Custom Applications for nanoScale Science

Administrative

- **Final Project Turn-in**
  - Due 7PM, Thursday May 3rd
  - Written report
    - Described in link from schedule page
    - Example sent out earlier
  - Videos and Paraview State Files
    - Upload to FTP server
    - Or Dropbox and tell me where to find
- **Demo to me and scientist**
  - At or before the final turn-in

Overview

- Three Custom microscope control & molecular manipulation applications
- Advanced Model Fitting and Analysis
- Coupling visualization and control (beyond toolkits)
- Scientist & computer scientist collaboration
- **A Crazy Idea**
Docker

- Ming Ouh-Young’s dissertation project
  - Showed NTE factor-of-2 speedup with haptics
  - 6-DOF positioning task
  - “Lock and Key” problem
  - Hard surface + electrostatic

Rendering SPM Data has always been a problem

What this rendering seems like to me
What they’ve done with it

• Simply Incredible!

• Imagine what they could do with ink!

nanoManipulator

A virtual environment interface to SPM

The Goal:
• Remove boundaries between user and sample
• Can we make experiments on the molecular scale as easy as rolling a pencil or pushing a golf ball?

Conception

• R. Stanley Williams
  – Then professor of Chemistry at UCLA
  – Now head of nanocomputing research at HP
• Warren Robinett
  – Then director of HMD research at UNC
  – Now doing nanocomputing research at HP
• My dissertation topic in Computer Science
  – Under direction of Frederick P. Brooks, Jr.
Interoperability

- Analysis PC
- 3D graphics
- GUI
- Optical microscope
- Force
- Commercial interface
- Text & measurement

nanoManipulator Collaborators

- Information & Library Science
- Education
- CS Dist. Sys.
- Psychology
- CS Graphics
- Physics
- Gene Therapy
- Chemistry
- Biology
- NIEHS
- RTP

Now a Commercial System!

- nanoManipulator DP-100
- 2001 R&D 100 Award Winner
- www.nanomanipulator.com
Adenovirus: Imaging icosahedral shape with advanced rendering

AFM Images

Color by slope: Flat=dark, Steep=bright

Specular highlights through directional illumination

Measurements on Individual Fibers

Lateral force vs. Tip position

Translocation Deformation

Stacking Carbon Nanotubes

Lateral force measurements on individual fibers.
Question: Which Interface is Best?
NIMS: SEM + AFM

Combine the best of:

SEM:
• Imaging
• Elemental analysis
• Ebeam lithography

AFM:
• Topography
• Local (mech., elect..) properties
• Manipulation

nM:
• Manipulation (XYZ control)
• Multiple Data Set Rendering
• Registration

Hitachi S4700
Topometrix Observer

SEM/AFM in action

• Hand-controlled AFM
• Zooms in on nanotube
• “Twangs” nanotube

Play movie
SEM/AFM in action

- Two paddles
  - Suspended on tube
- Tip comes down
- Paddle sticks
- Tries to pry off
- Game over

Measuring Torsion

- Force curves all at single point (+/-50nm) on single paddle
- Force gets 20x larger after repeats!

SEM/AFM

- Challenges:
  - Real-Time overlay/registration
  - E Beam Lith Integration
  - Optimized Integration of Data Sets
  - 3D manipulation—where is the tip?
3DFM: The Next Step in Biological Force Microscopy

• How to do force microscopy inside a cell?

* Puncture the cell membrane to image inside the cell?

One Solution: Put the Probe Inside the Cell

• Problems:
  – How to measure the probe’s position?
  – How to apply forces?
Our Solution
3-D Force Microscope

- Magnetic fields apply forces to magnetic particle
- Particle position is monitored using optical tracking
  1. Very specific forces
  2. Little localized optical heating
  3. Relatively high forces

3DFM: Concept Video

- Link to video

VTK UI Prototype

- 2D Video
- More controls
- Slivered surf
- Wireframe bd
Optical Layout: Laser tracking

Optical Tracking

- Incident beam (maximum in center)
- Bead Scattering
- Resulting pattern (maximum in center)
- Terrible Visualization
  - Rainbow scale
  - No shading on surfaces
  - Down/blue is more

Z Tracking, QPD Image
3D Tracking: Bead Capture

- Bead 2.8 microns in diameter attached to cilium
  - Two beats uncaptured
  - Several captured
  - Note background (XY)
  - Note focus (Z)
  - Video link

3dFM: Magnetic Drive

3DFM: From CS Point of View
Initial Experiment Target: CF

- CF gene controls Cl⁻ and Na⁺ transport through cells.
- Affects airway secretions (mucin).
- Mucociliary clearance is the first line of defense against inhaled particulates, aerosols, etc.
- Particulate-laden mucus transported by cilia
  - beating in a mucus-free periciliary liquid (PCL)
  - to the glottis where it is expelled and swallowed.

Tracked cillum beating at 15 Hz

Next Target: Optical Microscopy

- Enable Natural Exploration in X,Y, and Z
- Use all of the Data (video, motion)
- Construct 3D (+ time) scene
- Enable Flexible Review/Summary
Tools to help Scientists
Build Better Models

- Extract Model
- Display Model with Experiment
- Simulate scan of model with microscope
- Enable direct visual comparisons

Carbon Nanotubes

What the scientist infers

The Data

Computed Centerline
Location of Mitotic Spindle: Cory Quammen
Problem: What is the geometry of the mitotic spindle?
Investigator: Kerry Bloom, Biology
Optimization of a Structural Model

"Model-based deconvolution"

Rapid Microscope Simulation
“What Should I See?”
Dilation and Erosion using Arbitrary Tip

Putting it Together: Fibrin (Conceptual)
• Extract
  – Fibrin model from optical (Tube Tracer)
  – Estimate fluorophore locations (FSM-like)
• Track
  – Motion of fluorophores (FSM-like)
• Optimize
  – Find expected motion (Lin NSF grant)
  – Find expected image (Fluoro-sim)
  – Adjust model parameters for best fit (MIBO)
• Compare
  – Actual and simulated images (nM, ScalarStack)
  – Quantitative: Simulated and measured displacements
Comparing Two Surfaces: Chris Weigle

- Model vs. AFM Scan
- Manual vs. Automatic:
  - Tumor vs. Isodose

Viz: Multivariate 3D Display
David Feng

- Virtual Cell
  - Loew
  - P41 Collab

AFM + Simulate BSE from SEM:
Adam Seeger
GPU-Accelerated TEM Simulation: David Borland

Multislice (20 minutes)
Kinematic (Let’s see…)

AMF&A: Summary

- Scientist or image analysis estimates model of object(s) scanned by a microscope
- Computer produces detailed result of applying a specified transfer function (model of instrument behavior) to this model to produce “what should I see in the image if my model is correct?”
- Scientist or image analysis compares the detailed simulation with experiment image, “does my model predict this?”
- Scientist or optimization code adjusts model trying to make simulated image better fit experiment image, “is this better?”

Insight into Instrument Behavior
Insight into Model Correctness
The Right Tool for the Job...

• All-in-one, not optimal for any
  – Sears ShopSmith
  – Computer (WIMP) interface

• Finely-tuned for the task
  – Specific power tools: table saw, lathe, router
  – Automobile, airplane cockpit
  – Bill Buxton: Bow for violin
  – What computers should be

CS Through the Science Lens

• Changing relationships between scientists and computers
  – Taking numbers to computer priesthood
  – Entering numbers on office computer
  – Connecting data collection computer to instrument
  – The computer interface is the instrument interface

• Bad news: The knobs and poking around and tools each
designed for their function are replaced by keyboard and
mouse

• Good news: Enables arbitrary mappings (in particular, we
are looking for the natural and effective ones) and new
knobs, poking, tools
  – Requires careful crafting in Visualization and UI design

Science seen through CS Lens

• Scientists are a source of many problems
  – Some are solvable with pedestrian CS (Undergraduate use
    as learning tool, visualization course may do)
  – Some are stretches or require new application
    (Visualization Case Study, Masters Thesis)
  – Some are really hard (CS dissertations, whole new project
    directions)

• Our main goal is cool new research, in CS and PS
How does it go?

- Team Building
  - Goodwill forms as each feels heard, and valued
  - Trust and increased engagement comes as results arrive

- Arms Race
  - Scientists ask for capabilities "yesterday"
  - CS looking for features for "3 months from now"
  - With the AIMS system, CS is ahead!
  - Need to start the software at least as soon as HW

- Iterative design: Having a new tool for a task changes the task

Crazy Idea: DNA + Nanotube Comp 1 Bit Full Adder: Chris Dwyer
Crazy Idea: DNA + Nanotube Comp: Assembly of NAND gate

- Link to movie

What We Learned

- Available Visualization Techniques
  - 2D scalar, 3D scalar, Vector, Tensor, Multivariate
  - InfoVis, Bioinformatics
- Visual Perception
  - How do you pick from all the options?
- Advanced ParaView Techniques
- Working as a team for a client
  - Client feedback, peer feedback, team contracts
What We Did (for your CV)

- 12 Designs for real-world data sets
  - 5 team designs for homework
  - 3 rounds of team design for a client (final project)
  - Several in-class designs
- 38 Design critiques
  - 34 critiques of other homework designs
  - 4 critiques of final-project designs
- Formal Evaluation of visualization design

How Did We Do?

- Evaluations
  - www.digitalmeasures.com/login/unc/student
- Which were the most-useful parts?
  - Team design exercises?
  - In-depth final projects?
- Which seem to be the least-useful parts?
  - Particular lectures?
- Suggestions for improvements
SIMULATOR

“For that whole one and a half weeks there wasn’t a textbook in sight (and that itself is enough to make middle schoolers happy) because what they were doing wasn’t even in the textbook yet!”

“A pointer pointer was better to see the outline of the virus. This was my favorite station.”

“I’m thinking of growing up and becoming a professional virus killer.”

INTERVIEW A SCIENTIST

“I always thought that scientists were weird people with weird accents. I was wrong except for the accents.”

“Contrary to popular thought, especially mine, science can be fun and not all scientists are dorks and dumpy nerds.”

“I was amazed at how many different scientists would actually come to talk to us about their job. Being able to talk to a bunch of different scientists allowed me to get a new understanding of scientists.”

NANOMANIPULATOR

“Every student should get a chance to have this experience because they are losing out on the best experience ever.”

“I learned that viruses are slightly sticky, because they stick to surfaces. I also learned that their texture is a lot like play-doh because they will move to the shape that you make them.”
Advanced Model Fitting: Microscope Simulation

- Simulated AFM scanner
  - Scanned surface vs. model surface
  - "What should I be seeing?"
  - Ongoing collaboration with chemist Dorothy Erie to produce a model of what happens when proteins/DNA are scanned with an AFM

AFM Simulator Version Two

Beyond the Toolkits

- Why/When?
  - Extreme performance
  - Tightly-coupled systems

- How?
  - Extend the toolkits! (when you can)
  - Any way you can (when you must)
  - "A tale of two Systems..."
“A Tale of 2+ Systems...”

nM v1:

nM v3:

3DFM v1:

Tele-nM for Collaboration

Face-to-face:
• social interactions is natural
• cooperative physical activities are natural
• teams share a single user scientific instrument

Distributed:
• social interaction is mediated by technology
• shared physical activities are difficult
• the instrument must support access by multiple users over the network.

Bead Pulled in Circle

* Link to movie
VTK UI Prototype

- Parameter menus
- Bead Histogram
- Yellow trace
- Green estimate
- Translucent volume swept by bead
- Complicated path from Brownian motion simulator

3DFM: CS Challenges

- Data Visualization
  - Overlaying volume, surface, line-trace data: both visually and haptically
  - Displaying surfaces with uncertain borders
- Computation and Rendering
  - Real-time volume convolution and display (COSM)
  - Incremental updates of a subset of the volume
- Measurement and Control Theory
  - Tracking the bead, estimation of forces, viscosity and other system state parameters

What does it take?

- Sustained hard work across disciplines
  - P&A/MS: Rich Superfine, Sean Washburn, Mike Fazio, Lu-Chang Qin, Stefan Seenbeck, Stianam Pagulayko, Garvit Mathur, Sudeep Desai, Jyotish Patil, Jieyi Gu, Jeyli Chhab, Siddhu Panmaliud, Andrei Rutkin, Lloyd Carol, Michael Sladermann, Adam Hall, Aashish Puri, Rohit Bhatn, Dollar DVI
  - SILS/EDU: Diane Sonnenwald, Gail Jones, Dennis Kubasko, Michele Kozda, Tom Tender, Susan Nagle, April Mackaughlin
- Sustained funding
  - $1M+: NIH/NCRR (12+ yr), NSF/HPCC (5 yr), NSF/ROLE (3 yr), ONR/MURI (5 yr), ARO/DURIP (2 yr), Keck Foundation (1 time)
Administrative

- Evaluations
  - www.digitalmeasures.com/login/unc/student

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