A Web Services Based Architecture for Biomedical Applications

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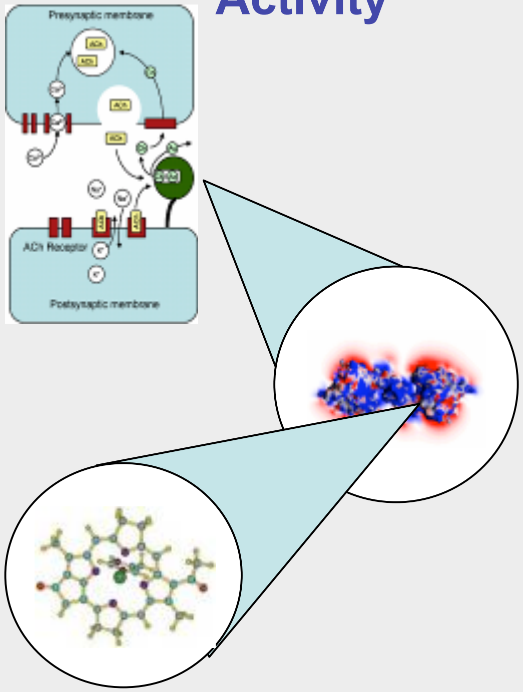
Goals

- Enabling integration across multi-scale biomedical applications
- Leveraging geographically distributed, disparate computational and data resources

Modeling and Analysis Across Scales

Modeling Synaptic Activity



Organisms

Organ

Tissue

Cell

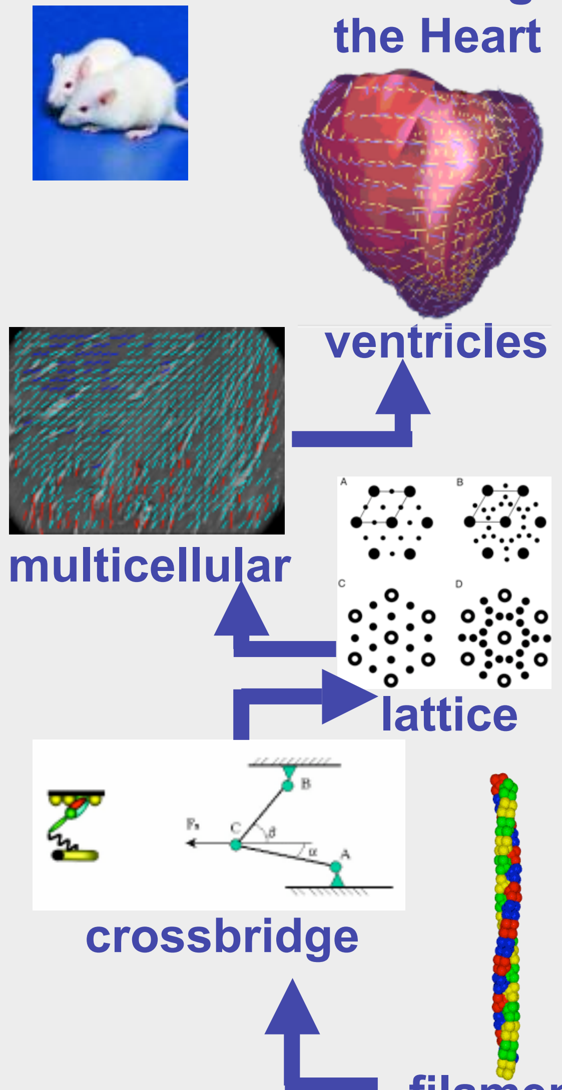
Subcellular

Macromolecular

Molecule

Atom

Modeling the Heart



ventricles

multicellular

lattice

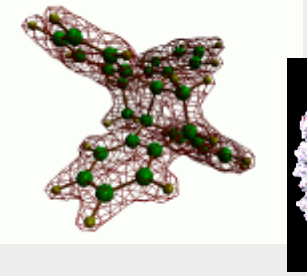
crossbridge

filament

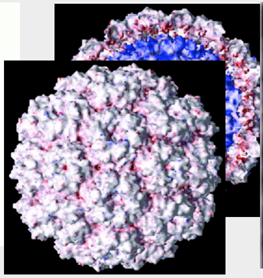
NBCR Tools Integrate Data, Construct Models and Perform Analysis across Scales

Computational Infrastructure for Multiscale Modeling

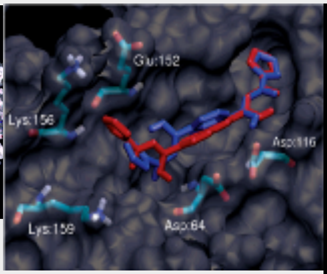
Set of Biomedical Applications



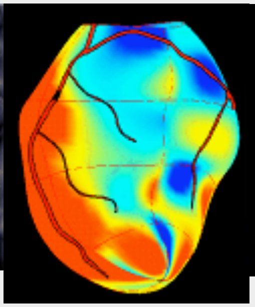
QMView
GAMESS



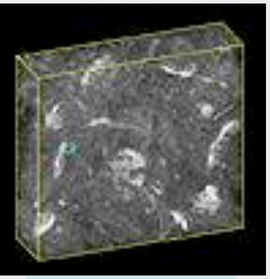
APBS



Autodock



Continuity

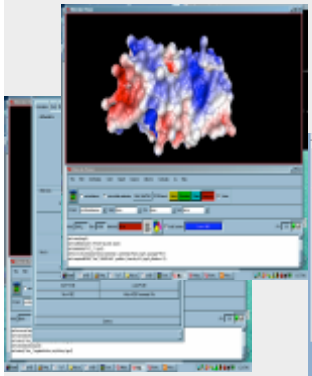


Gtomo2
TxBR

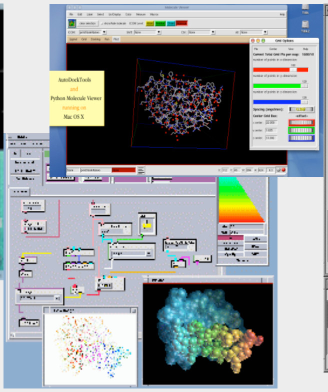
Infrastructure

Computational Grid

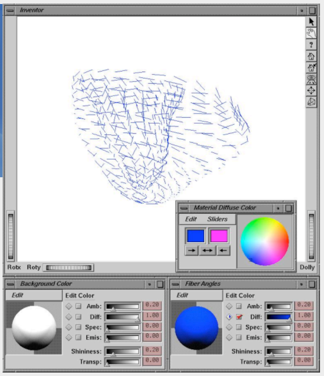
Rich Clients



APBSCommand

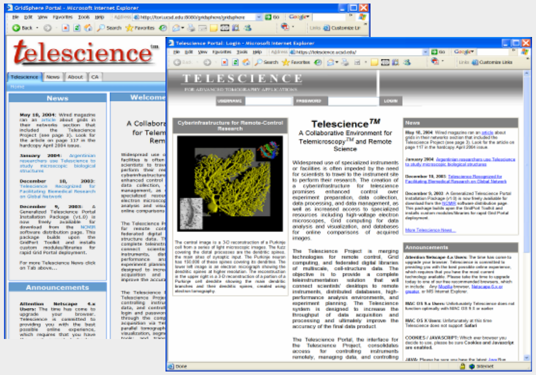


PMV ADT
Vision



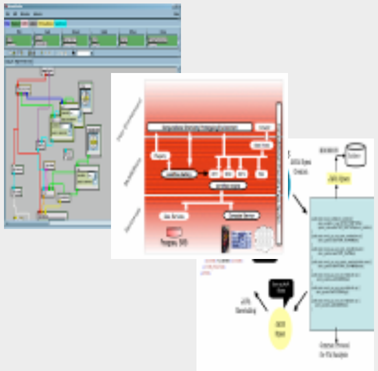
Continuity

Web Portals



Telescience Portal

Web Services



Workflow
Middleware

Requirements

- Making biomedical applications *Grid-aware*
  - Remote execution on Grid resources
    - Use of Grid-based schedulers
  - Support for multiple concurrent users
  - Access via disparate user interfaces
  - Use of standards-based security mechanisms
- Integration across multi-scale applications via the use of *Workflow* tools

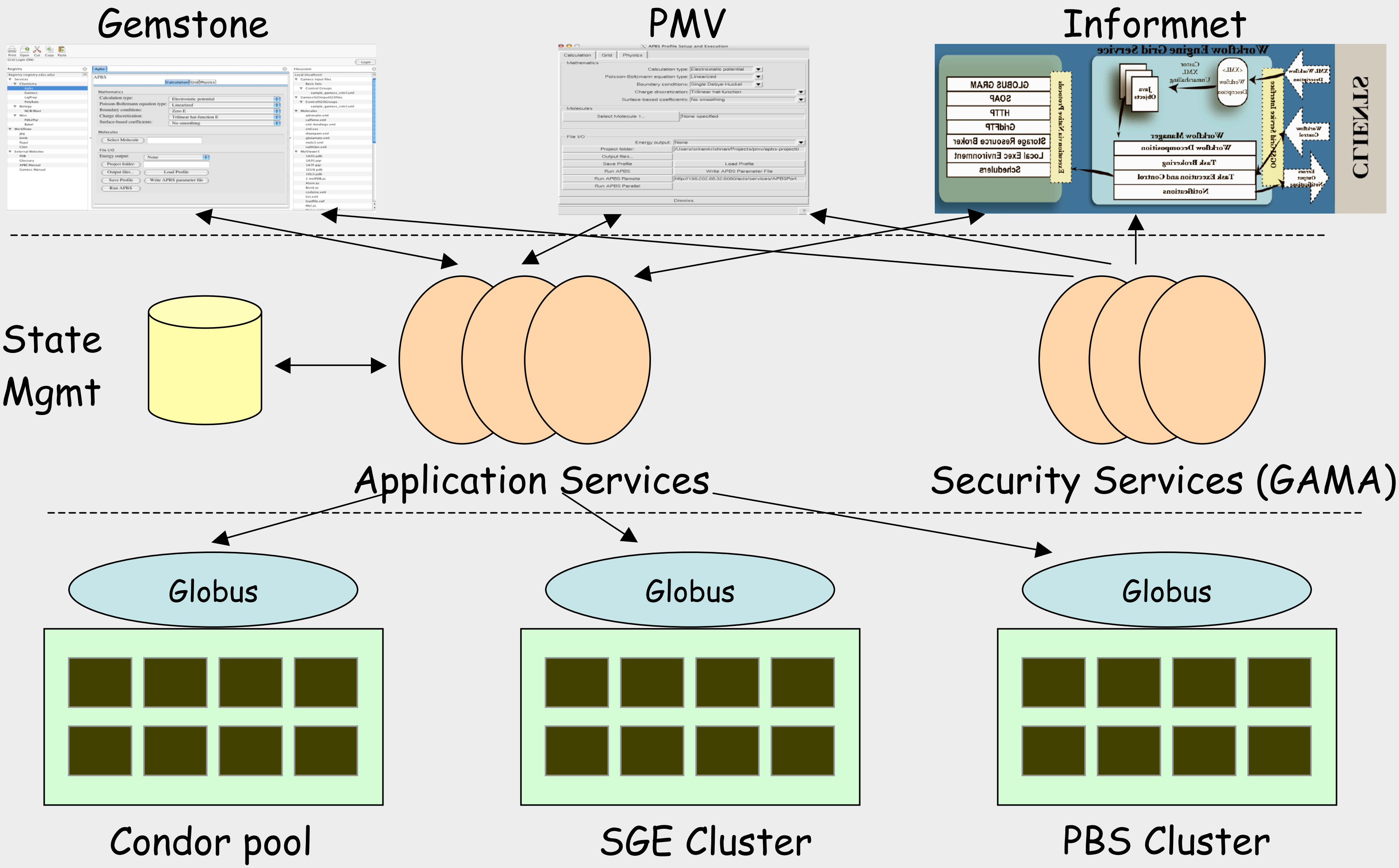
Towards a Services Oriented Architecture

- Applications are wrapped as services
  - Provide transparent execution on Grid resources
  - Users are free to use clients of their choice
  - Multiple standards-based security alternatives to choose from
- Services exchange strongly typed data defined using XML schemas
  - Aids in the creation of complex workflows

Talk Outline

- Motivation for a Services Oriented Architecture
- Overall end-to-end architecture
- Technical Details and Challenges
- Sample User Interfaces
- Status and Evaluation
- Conclusions

Architecture Overview



Print Open Cut Copy Paste

Grid Login (DN):

Login

Registry

Registry (registry.sdsc.edu)

- Services
  - Chemistry
    - Apbs
    - Gamess
    - LigPrep
    - PolyRate
  - Biology
    - NCBI Blast
  - Misc
    - Pdb2Pqr
    - Babel
- Workflows
  - jpg
  - kimb
  - flujul
  - Clint
- External Websites
  - PDB
  - Glossary
  - APBS Manual
  - Gamess Manual

Apbs

APBS

Calculation | Grid | Physics

Mathematics

Calculation type: Electrostatic potential

Poisson-Boltzmann equation type: Linearized

Boundary conditions: Zero E

Charge discretization: Trilinear hat-function E

Surface-based coefficients: No smoothing

Molecules

Select Molecule

File I/O

Energy output: None

Project folder:

Output files... | Load Profile

Save Profile | Write APBS parameter file

Run APBS

Filesystem

Local (localhost)

- Gamess input files
  - Basis Sets
  - Control Groups
    - sample_gamess_cntrl.xml
- Gamess%20input%20files
  - Control%20Groups
    - sample_gamess_cntrl.xml
- Molecules
  - adrenalin.xml
  - caffeine.xml
  - cml-bindings.xml
  - cml.css
  - diazepam.xml
  - glutamate.xml
  - mols3.xml
  - nafthlen.xml
- MolViewer5
  - 1A00.pdb
  - 1A00.pqr
  - 1A7F.pqr
  - 1GU8.pdb
  - 1OL0.pdb
  - 2 molPDB.as
  - Atom.as
  - Bond.as
  - codeine.xml
  - list.xml
  - loadfile.swf
  - Mol.as

APBS Profile Setup and Execution

Calculation | Grid | Physics

Mathematics

Calculation type: Electrostatic potential

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Molecules

Select Molecule 1... None specified

File I/O

Energy output: None

Project folder: /Users/sriramkrishnan/Projects/pmv/apbs-project0

Output files...

Save Profile | Load Profile

Run APBS | Write APBS Parameter File

Run APBS Remote http://198.202.88.32:8080/axis/services/APBSPort

Run APBS Parallel

Dismiss

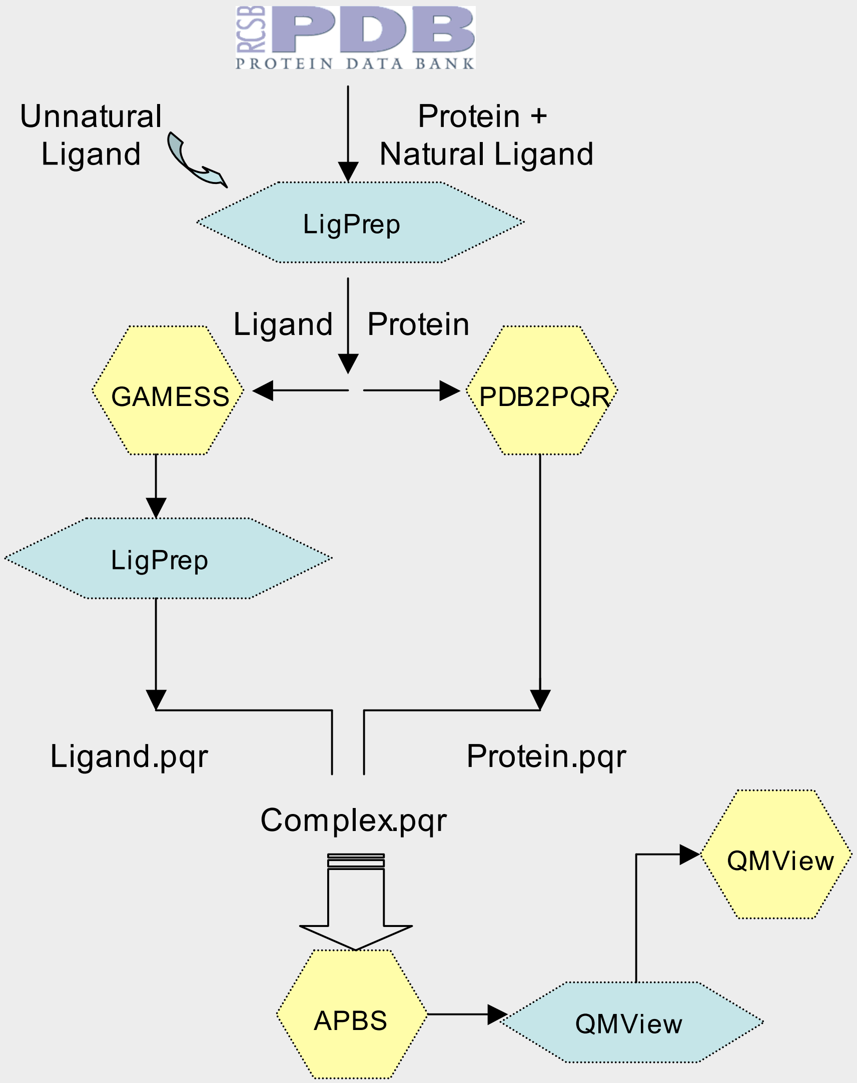
Technical Details and Challenges

- Application Services
  - Operations and Data Typing
- State Management
- Scheduling
- Security

Application Services

- APBS, GAMESS, QMView, LigPrep
  - Functionalities provided by the applications modeled as WSDL operations
  - Requests and responses for operations are strongly typed
    - Use of XML Schemas to define data structures passed around
  - Implementation details
    - Services *wrap* scientific codes - no (or minimal) modification required to these codes
    - Software tools used - Apache Axis, Jakarta Tomcat

Workflows and Strong Data Typing



Ligand-Protein Interaction

- Baldridge, Greenberg, Amoreira, Kondric
- GAMESS Service
  - More accurate Ligand Information via GAMESS-XML
  - Generation of Conformational Spaces
  - Assignment of parameters for APBS
- PDB2PQR Service
  - Protein preparation
- APBS Service
  - Generation of electrostatic information
- QMView Service or VMD Service
  - Visualization of electrostatic potential file
- Applications:
  - Electrostatics and docking
  - High-throughput processing of ligand-protein interaction studies
  - Use of small molecules (ligands) to turn on or off a protein function

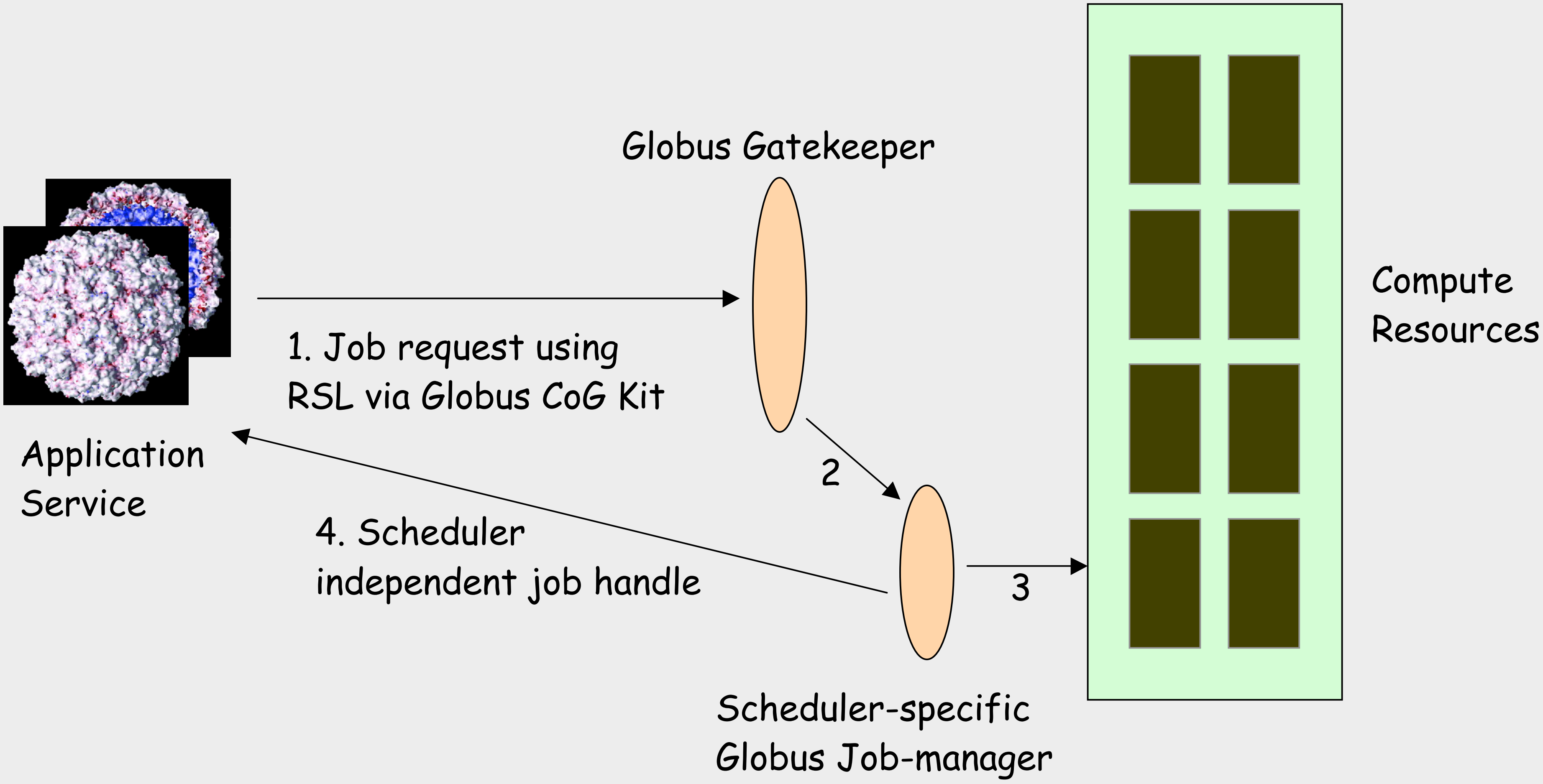
Service Operations

- Operations can be invoked synchronously, or asynchronously
- Synchronous Operations:
  - Block until the operation is finished
  - Outputs returned as a response to initial request
  - Suitable for short jobs
- Asynchronous operations:
  - Return immediately with a jobID
  - Can query for job status and outputs using the jobID
  - Suitable for long running jobs

State Management

- Application services are stateful
  - Metadata about job inputs and outputs
  - Job status for asynchronous jobs
  - Job history
- Use of a database for storing/retrieving service state
  - Access to PostgreSQL database via JDBC
- Future Work:
  - Web Service Resource Framework (WSRF) integration

Scheduling



Globus Gatekeeper

Application Service

1. Job request using RSL via Globus CoG Kit

2

3

4. Scheduler independent job handle

Scheduler-specific Globus Job-manager

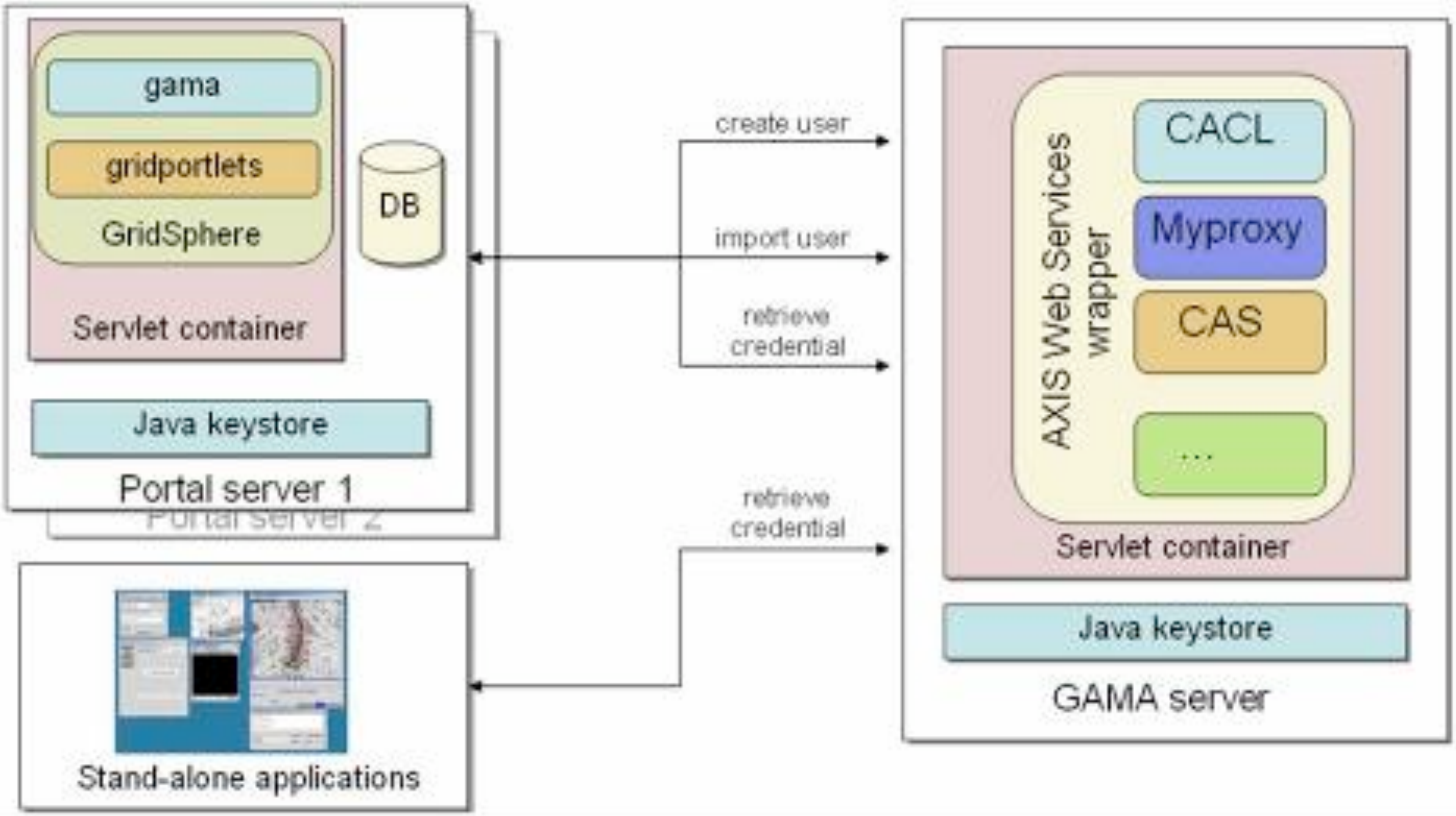
Compute Resources

Security

- GSI-based transport level (SSL) authentication
  - Use of Java CoG libraries and Tomcat to provide a secure socket connection
- Simple *grid-map* based authorization provided as an Axis Handler
  - Every Axis request passes through a chain of handlers before the target service is invoked
  - The grid-map Authorization Handler verifies if the client is authorized to access the service by looking up the grid-map using the Client’s Distinguished Name (DN).
- Future Work:
  - Message Level Security
  - SAML-based authorization techniques

Certificate Management

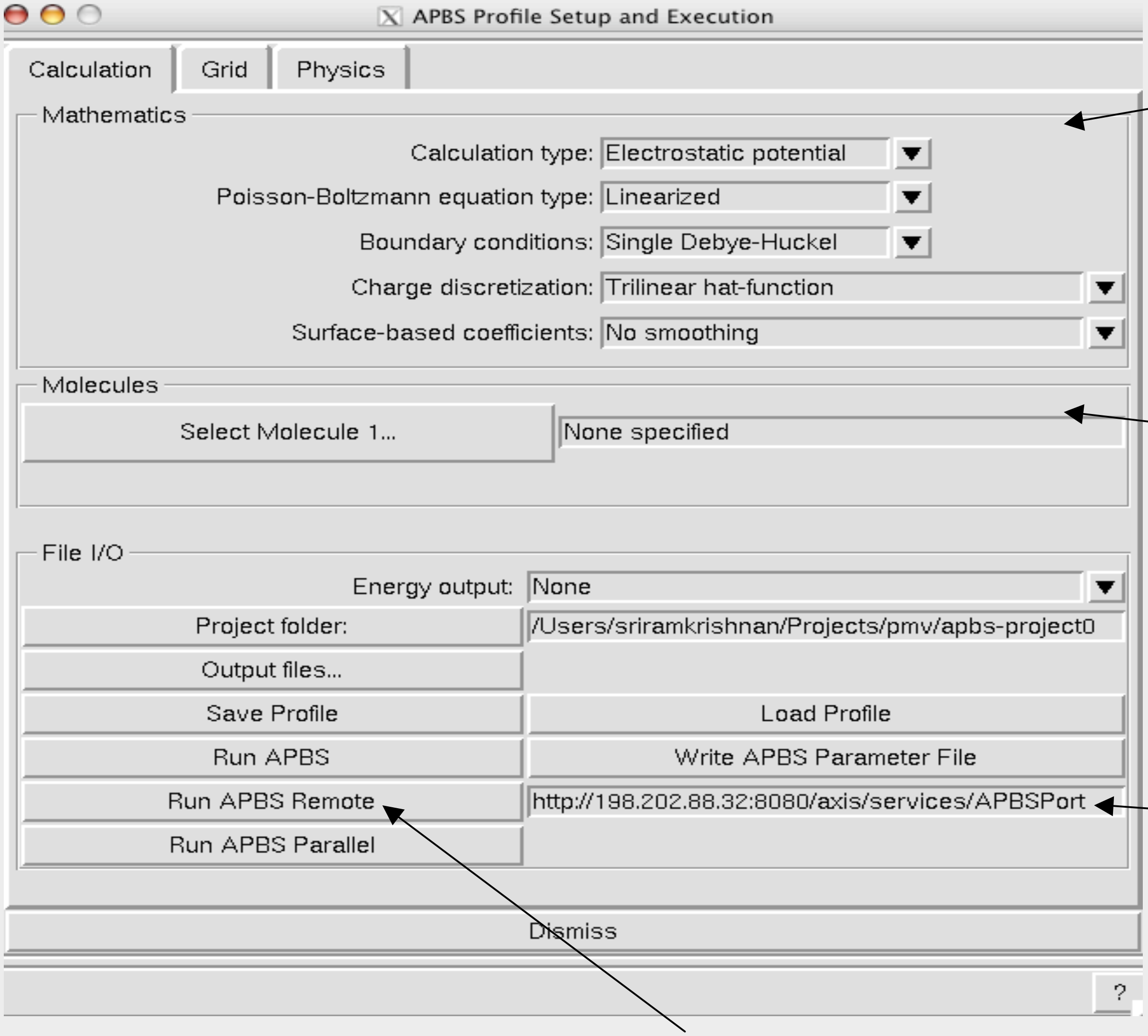
GAMA: Grid Account Management Architecture



User Interfaces

- Web services are language and platform independent
  - Can be accessed via a multitude of clients
- Java
  - Gridsphere-based Web portals
  - Workflow tools: Kepler, Informnet
- Python
  - Python Molecular Viewer (PMV)
  - Workflow tools: Vision
- Other
  - Gemstone: Mozilla-based Web services front-end

PMV APBS Client: Michel Sanner, et al



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Surface-based coefficients: No smoothing

Select Molecule 1... None specified

Energy output: None

Project folder: /Users/sriramkrishnan/Projects/pmv/apbs-project0

Run APBS Remote http://198.202.88.32:8080/axis/services/APBSPort

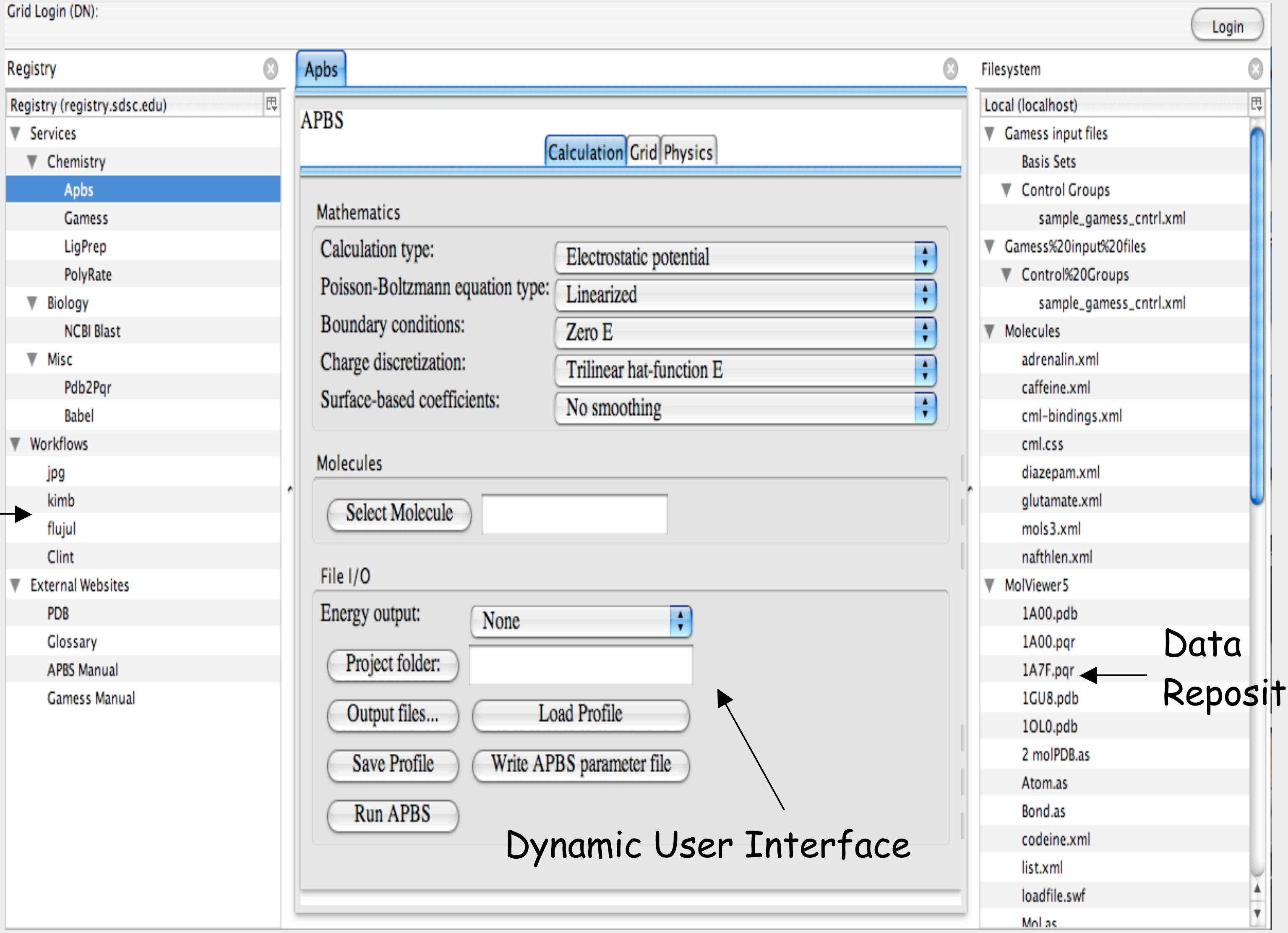
Calculation Parameters

Molecule Data

URL of APBS Web service

Invoke remote Web service

Gemstone: Karan Bhatia, et al



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APBS

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  - caffeine.xml
  - cml-bindings.xml
  - cml.css
  - diazepam.xml
  - glutamate.xml
  - mols3.xml
  - nafthlen.xml
- MolViewer5
  - 1A00.pdb
  - 1A00.pqr
  - 1A7F.pqr
  - 1GU8.pdb
  - 1OL0.pdb
  - 2 molPDB.as
  - Atom.as
  - Bond.as
  - codeine.xml
  - list.xml
  - loadfile.swf
  - Mol.as

Registry of Services

Dynamic User Interface

Data Repository

National Biomedical Computation Resource
an NIH supported resource center

San Diego Supercomputer Center

Initial Evaluation

- SOAP/HTTP not the most ideal technology to transfer large inputs and outputs
  - XML representation of molecule data (in PQR format) approximately an order of magnitude larger
  - Larger transfer times
- Axis de-serialization very expensive for large inputs
  - Large memory footprint
  - Very time consuming

Status and Software Availability

- Application services: http://nbcr.net/services
  - Alpha version of APBS service available for download and testing
  - GAMESS, QMView, LigPrep services available soon
- Gemstone: http://grid-devel.sdsc.edu/gemstone
- GAMA: http://grid-devel.sdsc.edu/gama
  - Version 1.0 available for download
- Informnet: http://grid-devel.sdsc.edu/informnet
- PMV: http://www.scripps.edu/~sanner/python

Summary

- An end-to-end infrastructure for Grid-enabling biomedical applications that provides:
  - Remote execution on Grid resources
    - Access to schedulers
  - State management
  - Concurrent access via disparate interfaces
  - Standards-based security
- Ability to use workflow tools for coupling multi-scale biomedical applications

(Incomplete) Acknowledgements

- Karan Bhatia
- Phil Papadopoulos
- Brent Stearn
- Steve Mock
- Kurt Mueller
- Sandeep Chandra
- Nadya Williams

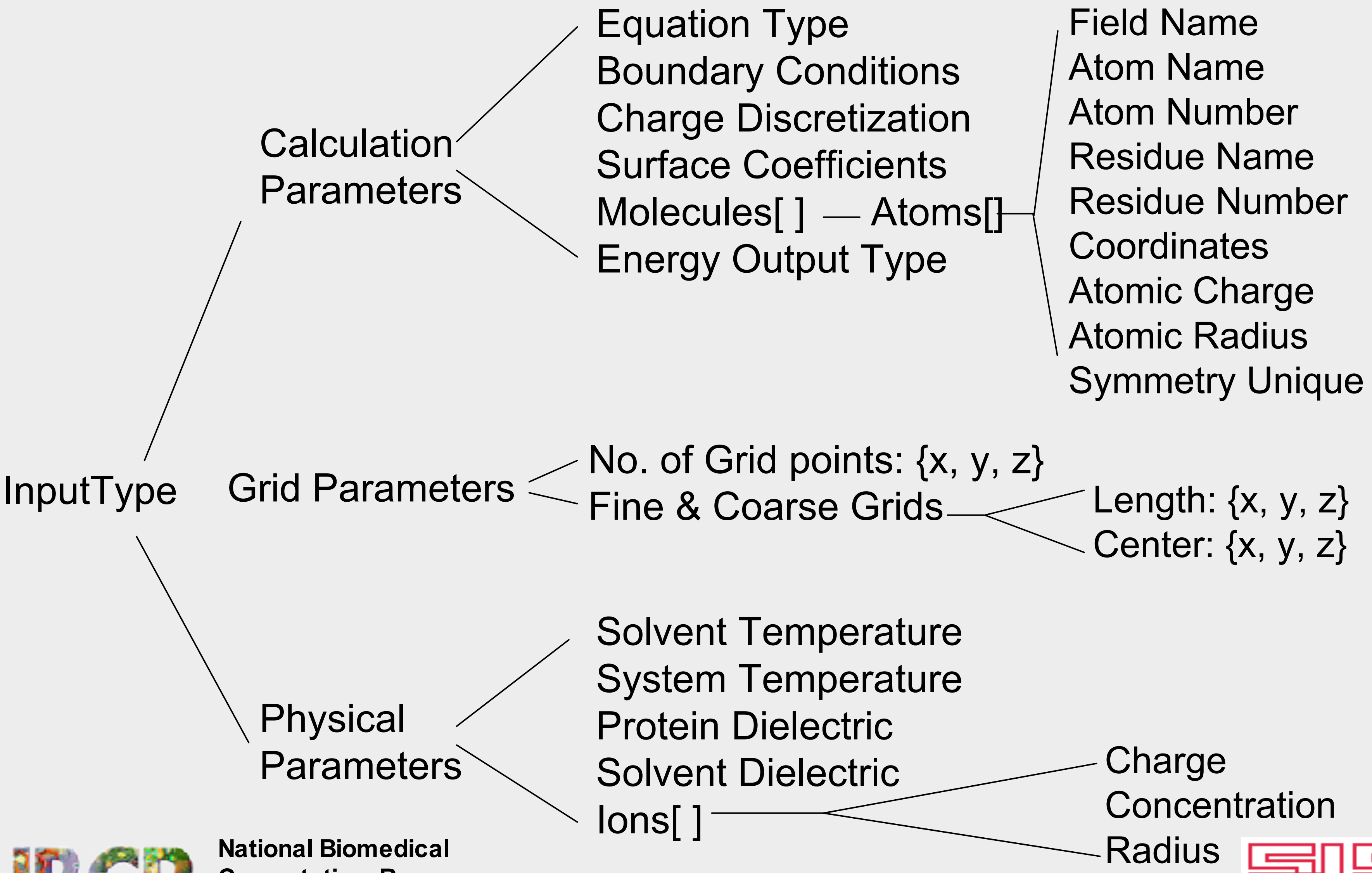
- Peter Arzberger
- Wilfred Li
- Kim Baldridge
- Jerry Greenberg
- Robert Konecny
- Michel Sanner
- Wibke Sudholt
- APBS Team

Appendix

Sample Service: APBS

- Operations provided:
  - calculateBindingEnergy
  - calculateSolvationEnergy
  - calculateElectrostaticPotential
- Operations accept and return strongly typed parameters in XML format
  - Described by an XML Schema
  - Data binding provided by stub generators in various languages
    - WSDL2Java provided by Apache Axis
    - WSDL2PY provided by Python ZSI

APBS Input Types



- InputType
  - Calculation Parameters
    - Equation Type
    - Boundary Conditions
    - Charge Discretization
    - Surface Coefficients
    - Molecules[ ] — Atoms[]
      - Field Name
      - Atom Name
      - Atom Number
      - Residue Name
      - Residue Number
      - Coordinates
      - Atomic Charge
      - Atomic Radius
      - Symmetry Unique
    - Energy Output Type
  - Grid Parameters
    - No. of Grid points: {x, y, z}
    - Fine & Coarse Grids
      - Length: {x, y, z}
      - Center: {x, y, z}
  - Physical Parameters
    - Solvent Temperature
    - System Temperature
    - Protein Dielectric
    - Solvent Dielectric
    - Ions[ ]
      - Charge
      - Concentration
      - Radius

SOAP Performance: Alternatives

- Parsing techniques
  - Streaming
  - Pull-based
- Binary XML
  - More compact representation of data
  - More efficient data transport and parsing
  - Smaller memory footprint
- Data Format Description Language (DFDL)
  - Definition of structure of binary and character files
  - Files transferred in their native formats
    - Smaller sizes, hence faster transfer