

Schrödinger Overview

Spain, Santiago

June, 2010

Jas and Dan *Applications Scientists*
Katia Dekimeche *Account Manager*



SCHRÖDINGER.

Welcome !!

Day 1: Structure Based Methods



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Day 1: Structure Based Methods

Registration and Coffee 9.30

10.00 MORNING

General Schrödinger overview and introduction

15 min

Intro to structure-based drug design

20 mins

Getting started with Maestro

60 mins

Structure-based virtual screening

60 mins

Lunch 13.00 - 14.00

14.00 AFTERNOON

Structure-based lead optimization

60 mins

Advanced Docking (IFD, loop refinement)

60 mins

Wrap-Up 16.00

Summary, Feedback ...

20 mins

Free sessions ...

Welcome Back !!

Day 2: Ligand Based Methods



Day 2: Ligand Based Methods

Breakfast 9.30

10.00 MORNING

Introduction to ligand-based drug design	30 mins
Ligand Preparation and Conformational Searching	30 mins
Ligand-based virtual screening	
– Manual Generation of Pharmacophores	45 mins
– Automatic Generation of Pharmacophores	45 mins
– 3D QSAR	10 mins

Lunch 13.00 - 14.00

14.00 AFTERNOON

Looking for Alternate Cores/ Compounds by Shape	30 mins
Shape Based Searching	30 mins
An interface for 2d Molecules and 2d QSAR	30 mins
Techniques for finding Diverse Compounds	30 mins

Wrap-Up 16.00

Summary, Feedback ...	20 mins
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Presentation Overview

- Company Overview
- Suite Overview
- Software Licenses
- How to Get Started and Download
- Conclusions

Company Overview

- Privately held company, founded in 1990
- Staff of ~120, 50% Ph.D.'s
- Clients
 - Over 1000 client sites
 - ~300 commercial sites
- Main sites
 - New York, NY
 - Portland, OR
 - San Diego, CA
 - Mannheim and Munich, Germany
 - Camberley, UK
 - Hyderabad, India
 - Distribution Partners in Japan, China, Korea, Hungary, and Italy

Scientific Advisory Board

- Richard A. Friesner
 - *Chairman of SAB & Founder*
- Paul A. Anderson
 - *Esteemed medicinal chemist from Merck; lead efforts to develop TRUSOPT, ZOCOR, CRIXIVAN, and SUSTIVA*
- Bruce J. Berne
 - *Higgins Professor of Chemistry, Columbia University*
- Ronald Breslow
 - *Professor, Departments of Chemistry and Biology, Columbia University*
- Barry Honig
 - *Professor, Department of Biochemistry and Biophysics, Columbia University*
- Wayne C. Guida
 - *Professor, Drug Discovery Program at H. Lee Moffitt Cancer Center*
- William L. Jorgensen
 - *C. P. Whitehead Professor of Chemistry, Yale University*
- Ronald M. Levy
 - *Professor of Chemistry, Rutgers University*
- Matthew Jacobson
 - *Professor, Department of Pharmaceutical Chemistry, UCSF*
- Mark Murcko
 - *Vice President, CTO and Chair of the SAB of Vertex*

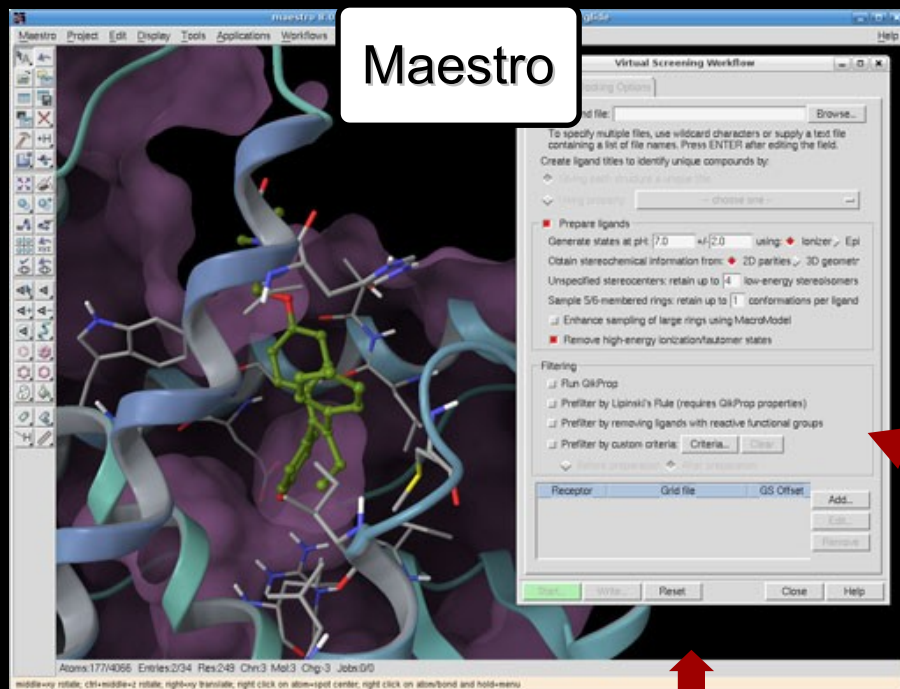
Suite Overview

- Visualization and Automation
- Small Molecule Modeling and Simulations
- Macromolecular Modeling and Simulations
- Lead Discovery
- Lead Optimization



Visualization and Automation

Maestro



Python

```
# Create a notebook
self.notebook = ...
self.notebook.pack(fill='both', expand=1)
self.tabs = {}

# Call functions
self.mini_tab = MiniTab( self )
self.tabs[self.MINI] = self.mini_tab

self.torsion_scan_tab = TorsionScanTab( self )
self.tabs[self.TORSION_SCAN] = self.torsion_scan_tab

self.csearch_tab = CSearchTab( self )
self.tabs[self.CSEARCH] = self.csearch_tab

self.esp_tab = ESPTab( self )
self.tabs[self.ESP] = self.esp_tab

self.current_tab = self.mini_tab

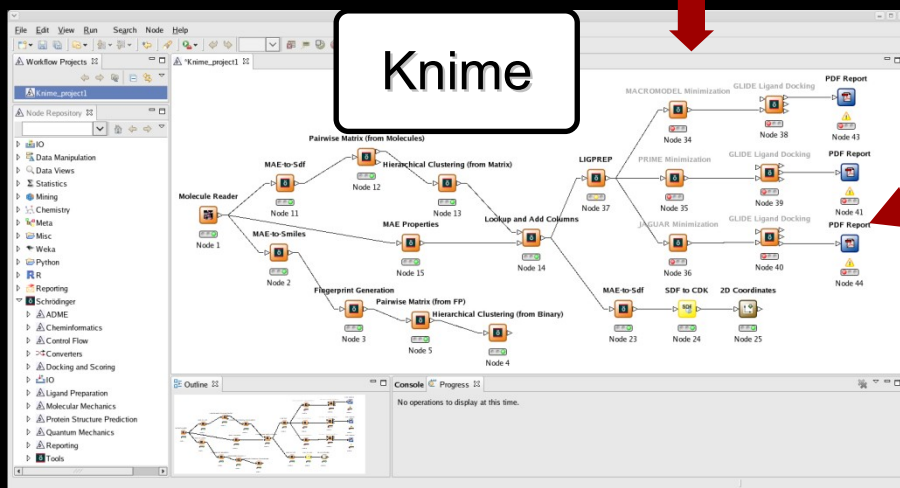
# Build the Close button:
self.close_box = stk.ButtonBox(self.root)
self.close_box.pack(fill='none', expand=0, padx=10, pady=10,
                    side=stk.RIGHT)

self.close_box.add("Close", command=self.close )
self.close_box.setdefault(0)

self.run_box = stk.ButtonBox(self.root)
self.run_box.pack(fill='none', expand=0, padx=10, pady=10,
                  side=stk.LEFT)

self.run_box.add("Run", command=self._runCB)
```

Knime



Maestro

Toolbar

Help!

The screenshot displays the Maestro software interface. The main workspace shows a 3D molecular model of a protein-ligand complex. The protein is represented by a ribbon diagram with orange, yellow, and blue segments. The ligand is shown as a stick model with cyan, orange, and red atoms. The workspace is labeled "Workspace" in red text.

The toolbar on the left contains various icons for file operations, editing, and visualization. The top menu bar includes "Object", "Edit", "Display", "Tools", "Applications", "Workflows", and "Scripts". The status bar at the bottom of the workspace displays the following information: "rms:70/9576 Entries:2/104 Res:1726 Chn:595 Mol:594 Chg:-12 Jobs:0/0".

The Project Table at the bottom is titled "Table --- intro_maestro_examples" and contains the following data:

In	Title	Surf	Hyp	Vib	Entry ID	Entry Name	PDB ID	PDB CRYST1 a	PDB CRYST1 b	PDB CRYST1 c	PDB CRY
-	ACHe crystal structs after alignment										
◆	1EVE retains original coordinates				11	1eve.1	1EVE	111.925	111.925	136.896	90.000
◆	1B41 aligned on top of 1EVE				10	1b41.1	1B41	148.990	148.990	247.010	90.000
+	Additional AChE structures to experim...										

The Project Table is labeled "Project Table" in red text. The table has 12 columns and 5 rows. The first row is a header, and the subsequent rows contain data for different crystal structures. The table is titled "Table --- intro_maestro_examples".

Workspace

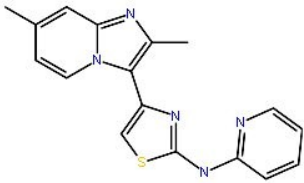
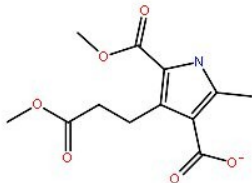

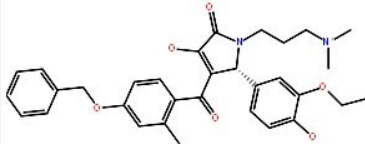
Project Table

2D Viewer in the Project Table

Project Table --- Scratch Project

Table Select Entry Property Group ePlayer

2D

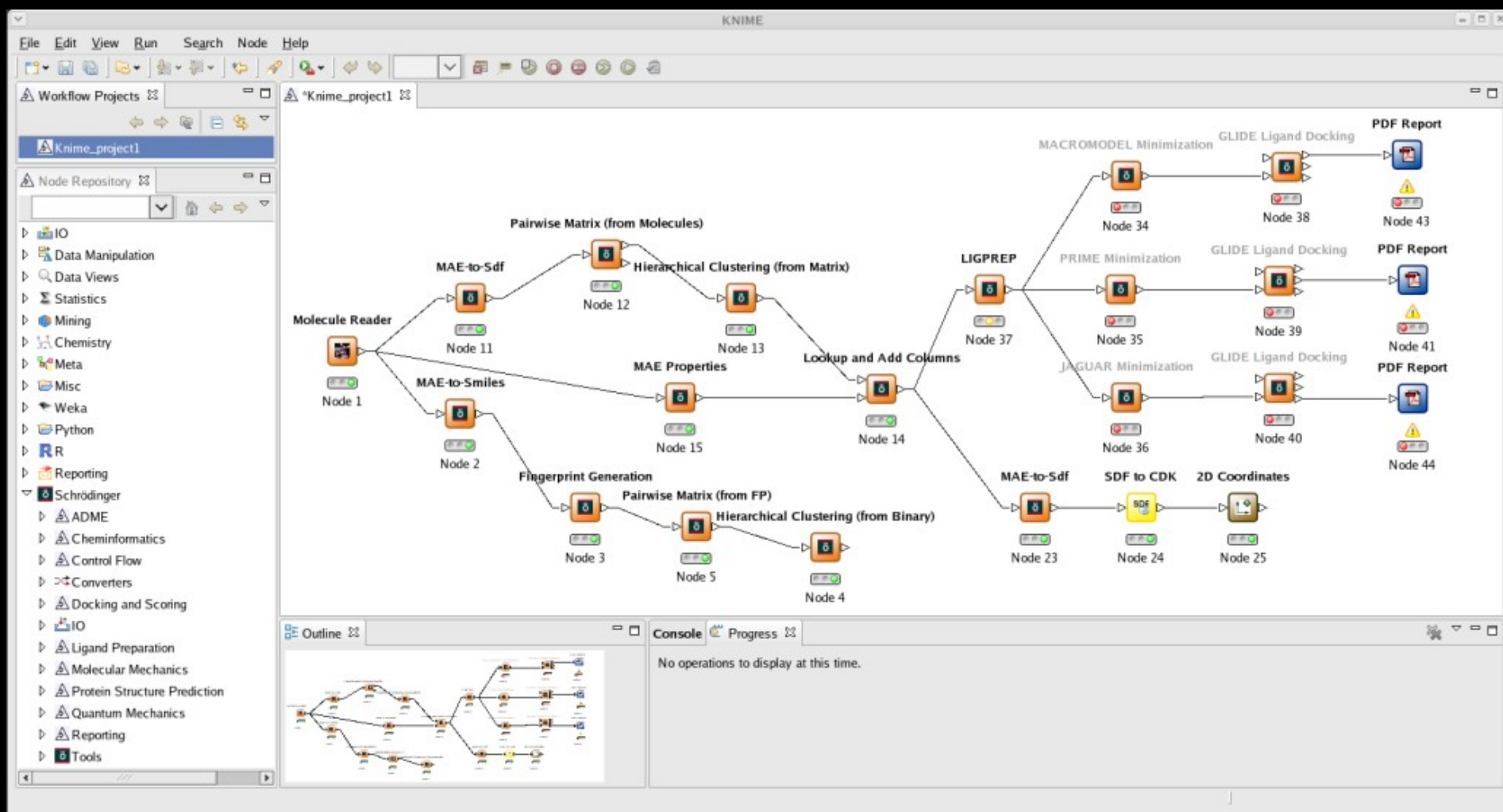
Row	In	2D Structure	Title	Au	glide hbond	glide metal	glide rewards	glide evdw	glide ecoul	glide erotb	glide esite	glide emodel	glide energ
13	<input type="checkbox"/>		151943		-0.314686	0.000000e+0...	-2.059205	-40.992566	-3.327766	0.542664	0.000000e+0...	-60.384022	-44.320332
14	<input type="checkbox"/>		451167		-0.438492	0.000000e+0...	-2.448495	-32.666768	-8.220819	0.992083	-0.021814	-62.087790	-40.887587
15	<input type="checkbox"/>		617674		-0.104345	0.000000e+0...	-1.627061	-40.941879	-0.551073	0.170468	-0.010980	-57.598426	-41.492952
16	<input type="checkbox"/>		689972		0.000000e+0...	0.000000e+0...	-0.285627	-42.011685	-11.198709	0.695405	0.000000e+0...	-73.265857	-53.210394

2D structure height:

Entries: 51 total, 51 shown, 1 selected, 1 included Groups: 1 total, 0 selected

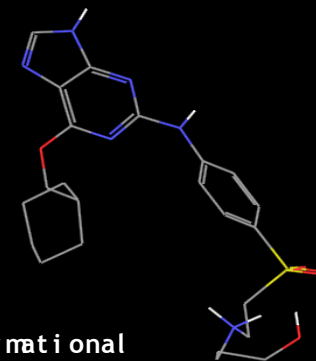
Close Help

KNIME Extensions

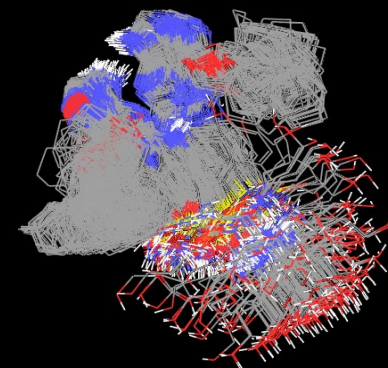


Small Molecule Modeling and Simulations

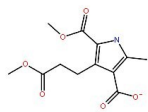
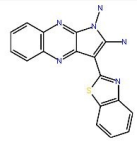
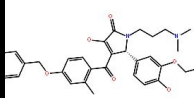
- 1D/2D to 3D Structure Generation
- Conformation Generation and Clustering
- Property Generation and Filtering
- Molecular Mechanics
- Molecular Dynamics
- Quantum Mechanics

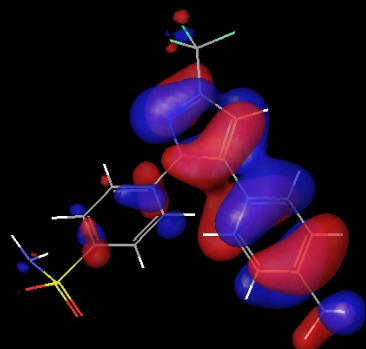
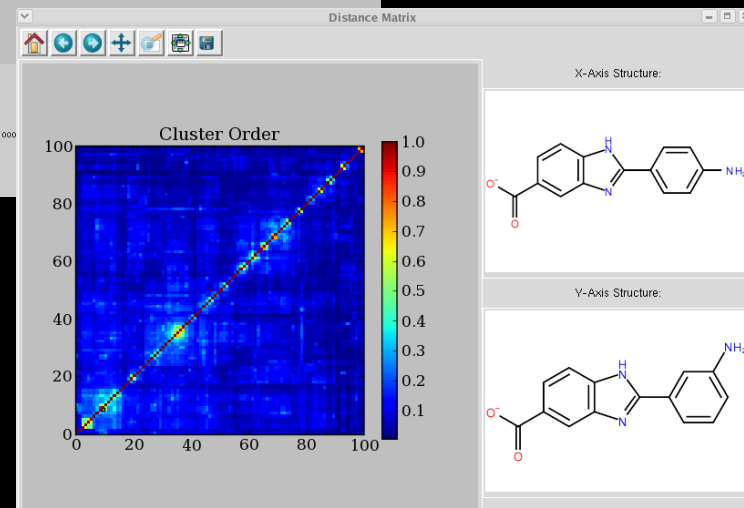


Conformational Analysis

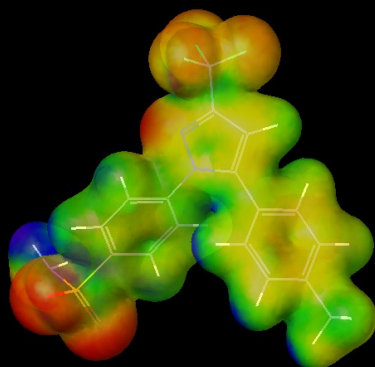


Property Prediction and Analysis

	451167	-0.430492	0.000000e+00	-2.448495	-32.666768	-8.220819	0.992083
	617674	-0.104345	0.000000e+00	-1.627061	-40.941879	-0.551073	0.170468
	689972	0.000					



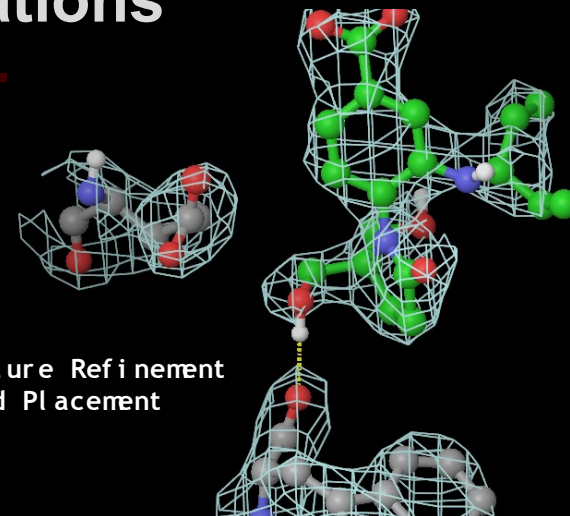
Molecular Orbitals



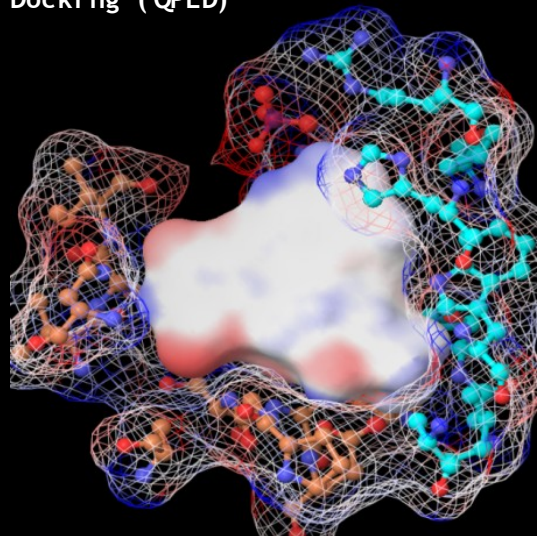
Electrostatic Potentials

Macromolecular Modeling and Simulations

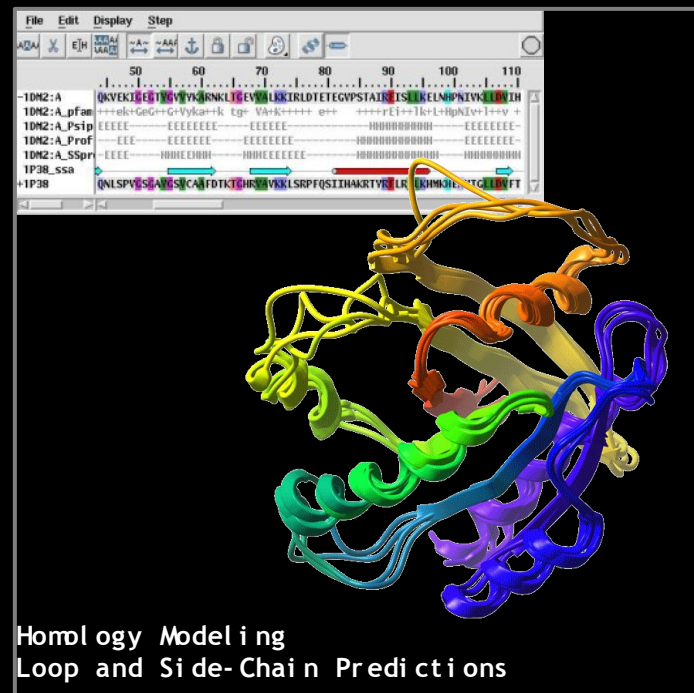
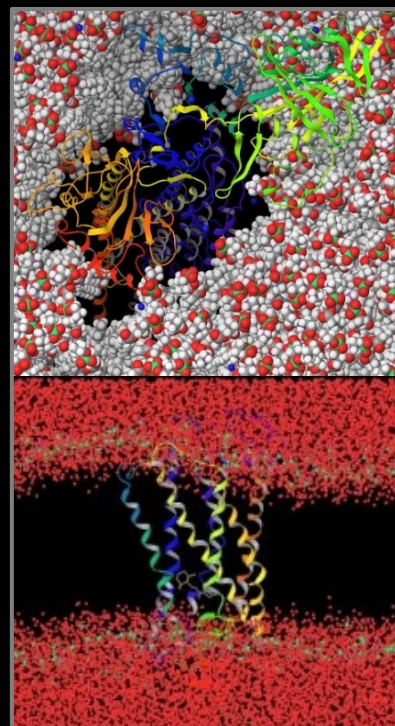
- Structural Biology – Crystallography
- Protein Modelling and Bioinformatics
- Molecular Mechanics
- Molecular Dynamics
- QM/MM



Quantum Polarized Ligand
Docking (QPLD)



Molecular Dynamics

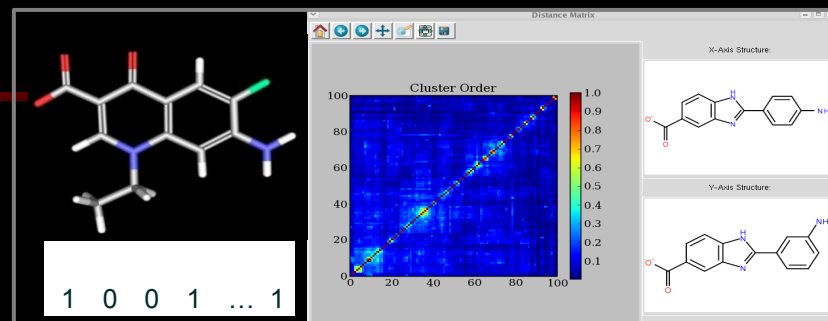


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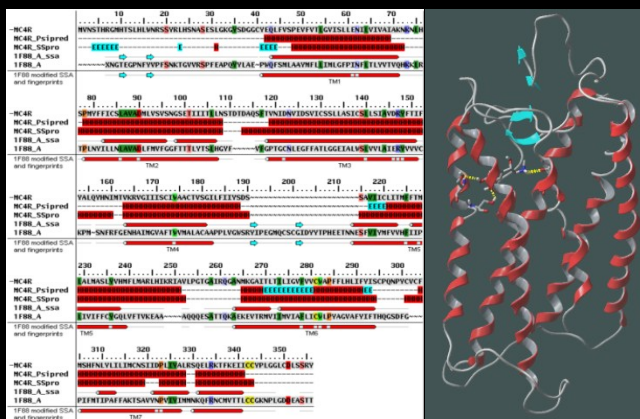
Lead Discovery

- Cheminformatics
- Ligand-Based Discovery
- Structure-Based Discovery

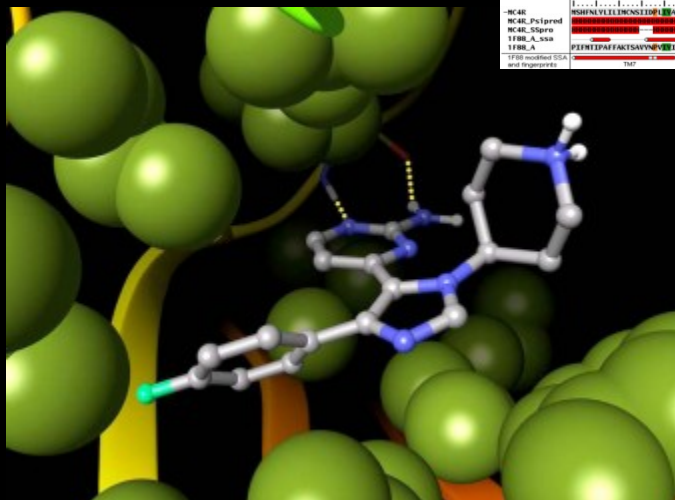
Fingerprints and Clustering



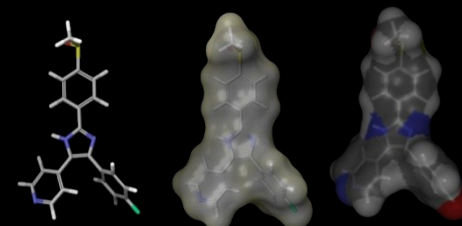
Prime and GPCR Modeling



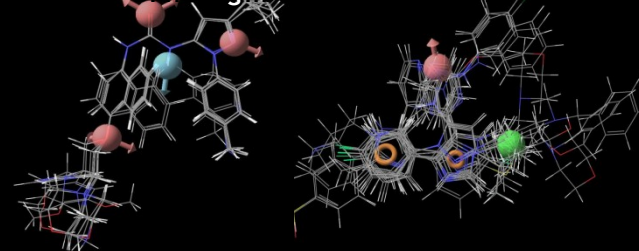
Virtual Screening



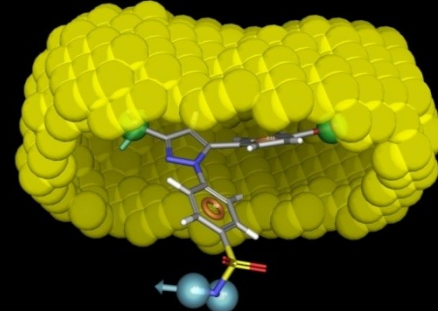
Shape-Based Searching



Biophore Modeling with Multiple Binding Site Detection

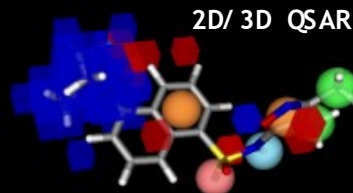


Excluded Surfaces

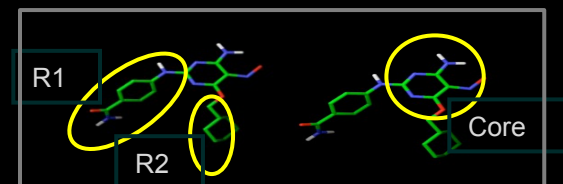


Lead Optimization

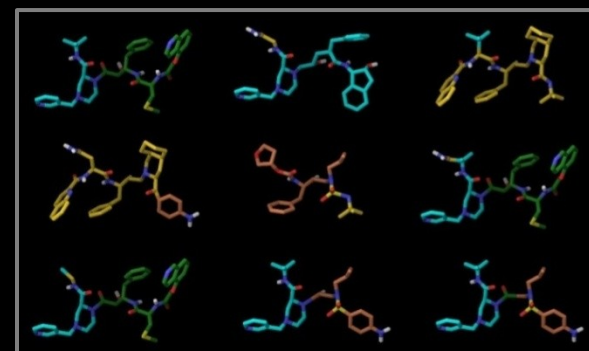
- 2/3D QSAR
- Combinatorial Chemistry
- Fragment-Based Design
- Structure-Based Discovery
- Absolute and Relative Binding Affinity



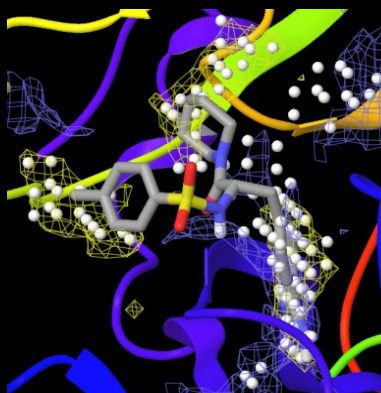
Focused Library Design



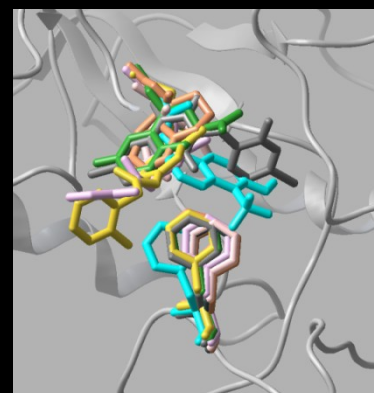
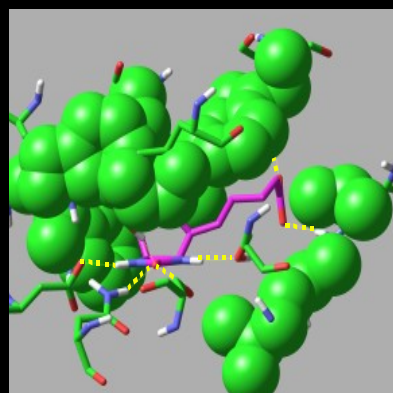
BREED



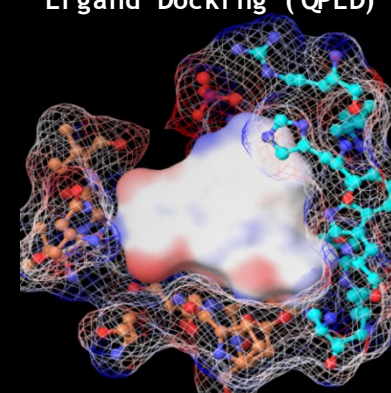
Binding Site Analysis



Extra Precision (XP) Docking Induced-Fit Docking (IFD)



Quantum Polarized
Ligand Docking (QPLD)



Suite Overview with Module Names

- Visualization and Automation
 - *Maestro, Canvas, KNIME Ext, Python*
- Small Molecule Modeling and Simulations
 - *LigPrep, Epik, QikPrep, MacroModel, Jaguar, Canvas*
- Macromolecular Modeling and Simulations
 - *PrimeX, Prime, MacroModel, Desmond, QSite*
- Lead Discovery
 - *Canvas, Phase, Glide, CombiGlide, GPCR Modeling*
- Lead Optimization
 - *Phase, CombiGlide, SiteMap, Glide, IFD (Glide + Prime), QPLD (Glide + QSite)*



Schrödinger Academic Offer

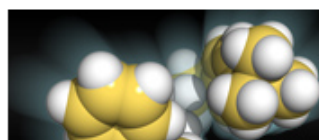
- For Academics we offer parts of the suite for free:
 - ✓ Unlimited usage of the GUI and workbook **Maestro**:
<http://www.schrodinger.com/getmaestro>
 - ✓ Free **KNIME extensions** (workflow tool)
 - ✓ Free highly parallelizable MD package **Desmond** (D.E. Shaw Research) : `Desmond@DEShawResearch.com`
 - ✓ Protein crystal structure refinement package, **Prime X**, provided free of charge until December 31, 2010:
<https://www.schrodinger.com/getprimex>
 - ✓ Back-ends licensed with academic discounts
 - ✓ Additional Teaching licenses for temporary use in educational efforts

How can you get started?

Additional information

- Schrödinger on line support available: help@schrodinger.com
- Scripts Center: <https://www.schrodinger.com/scriptcenter/>
- Schrödinger Spring 2010 Seminar Series, topics & registration:
<http://www.schrodinger.com/Spring2010Webinars.html>
- Training Videos available on line:
<http://www.schrodinger.com/supporttraining/18/>

Schrödinger Spring 2010 Seminar Series



Spring 2010 seminar series
presented by SCHRÖDINGER

The Schrödinger Spring 2010 Seminar Series features six webcast seminars on topics that cover a wide range of modeling methodologies and tools. There is no cost to attend the available to all attendees, and will also be made available to registrants who are unable to view the live events.

[English](#) : [San Francisco Time](#)

☐ Show past events

Upcoming Events

<input type="checkbox"/>	Date & Time ▼	Event	Panelist		
<input type="checkbox"/>	May 25, 2010 6:00 am	Schrödinger Suite 2010: New programs, enhancements, and features (Early time slot)	Dr. Woody Sherman - Schrödinger Vice President of Applications Science		Open
<input type="checkbox"/>	May 25, 2010 10:00 am	Schrödinger Suite 2010: New programs, enhancements, and features (Late time slot)	Dr. Woody Sherman - Schrödinger Vice President of Applications Science		Open
<input type="checkbox"/>	May 27, 2010 6:00 am	Simplifying compound docking with KNIME	Dr. Robert Happel - Boehringer Ingelheim, Vienna		Open
<input type="checkbox"/>	Jun 1, 2010 6:00 am	Getting started with PyMOL (Early time slot)	Dr. Jason Vertrees - PyMOL product manager		Open
<input type="checkbox"/>	Jun 1, 2010 10:00 am	Getting started with PyMOL (Late time slot)	Dr. Jason Vertrees - PyMOL product manager		Open
<input type="checkbox"/>	Jun 3, 2010 6:00 am	Structure-based modeling of GPCRs (Early time slot)	Dr. Thijs Beuming - Schrödinger Applications Scientist		Open
<input type="checkbox"/>	Jun 3, 2010 10:00 am	Structure-based modeling of GPCRs (Late time slot)	Dr. Thijs Beuming - Schrödinger Applications Scientist		Open
<input type="checkbox"/>	Jun 8, 2010 6:00 am	Glide development overview: Scientific advancements and performance benchmarks in Schrödinger Suite 2010 (Early time slot)	Dr. Matt Repasky - Glide product manager		Open
<input type="checkbox"/>	Jun 8, 2010 10:00 am	Glide development overview: Scientific advancements and performance benchmarks in Schrödinger Suite 2010 (Late time slot)	Dr. Matt Repasky - Glide product manager		Open
<input type="checkbox"/>	Jun 10, 2010 6:00 am	Development and validation of novel methods for generating structure-based pharmacophores using energetic analysis (Early slot)	Dr. Noeris Salam - Schrödinger Applications Scientist		Open



Resources & Downloads - Support Center

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Downloads

Sales

Script Center

Support



Seminars

KNIME Workflows

Request Logon

Log On

Overview

We are committed to providing our users with the best technical and scientific support. You may contact the Schrödinger Tech Support team by emailing help@schrodinger.com, or by calling  (503) 299-1150 .

In addition, we encourage you to take advantage of these on-line resources that are available here:

- [Docs & Known Issues](#) allow you to access all user manual and helpful information regarding known issues.
- [FAQs](#) provide answers for many of the commonly-asked questions.
- [Training Videos](#) allow you access to a series of short videos available for viewing on-line. These videos take you step-by-step through some common tasks and workflows.

Support Center Resources

Overview

- > [Docs and Known Issues](#)
- > [FAQs](#)
- > [Training Videos](#)
- > [Update User Info](#)

Resources & Downloads - Support Center

Home > Resources & Downloads > Support > **Training Videos**

Downloads

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Download Training Videos

The videos below are in Flash format. The Flash Player is available from the [Adobe](#) website. Some videos are also available in QuickTime format. QuickTime is available from the [Apple](#) website.

The following Training Videos are available for this product:

Topic (click to view)	Time	Upload date
Glide grid generation	8:28	07/16/2009
Setting up a Glide docking calculation	9:38	07/16/2009
The Glide XP Visualizer	8:34	07/16/2009

Support Center Resources

[Overview](#)

> [Docs and Known Issues](#)

> [FAQs](#)

> **Training Videos**

[Canvas](#)

Glide

[MacroModel](#)

[Maestro](#)

[Phase](#)

[PrimeX](#)

[Protein Preparation Wizard](#)

[QSite](#)

[Virtual Screening Workflow](#)

> [Update User Info](#)

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Docs and Known Issues

The following PDF Documents are available for download...

General Information 2009

- [All Documentation](#)
- [Installation Guide](#)
- [Job Control Guide](#)
- [Job Options Supported, by Product](#)
- [Known Issues](#)
- [Mopac Guide](#)
- [Protein Preparation Guide](#)
- [Running Distributed Schrödinger Jobs](#)
- [Schrödinger Utilities](#)
- [Scripting with Python](#)
- [Unix Quick Install Guide](#)
- [Windows Quick Install Guide](#)

General Information 2008

- [All Documentation](#)
- [Installation Guide](#)
- [Job Control Guide](#)
- [Job Options Supported, by Product](#)
- [Known Issues](#)
- [Running Distributed Schrödinger Jobs](#)
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- [Running Distributed Schrödinger Jobs](#)

Support Center Resources

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[General Information](#)

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Contact

katia.dekimeche@schrodinger.com

help@schrodinger.com

