# RosettaCon *Workshop* 2,007

"Bridging Industry and Academia"



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#### Presented by Rosetta Design Group

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# **ROSETTA's Origins**

In 1999, a collection of scripts and programs used to predict the tertiary structures of proteins from their primary amino acid sequences was christened "Rosetta" by David Baker and colleagues at the University of Washington in their paper entitled, "Ab Initio Protein Structure Prediction of CASP III Targets Using ROSETTA".

The Critical Assessment of Techniques for Protein Structure Prediction (CASP) is a biennial competition of computational protein structure prediction technologies that was established in 1994. In the competition, protein sequences are provided for which crystal structures have been solved but not yet released to public databases, eliminating the potential bias that arises from algorithms trained or developed to produce specific structures. The CASP competitions have always played a central role accelerating the development of Rosetta, despite the fact that the Rosetta algorithms have expanded to include functionality well beyond structure prediction.

In CASP 5, ROBETTA, an automated server developed in the Baker laboratory integrating the Rosetta algorithms with other bioinformatics software, placed first, even above predictions made by top scientists manually guiding a wide variety of algorithms. In CASP 6, ROBETTA lost the lead but rather comically, those placing above ROBETTA in the top five had used ROBETTA as the starting point for their predictions. The success of the Rosetta algorithms in accurately modeling macromolecules has led to its establishment as a benchmark for computational development in the field.

# **Development of ROSETTA**

Rosetta, the algorithms and community, grew in subsequent years, as interests in macromolecular modeling developed beyond tertiary structure prediction and post-doctoral scholars from the Baker laboratory began their own laboratories (see below).



To allow for continued collaboration, Gabrielle Campbell and colleagues in the University of Washington's Tech Transfer Office worked with the Rosetta Community to establish the Rosetta Commons consortium. The consortium is governed by an executive committee composed of the principle investigators of each laboratory. Developers in the consortium sign participation agreements with rules regarding contribution and copyright. Revenues from licensing go directly towards supporting development of the code by funding RosettaCon, an annual developers' meeting, and allowing for dedicated development support staff. This unique arrangement allows for continued innovation through combining the strengths of the open source model of development with a coherent organizational structure. Since inception of the Rosetta Commons, the Rosetta Algorithms have been widely adopted by hundreds of academic labs in more than 35 countries. Currently, there are an average of 70-80 new users per month. In addition, most of the major pharmaceutical companies have licensed the suite for drug discovery applications.

### About the Rosetta Design Group

The Rosetta Design Group LLC was founded to meet the growing need in the pharmaceutical industry for macromolecular design, consulting, software development, support, and training services, with a particular emphasis on the Rosetta software suite for macromolecular modeling.

As a participating institution in the Rosetta Commons, RDG actively contributes to the development of Rosetta and is the only company sanctioned by the Rosetta Commons to provide user support to licensees and academic users. Unlike large vendors of modeling software, RDG remains close to the leading academic researchers that fuel innovation. RDG is dedicated to ensuring that its clients have the support they need to use the complex and rapidly evolving software needed for R&D.

In addition to support, RDG provides contract R&D services involving macromolecular modeling. With formal and informal ties to academic scientists in the Rosetta Commons, considerable in-house computing power, and a standing agreement with UNC for use of its massively parallel IBM BladeCenter research computing clusters, RDG is strategically poised to solve the most challenging problems our clients may face in macromolecular modeling.

#### SCIENTIFIC ADVISORY BOARD:

**Dr. Brian Kuhlman** is an Assistant Professor in the Department of Biochemistry and Biophysics at UNC Chapel Hill. His laboratory develops and applies new technology for protein design. Their methods have been used to stabilize proteins, alter specificity in proteinprotein interactions and design completely novel protein structures. Dr. Kuhlman is the original developer of the RosettaDesign modeling software. He is a 2004 recipient of the AAAS Newcomb Cleveland Prize and the 2004 Foresight Institute prize in nanotechnology. He has recieved young investigator awards from the Searle and Beckman Foundations. He recieved his PhD in Chemistry from the State University of New York at Stony Brook.

#### MANAGING PARTNER

Dr. Xavier Ambroggio founded RDG and works to cultivate strong relationships with highly motivated individuals based on trust, respect, and mutual benefit. He joined the Commons as an NIH-NRSA postdoctoral fellow with Dr. Kuhlman at UNC, where he modified Rosetta to optimize a single amino acid sequence for multiple target structures. Also an experimentalist, he validated the new algorithms by designing a protein that undergoes a zinc-mediated transition between different folds. Dr. Ambroggio was an NSF doctoral fellow at Caltech, where he studied with Doug Rees and Ray Deshaies the structural and biochemical properties of the 19S proteasome. He received a Moore Discovery Grant for his research and a Helen G. and Arthur McCallum Fellowship prior to his NSF fellowship award. He holds a BS in biology from Mason, where he was awarded scholarships from the biology department and the Golden Key National Honor Society.

#### **EXECUTIVE ADVISOR**

Gabrielle Campbell brings a strong background in new tech management to RDG. She has managed a portfolio of over 100 emerging computational biology technologies at UW's Tech Transfer Office, handling IP protection and licensing. As a Bosch Fellow, she studied the biotech start-up environment in Germany and worked with GPC Biotech AG and the Bavarian Ministry of Economics. She completed an MBA at UW studying the management of new technologies after working in biotech. Prior moving to Seattle, she did marketing communications and lobbying for the Health Care Group of Hill and Knowlton Public Affairs Worldwide in Washington DC, where her clients were major pharmaceutical companies and non-profit research institutes. Ms. Campbell holds a BA in cell biology from U Penn.

Dr. Jeffrey J. Gray is an Assistant Professor in Chemical & Biomolecular Engineering at Johns Hopkins with a secondary appointment in the Sidney Kimmel Comprehensive Cancer Center. Dr. Gray is the original developer of RosettaDock, an algorithm for predicting the structure of protein complexes from individually determined structures. In CAPRI, an international blind prediction challenge, RosettaDock predicted several targets including some for which homology modeling was used to create the monomer structures, a breakthrough in the field. In recent work, Dr. Gray's research group predicted the mechanism of an anti-cancer therapeutic antibody that binds to endothelial growth factor receptor (EGFR). His group also works on simulation of allostery, the interaction of proteins with solid surfaces, and simulating pHdependent conformational change. Dr. Gray has been funded by NIH, the ACS, and supported by IBM and Gigatrend. He was named a Beckman Young Investigator in 2005.



# **RosettaCon2007 Academic Participants**

Laboratory of David Baker University of Washington, Seattle

> Summer Thyme Andrew Wollacott Sagar Khare John Karanicolas Vatsan Raman Lin Jiang Florian Richter Justin Siegel Chu Wang Mike Tyka David Kim Rhiju Das Sarel Fleishman Ian Davis Will Sheffler Yasuo Yoshikuni **Oliver Lange** Eric Althoff Ben Blum Bin Qian Ingemar Andre Liz Kellogg Alexandre Zanghellini **Bjorn Wallner** Daniela Röthlisberger Brian Kidd Adrien Treuille Seth Cooper Jim Havranek James Thompson Nobuyasu Koga

Laboratory of Bill Schief University of Washington, Seattle

> Andrew Ban Possu Huang Sergey Menis Chris Carrico

Laboratory of Phil Bradley FHCRC, Seattle Amy Ticoll Laboratory of Brian Kuhlman University of North Carolina Chapel Hill

> Ron Jacak Grant Murphy Doug Renfrew Andrew Leaver-Fay Jack Snoeyink Eun Jung Choi Yi Liu Deanne Sammond Gurkan Guntas

Xavier Ambroggio Rosetta Design Group, Chapel Hill

Laboratory of Jeffrey Gray Johns Hopkins University, Baltimore

Monica Berrondo Sid Chaudhury Michael Daily Ryan Harrison Eric Kim Sergey Lyskov Arvind Sivasubramanian

Laboratory of Tanja Kortemme University of California San Francisco

> Colin Smith Dan Mandell Elisabeth Humphris Greg Friedland Mariana Babor Anthony Linares Ryan Ritterson

Laboartory of Richard Bonneau New York University

> Glenn Butterfoss Kevin Drew

Laboratory of Jens Meiler Vanderbilt University, Nashville

> Kristian Kaufmann Laura Mizoue Carie Fortenberry Beth Repasky Nathan Alexander Julia Koehler David Nannemann Rene Staritzbichler Nils Woetzel

Charlie Strauss Los Alamos National Lab

Laboratory of Ora Schueler-Furman The Hebrew University, Jerusalem

> Barak Raveh Nir London

Alan Yen UW TechTransfer University of Washington, Seattle

Gabrielle Campbell Association of American Medical Colleges, Washington DC

Lars Malmstroem Goodlett lab University of Washington, Seattle

Anastassia Alexandrova Jorgensen lab Yale University, New Haven

David Anderson UC Berkeley Space Sciences Lab

Fox Chase Cancer Center Guoli Wang Roland Dunbrack

# Workshop Agenda

Workshop Agenda		THURSDAY, August 2nd, 2007			
FRIDAY, August 3rd, 2007		3:00 - 6:00 p	m Cł	neck In	
7:30 - 8:30 am	Breakfast with the Rosetta Community	6:00 - 7:00 p	$\mathbf{m} = \begin{bmatrix} Di\\ Cd \end{bmatrix}$	inner with the Rosetta	
9:00 - 9:15 am	<b>Keynote Address</b> David Baker, UW	<b>9:00 - 11:00</b> )	pm Di	rinks	
9:15 - 9:40 am	Introduction to Rosetta An Overview of Code Organization and Scientific Philosophy Chu Wang, Baker Lab, UW				
9:40 - 10:00 am	Scoring Functions and Optimization Routines Glenn Butterfoss PhD, Bonneau Lab, NYU				
10:00 - 10:25 am	<b>Protein Design with a Flexible Backbone</b> Brian Kuhlman PhD, UNC				
10:25 - 10:45 am	Juice & Coffee Break				
10:45 - 11:10 am	<b>Investigating Protein Small-Molecule Interfaces with Rosetta</b> Kristian Kaufmann, Meiler Lab, Vanderbilt				
11:10 - 11:35 am	Design of New Protein Catalysts using Rosetta Alexandre Zanghellini, Baker Lab, UW				
11:35 – 12:00 pm	Design of Novel Immunogens Bill Schief PhD, UW				
12:00 - 1:15 pm	Lunch with the Rosetta Community				
1:15 - 1:45 pm	<b>Knowledge-based Spatial Constraints in Rosetta</b> James Thompson, Baker Lab, UW				
1:40 - 2:15 pm	<b>Antibody Structure Prediction and the Use of Mutagenesis in Docking</b> Arvind Sivasubramanian PhD, Gray Lab, JHU				
2:15 - 2:50 pm	<b>The FunHunt classifier for funnel discrimination</b> Ora Furman-Schueler PhD, The Hebrew University				
2:50 - 3:10 pm	Juice & Coffee Break				
3:10 - 3:40 pm	Making Directed Libraries Using Rosetta Gurkan Guntas PhD, Kuhlman Lab, UNC				
3:40 - 4:15 pm	<b>Protein Interface Design</b> Tanja Kortemme PhD, UCSF	SATUR 7:30 - 8	<b>SATURDAY, August 4th, 2007</b> <b>7:30 - 8:00 am</b>		
4:15 - 4:45 pm	On-the-fly Energy Calculations in Protein Interface Design	8:00	am	Rosetta Community Box Lunch Pick-Up	
4:45 - 5:00 pm	Closing Remarks	8:00 - 11	:00 am	Check Out / Hike Departure	
	Aavier Amoroggio PhD, UNC, KDG	12:00 - 1	:00 pm	Lunch for Stragglers	
6:00 - 7:30 pm 9:00 - 11:00 pm	Dinner with the Rosetta Community Drinks & Snacks on the Terrace	1:00 - 1	:30 pm	Departure for Stragglers	

# Your Stay at Sleeping Lady



We look forward to welcoming you as our guest. To ensure you feel at home during your stay with us, we've provided the following information about our site. Please do not hesitate to contact us at 800-574-2123 if you have any questions.

- Check-in time is 3:00 p.m.; Checkout is 11:00 a.m.
- Our **Registration Desk** and **Gift Shop** are staffed 24 hours a day and look forward to serving you.
- We have a **non-smoking policy** indoors and out. Guests not adhering to the policy will be charged a minimum of \$150. Please help us keep Sleeping Lady smoke-free.
- Due to the four seasons we experience and our natural environment we recommend **business casual attire** and **non-slip footwear**. High heels are strongly discouraged.
- Sleeping Lady is a walking site. Please park your **vehicles** in the guest parking lot. No motor vehicles may be driven on site. A wheelchair is available upon request.
- Luggage carts are available directly outside the main office for the convenience of our guests.
- The **Woodland Rock Pool** is open 24 hours a day seasonally (mid April-September) and the adjoining **hot pool** is open year round. Both are accessible via your room key. Swimsuits are required.
- The **Sauna** and cold plunge is open 24 hours a day.
- If you would like to schedule a **massage**, please call us at the number above. 24-hour advance reservation is recommended.
- **Grasshopper Fitness Center** adjacent to the Sauna building is open 24 hours a day and is accessible via your room key.
- Roki, our resident Icelandic Sheep Dog will likely welcome you upon your arrival or make your acquaintance some time during your stay. Those with pet allergies should note that Sleeping Lady also hosts a resident cat, Kiska. Dog lovers Ask about our Canine Companion Program.
- There are **no televisions** in our guest rooms. We invite you to take our self guided art walk, a leisurely stroll down by the river or through our organic garden. We offer **seasonal equipment rental** including snowshoes, cross-country skis, bicycles and trail passes and information on the seemingly endless recreational opportunities surrounding our site.
- There are **telephones**, wireless and dial up Internet access in all the guest rooms and meeting spaces.
- Our friendly barkeep at **The Grotto Bar** keeps the music and beverages flowing, with wine, beer, spirits and soft drinks to choose from. Open daily at 4:30 10:00 p.m., or later at the barkeep's discretion.
- **Dining Hours**: Dinner is served from 6-7 p.m. Breakfast, 7:30-8:30 a.m. weekdays, 8-9 a.m. weekends. Lunch is served from noon-1 p.m. All meals are served in the Kingfisher Dining Lodge.
- **O'Grady's Pantry,** offers in between meal snacks, espresso, a wide selection of teas and juices, as well as a fine collection of Northwest wines, beers and spirits.



#### **OFFICE & GIFT SHOP** 1.

Registration and guest services include check-in desk, gift shop, management office, and faxing and copying. Adjacent luggage depot offers carts for guests to transport luggage to rooms and bicycles for guest's rental.

MERGANSER 2.

Administrative offices.

3 FLICKER

Comfortable meeting cabin with space for up to 40.

WOODPECKER 4.

Seats up to 150. Built in audio-visual system.

CHIHULY'S "ICICLES"

Dale Chihuly's blown glass sculpture, dedicated in December 1996, is his only permanent outdoor installation.

**KINGFISHER DINING LODGE & TERRACE** 6.

Menus feature Northwest cuisine with an international flair and offer fresh seasonal herbs, complimented by vegetables and fruits grown in the organic garden. Meals served buffet style. Breakfast starting at 7:30, lunch at 12, dinner at 6:00. Saturday & Sunday breakfast at 8:00.

#### **RIVER MEADOW** 7.

Barbecue and picnic area. Outdoor stage for seasonal performances.

FIRE CIRCLES 8.

One circle is located behind Kingfisher Dining Lodge overlooking the Icicle River, another is adjacent to the office and the third is outside of the Grotto Bar.

#### 9. **CHAPEL THEATER & SALMON GALLERY** A 185-seat performing arts theater. A grand piano, audiovisual conference equipment, a 12-foot projection screen and meeting/dressing rooms. The Salmon Gallery has a fireplace

and piano, and accommodates receptions for up to 180. NUTHATCH 10.

Cozy meeting cabin with wood stove and space for up to 30.

11. ROCK CLUSTER #100-109

Ten units with private baths in a setting of granite boulders. Each unit sleeps 2-4

12. GROTTO BAR

An evening gathering place around a rocky fireplace for guests to relax over wine, beer and spirits. Seats 35. Seasonal outdoor beer garden and fire circle.

13. SOFT DRINK & ICE MACHINE

#### 14. ROOKERY #157

On Woodpecker Hill, this cabin accommodates up to eight in a large room with double-decker beds. Two showers.

15. EYRIE #158

On Woodpecker Hill, this secluded lookout cabin features a king-size bed, one queen Murphy bed, wood stove, whirlpool bath and refrigerator.

#### 16. WOODLAND ROCK POOLS

Up the hill in a clearing is the boulder-lined swimming pool and year-round hot pool. Extra towels in Sauna House.

**17. DANCE** 

A meeting space accommodating up to 60.

#### 18. SAUNA & MASSAGE ROOM

Relax in the sauna or schedule a massage. This cabin has a sitting room and an outdoor, screened terrace with a cold plunge pool. Open 24 hours. Towels provided.

#### 19. OUAIL

Quail features state-of-the-art AV equipment, a wood stove, and seats up to 125. Large windows frame the mountains.

#### 20. TADPOLE

Tadpole features state-of-the-art AV equipment, a wood stove, and seats up to 80. Large windows look out on pond, meadow and mountains.

#### 21. FOREST CLUSTER #151-156

These three cabins have two units each, all with private baths. Each unit sleeps 2-4. One wheelchair accessible unit.

22. LIBRARY & GUEST COMPUTER WORKSTATION Lined with hand-crafted bookshelves, this cozy cabin has a wood stove and comfortable seating. Curl up with a book.

#### 23. POND CLUSTER #140-149

Ten units with private baths. Each unit sleeps 2-5. A pond extends into the courtyard.

#### 24. FOUNTAIN CLUSTER #130-139

Ten units with private baths. Each unit sleeps 2-5. Includes two connecting units and a wheelchair accessible unit. Built around a Tsutakawa fountain.

#### 25. TSUTAKAWA FOUNTAIN

Gerard Tsutakawa's water sculpture is a cast bronze column within the courtyard pool of Fountain Cluster. Forms and symmetry in nature provide the inspiration for this artwork.

#### 26. MEADOW CLUSTER #120-129

Ten units with private baths. Each unit sleeps 2-5. Includes two connecting units and a wheelchair accessible unit.

#### 27. DIPPER

Cozy meeting cabin with wood stove and space for up to 30.

28. COTTONWOOD CLUSTER #110-119 Ten units with private baths. Each unit sleeps 2-5.

#### 29. ORGANIC GARDEN

Seasonal produce for Kingfisher Dining Lodge. Guests are welcome to visit the garden.

#### **30. O'GRADY'S PANTRY**

The Pantry, at the entrance to Sleeping Lady, sells espresso, soups, salads, sandwiches, ice cream and other desserts from Kingfisher Dining Lodge, seasonal produce and flowers from our organic garden, beer, wine, and spirits.

#### 31. FITNESS ROOM & COIN LAUNDRY

Features cardiovascular, weight and stretching equipment, coin operated washer and dryer, changing rooms and shower. Open 24 hours, use room key for access.

#### 32. ICICLE BROADCASTING CO. Home of KOHO radio, 101.1 FM, local music and news

station for Leavenworth and Central Washington.

**PUBLIC TELEPHONES** are located at the entrances to Kingfisher Dining Lodge, the main office, and the rear entrance to the Salmon Gallery.

#### **VOLLEYBALL AND HORSESHOES**

Located near the organic garden entrance. Equipment is available at the front desk.

#### 7375 Icicle Road, Leavenworth, WA 98826

e-mail: info@sleepinglady.com www.sleepinglady.com





(509) 548-6344 • (800) 574-2123 • Fax (509) 548-6312



SLEEPING LADY MOUNTAIN RETREAT

T he music of her rivers, the fragrance of her trees and the mystery of her rocks, combine to welcome visitors and restore the human spirit.





# Map & Driving Directions

#### Directions

#### From Seattle via Interstate 90

Travel east on Interstate 90 past Cle Elum. Take the Wenatchee Exit 85 Go east on State Rt. 970 for 11.9 miles to US 97. Follow Highway 97 north over Blewett Pass for 35 miles to the junction of Highway 2. Turn left and travel west on Highway 2 for 5.6 miles through downtown Leavenworth to the west edge of town. Turn left on Icicle Road (just before milepost 99) and travel approximately 2.5 miles and past the Leavenworth National Fish Hatchery. Turn left into Sleeping Lady. Do not follow the major curve to the right which leads into Icicle Canyon.

#### From Seattle via Highway 2

Travel north on Interstate 405 from Seattle/Bellevue to Bothell where it meets Highway 522 east to Monroe. Head east on Highway 2 for 85 miles over Stevens Pass to the west boundary of Leavenworth. Turn right on Icicle Road. Follow directions above.

#### From Spokane via Interstate 90

Travel west on Interstate 90 to the junction of Highway 281 near George. Travel north on Highway 281 to Quincy. Turn left on Highway 28 and travel west to Wenatchee to Highway 2. Travel on Highway 2 to the west boundary of Leavenworth. Turn left on Icicle Road. Follow directions above.

#### From Portland, Oregon

Take I-5 north to Seattle. Go east on I-90 over Snoqualmie Pass. Past Cle-Elum follow signs to US-97 and Wenatchee over Blewett Pass. Turn left on Hwy 2 and travel 5 miles to Leavenworth. At the west end of town turn left on Icicle Road. Follow directions above. An alternative is Hwy 2 over Stevens Pass.

#### Want to know the road conditions before you go?

Find pass conditions, construction reports, and other transportation information on the traffic by clicking on <u>HTTP://traffic.WSDOT.WA.Gov/Sno-info/</u>

#### Airports

Sea-Tac International Airport is located south of Seattle and is 131 miles from Sleeping Lady. A wide range of airline carriers provides service to this international hub. Pangborn Memorial Airport in East Wenatchee is located 34 miles from Sleeping Lady. Horizon Airlines provides five direct flights per day between Seattle and East Wenatchee.

