

## System

different topologies,  
initial coordinates,  
constraint and FEP  
tag files

Complex

Ligand

## Thermodynamic State

$\lambda = 0.0$

$\lambda = \lambda + \Delta$

$\lambda = 1.0$

$\lambda = 0.0$

$\lambda = \lambda + \Delta$

$\lambda = 1.0$

## Replica

different initial  
velocities

$r_1$

$r_2$

$r_5$

$r_1$

$r_2$

$r_5$

$r_1$

$r_2$

$r_5$

$r_1$

$r_2$

$r_5$

$r_1$

$r_2$

$r_5$

$r_1$

$r_2$

$r_5$