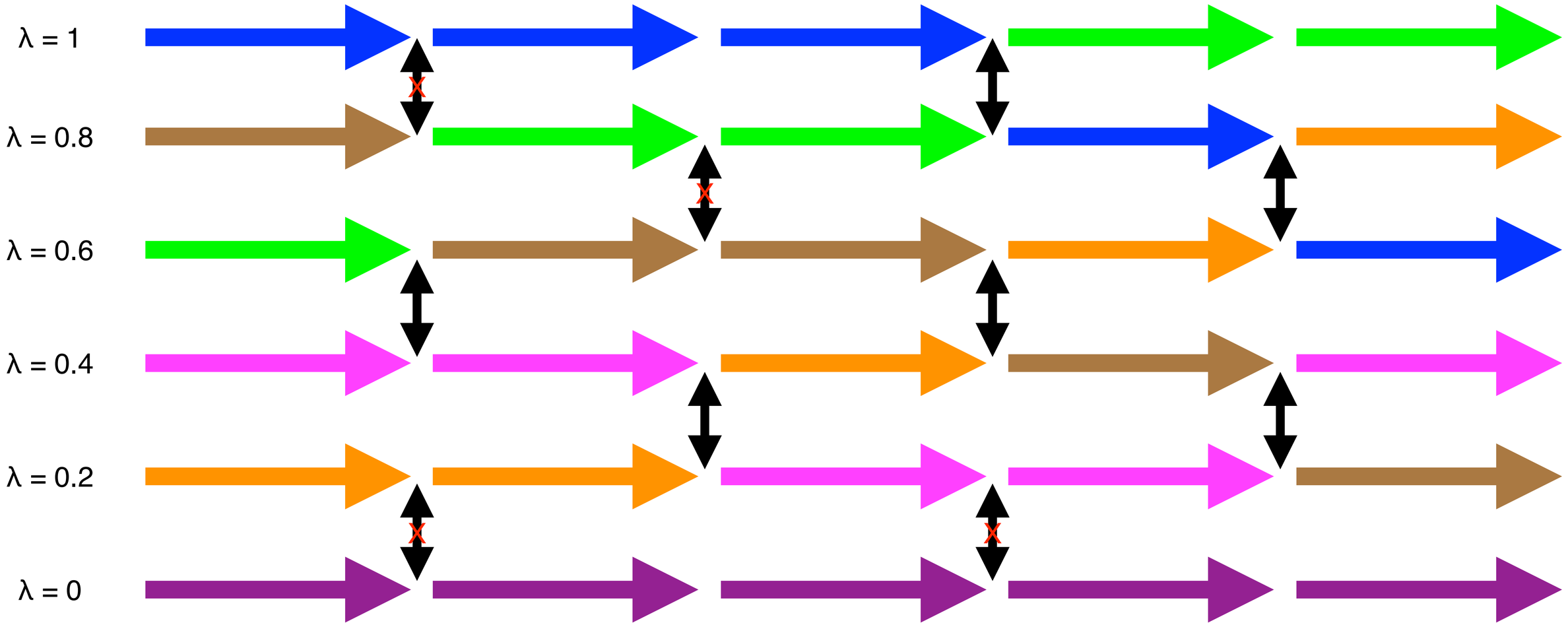
4/7/2020 Week 12 Module 1
Analysis of Binding Free Energy Calculations

- This module will consist of
  - a mini-lecture describing how YANK does free energy calculations
  - a description of how to analyze free energy calculations with YANK
- At the end of this module, you should also be able to analyze a binding free energy calculation with YANK

How does YANK work?

- YANK performs alchemical binding free energy calculations
- The thermodynamic cycles
  - include
    - complex phase: decoupling the ligand from the receptor and solvent
    - solvent phase: coupling the ligand with bulk solvent
  - are described here: http://getyank.org/latest/theory.html
- It uses several specialized algorithms
  - Thermodynamic states are coupled by replica exchange: configurations from different thermodynamic states are periodically exchanged
  - Equilibration time is automatically estimated based on the sum of potential energies in all states. http://getyank.org/latest/algorithms.html#automated-equilibration-detection
  - Free energies are computed with the multistate Bennett acceptance ratio (MBAR). http://getyank.org/latest/algorithms.html#analysis-with-mbar
  - These and others are described here: http://getyank.org/latest/algorithms.html

Replica exchange



Analysis with YANK

- See http://getyank.org/latest/analysis.html#analysis-usage
- You can perform automatic analysis with
  - yank analyze --yaml={Some YAML file which ran with ``yank script``}

```
ccb:[~/YANK]: yank analyze --store=/home/bxie4/restraint_simulation/YANK/TEST_SYSTEMS/bromodomain/3mxf/40flat_output_rep
eat1/experiments
/home/bxie4/local/miniconda3/lib/python3.6/site-packages/openmmtools/multistate/__init__.py:75: UserWarning: Warning: op
enmmtools.multistate API is experimental
  warnings.warn('Warning: openmmtools.multistate API is experimental')
/home/bxie4/local/miniconda3/lib/python3.6/site-packages/yank/multistate/utils.py:253: FutureWarning: Using a non-tuple
sequence for multidimensional indexing is deprecated; use `arr[tuple(seq)]` instead of `arr[seq]`. In the future this wi
ll be interpreted as an array index, `arr[np.array(seq)]`, which will result either in an error or a different result.
  equilibrated_data = cast_data[slc]
Free energy            :    99.786 +- 0.005 kT (59.489 +- 0.003 kcal/mol)
DeltaG solvent         :    99.786 +- 0.005 kT

Enthalpy               :   100.720 +- 0.034 kT (60.045 +- 0.020 kcal/mol)
```

Analysis with YANK

- You can also generate a simulation report in the form of a jupyter notebook
  - yank analyze report --store={experiments} --output={mynotebook.ipynb} {--format ipynb}
  - Let's look at examples
    - https://github.com/choderalab/yank/blob/master/Yank/reports/YANK_Health_Report_Example.ipynb
    - https://github.com/daveminh/Chem456/blob/master/static_files/tutorials/bromodomains-YANK/3mxf.ipynb