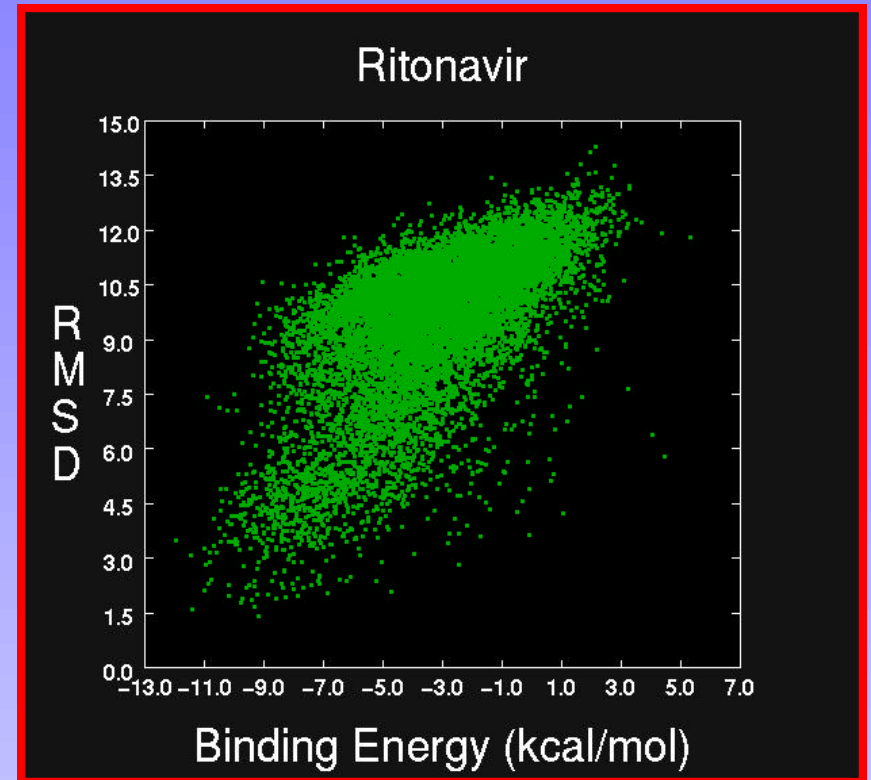
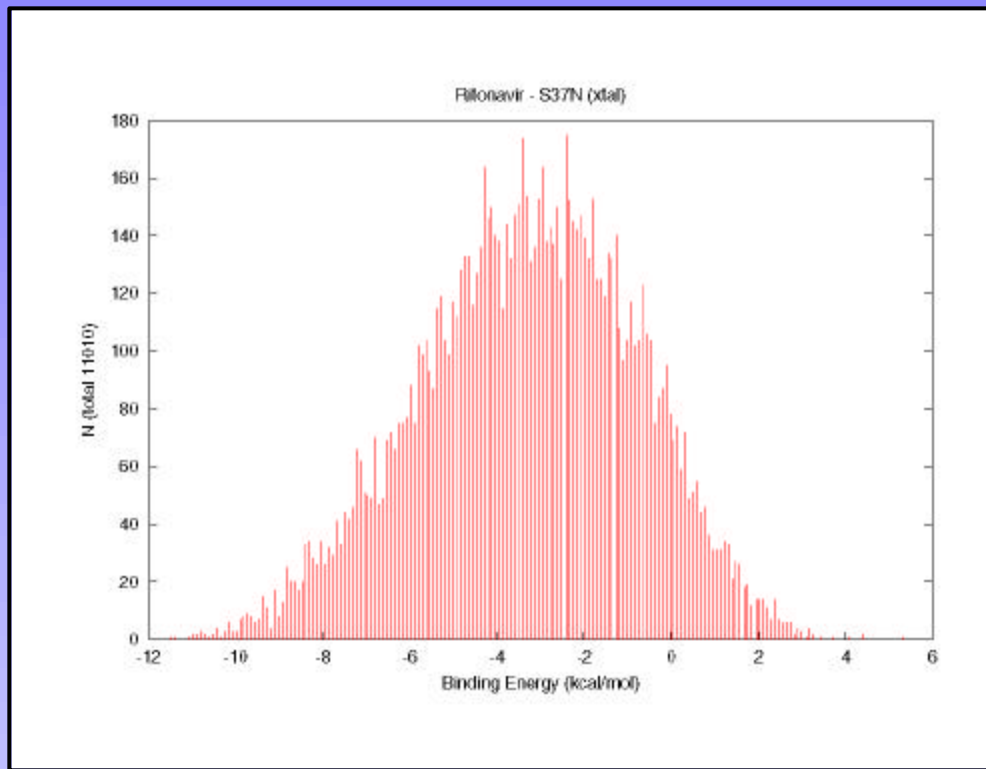


# Evaluating the Resistance-evading Potential of HIV Protease Inhibitors

William Lindstrom, David Goodsell, Garrett Morris and Arthur Olson

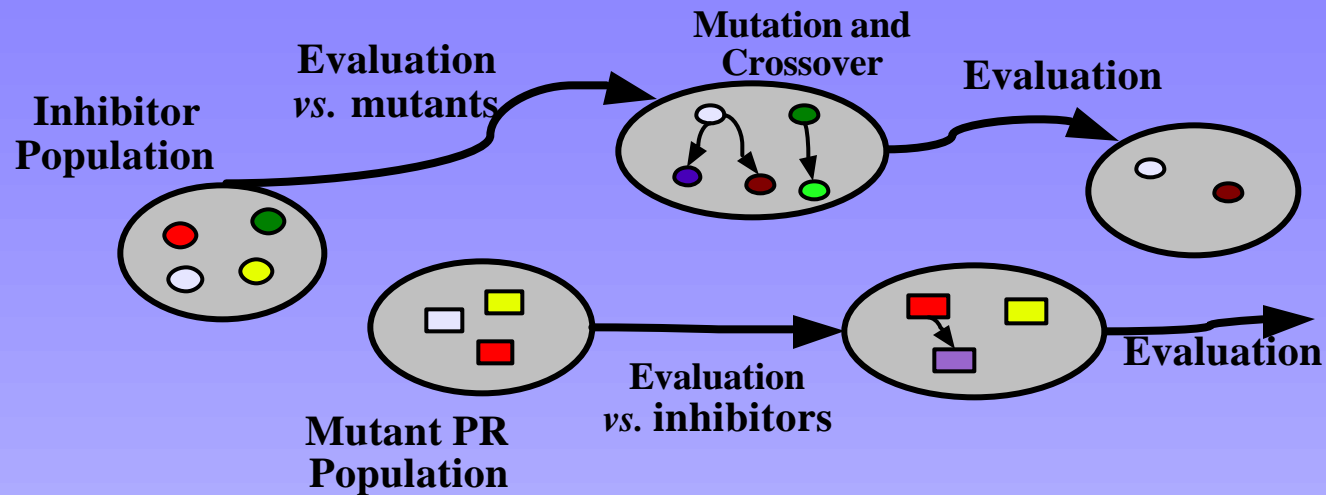
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# Ritonavir Redocking



? The relatively normal distribution of energies indicates that in this case most dockings terminated before convergence.

# Coevolutionary Strategy



- ? Diverse populations of inhibitors and PR mutants "compete" iteratively.
- ? Selection for inhibitor with minimax optimal activity with respect to mutant PR population.
- ? Fitness derived from volume?based binding free energy model of inhibitors and substrates.
- ? Rosin *et al.* (1999) *Proc. Natl. Acad. Sci. USA* **96**, 1369.

# Distributed Computing Architecture



AutoDockTools  
Entropia API  
Database Access  
Docking Database

Specification  
and Analysis



Task  
Server



Volunteer PCs  
running  
AutoDock

- ? 49,000 client downloads
- ? Performance: ~ 1000x SGI workstation
- ? Local distributed clustering analysis