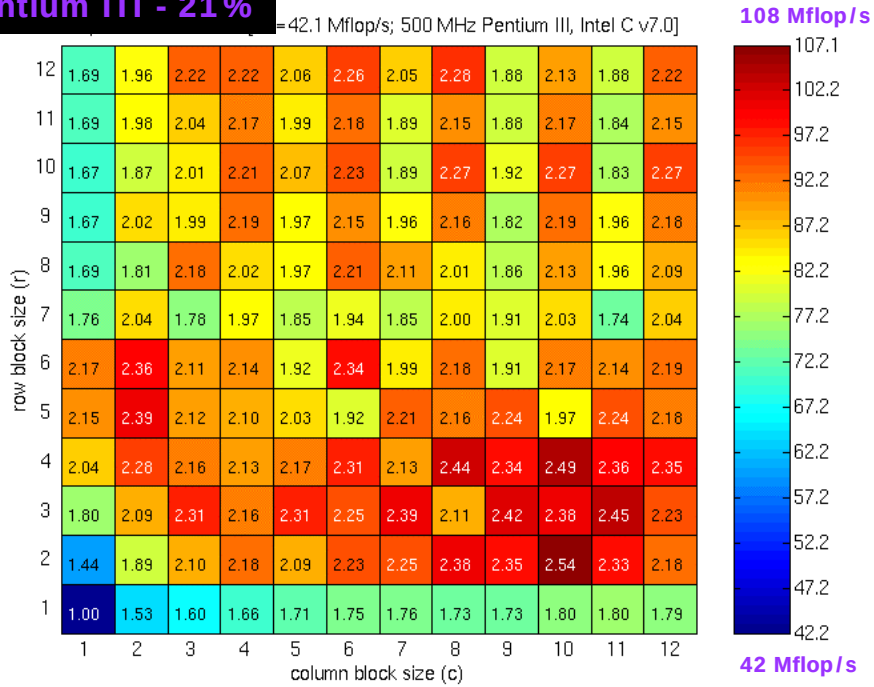
Power4 - 16%



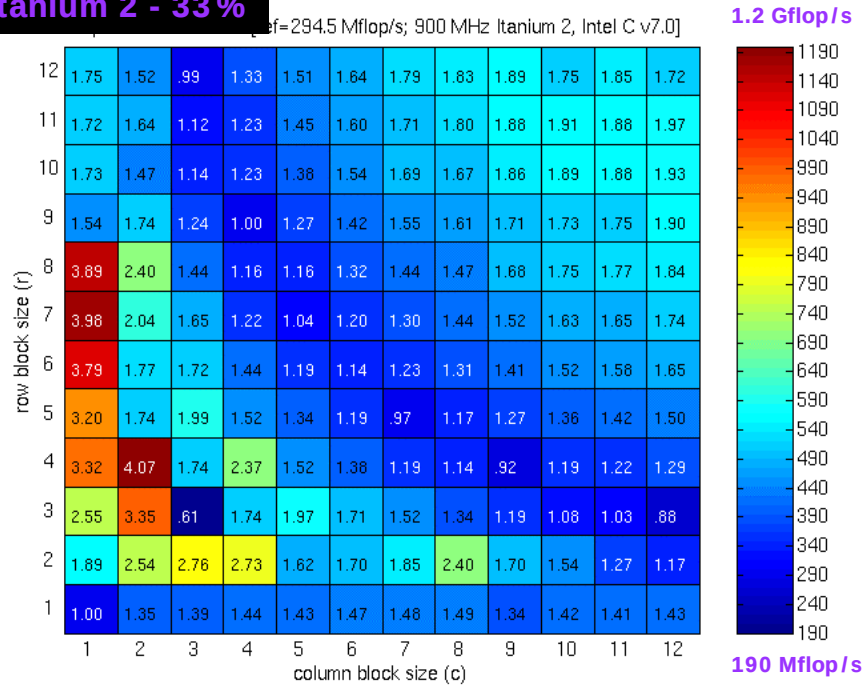
Ultra 3 - 5%



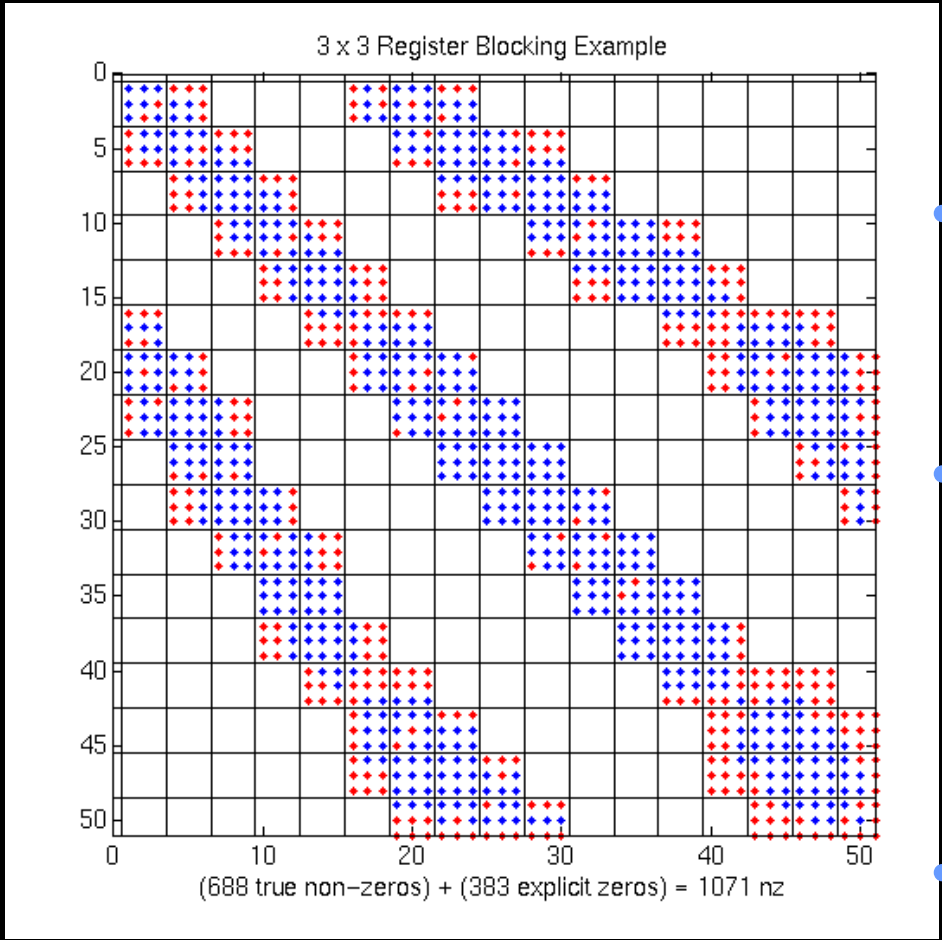
Pentium III - 21%



Itanium 2 - 33%



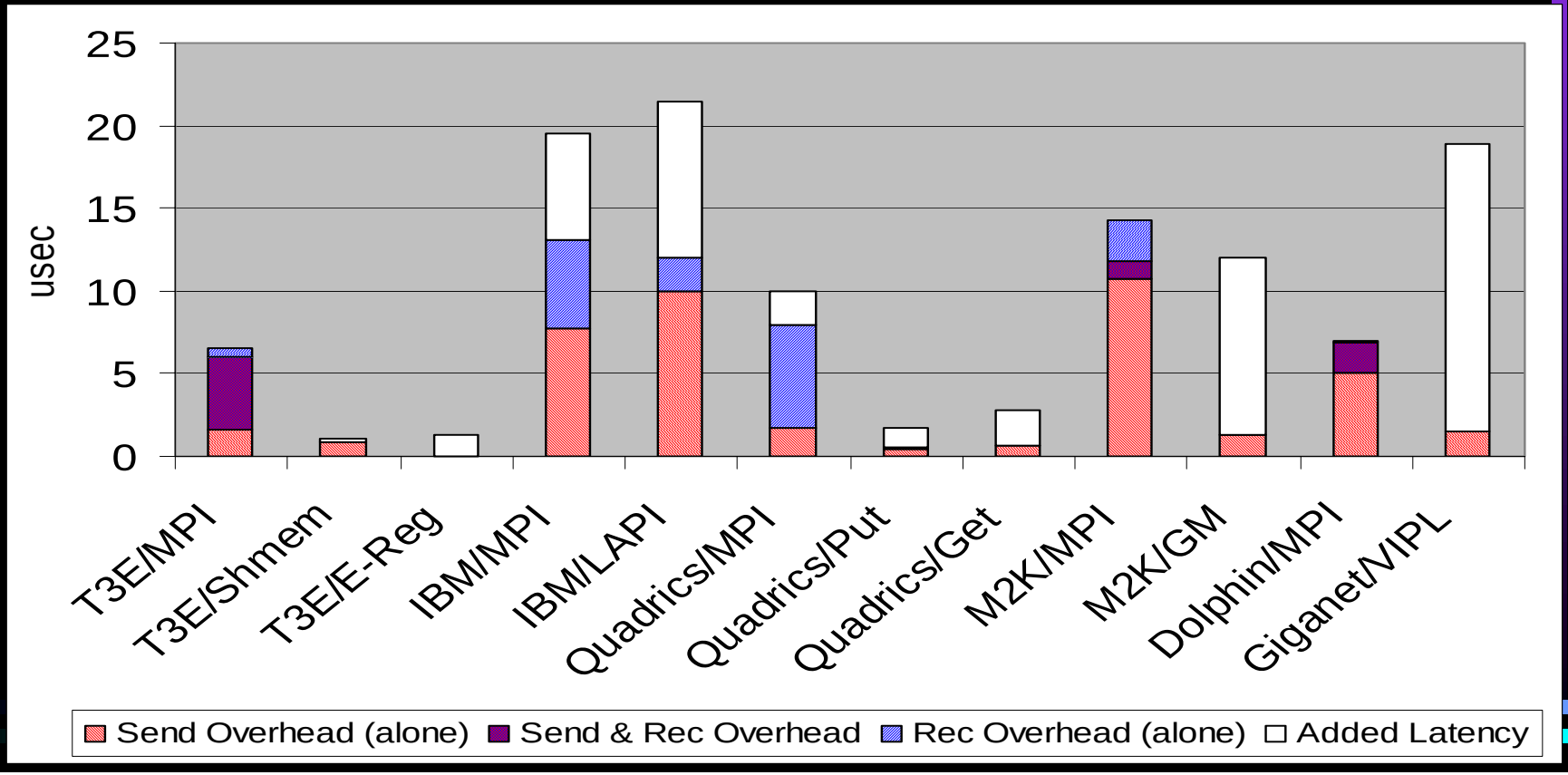
Extra Work Can Improve Efficiency!



- More complicated non-zero structure in general
- Example: 3x3 blocking
  - Logical grid of 3x3 cells
  - Fill-in explicit zeros
  - Unroll 3x3 block multiplies
  - “Fill ratio” = 1.5
- On Pentium III: 1.5x speedup!

Network Performance Tuning

- Two-sided message passing (MPI) is not the fastest form of communication
- Low latency/overhead allows for easier implementations



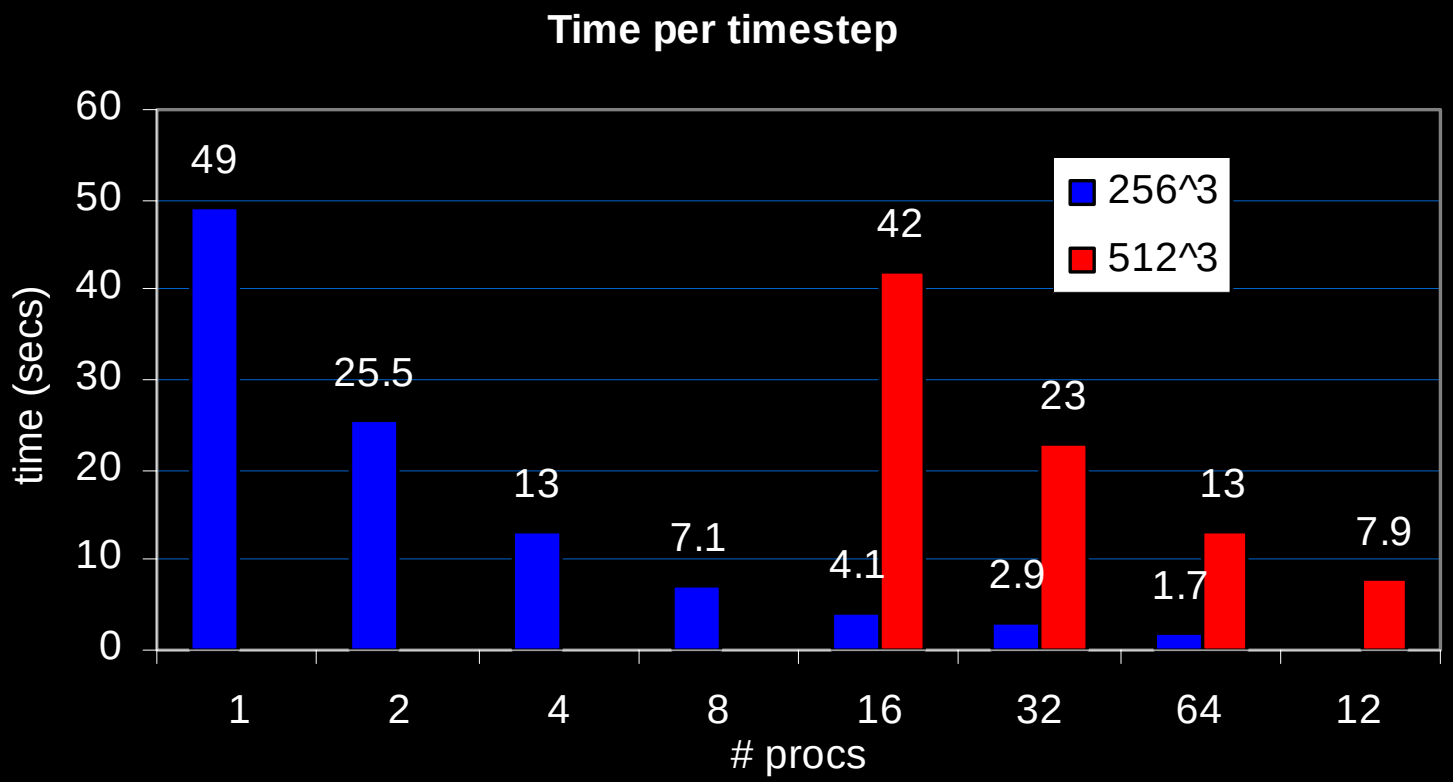
Putting it all together

Performance of the Immersed Boundary code using:

- Titanium
- GASNet
- Automatically tuned FFTs (FFTWs)

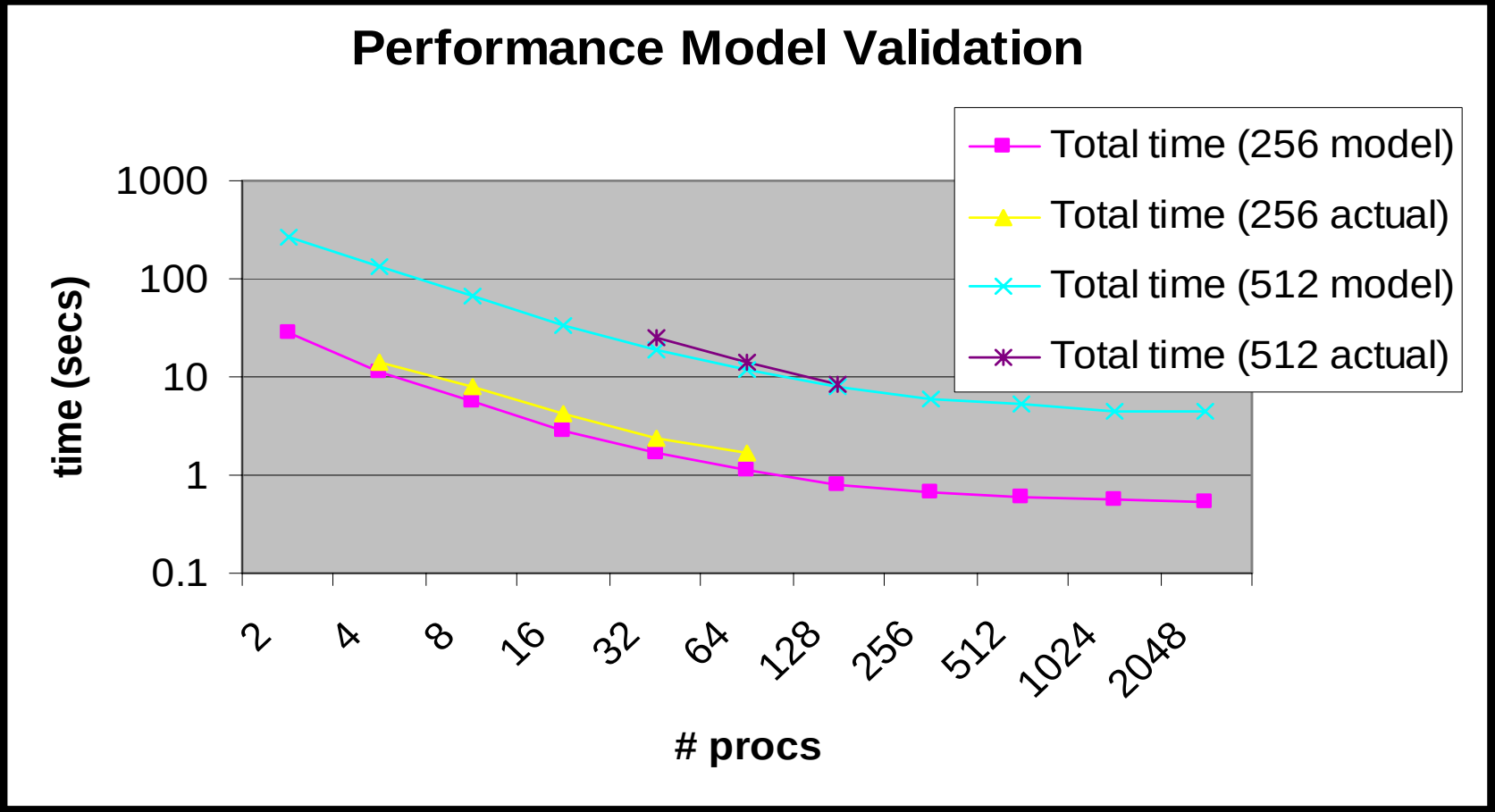
  (No sparse matrices yet)

Scaling Behavior (Synthetic Problem)



- Measured on the IBM SP at NERSC
- Also run on Itanium/Myrinet clusters and elsewhere

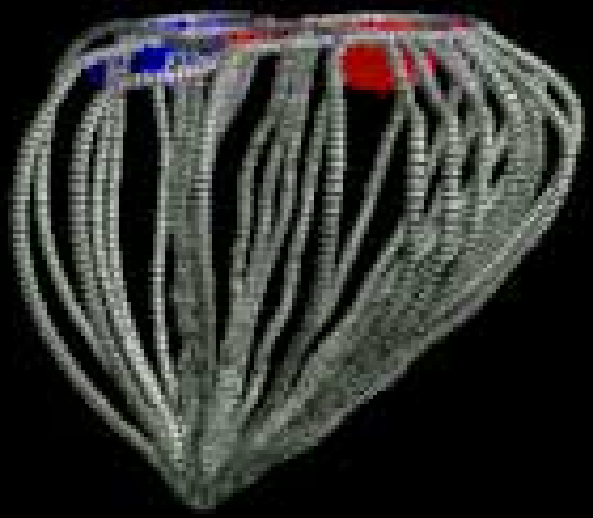
A Performance Model



- 512^3 in < 1 second per timestep not possible
- 10x increase in bisection bandwidth would fix this

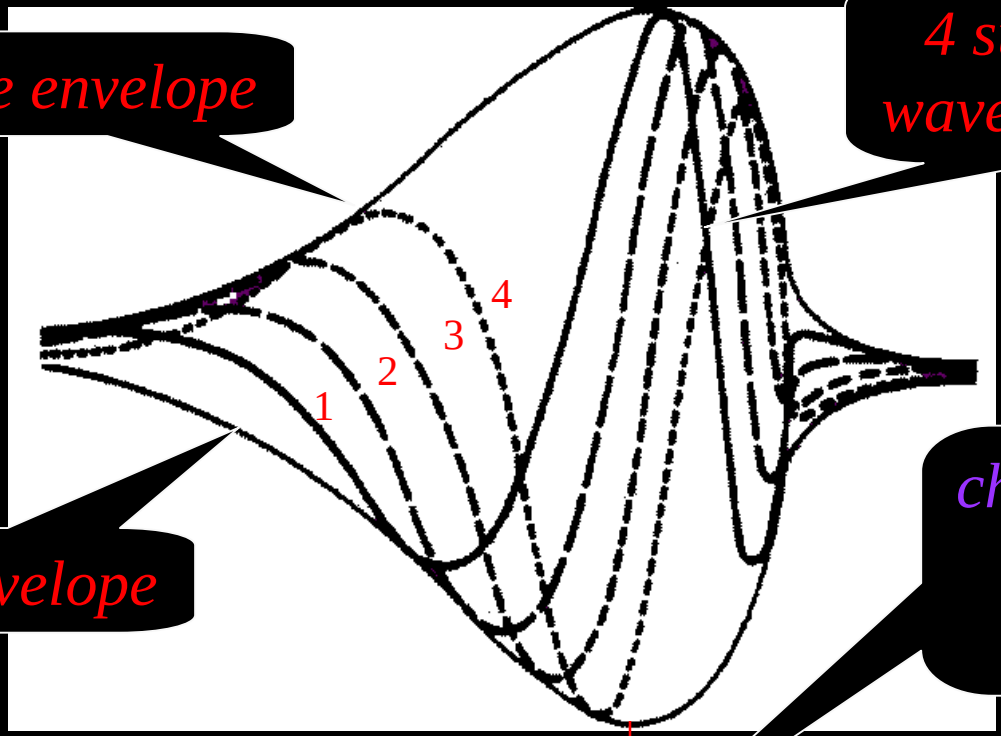
Heart Simulation

Animation of lower portion of the heart

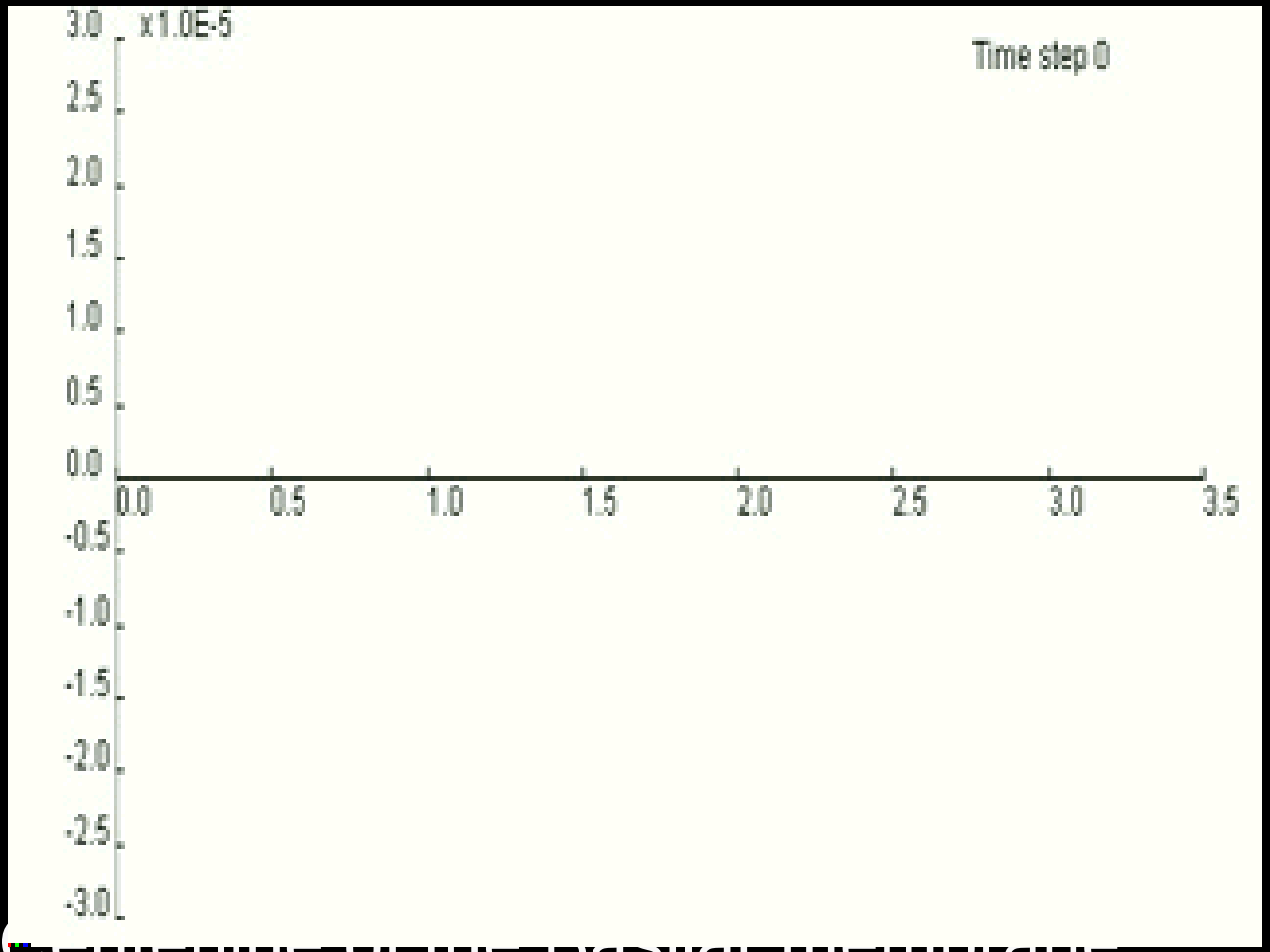


Source: www.psc.org

Traveling Wave in the Cochlea



Sound Wave Propagation in Cochlea



- Centerline of the Basilar membrane
- Response to 10 KHz frequency input

Future Research

- Variable timestepping
- Improved scalability
  - Finer decomposition of materials and fluid
  - Multigrid or other solvers
- Second-order accurate method
- Adaptive Mesh Refinement
- Multi-physics models
  - Incorporating diffusion, electrical models, etc.
  - Needed for cardiac muscle contraction
  - Needed for Outer Hair Cell in cochlea

Collaborators

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- Alex Aiken
- Phillip Colella, LBNL

Bebop faculty
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- Jason Duell, LBNL
- Paul Hargrove, LBNL
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- Sabrina Merchant
- Kaushik Datta
- Dan Bonachea
- Rich Vuduc
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- Omair Kamil
- Ben Liblit
- Meling Ngo
- Geoff Pike, ISI
- Jimmy Su
- Siu Man Yau
- Shaoib Kamil
- Benjamin Lee
- Rajesh Nishtala
- Costin Iancu, LBNL
- David Gay, Intel
- Armando Solar-Lezama

http://titanium.cs.berkeley.edu/
http://upc.lbl.gov
http://bebop.cs.berkeley.edu

* Primary researchers on the IB simulation