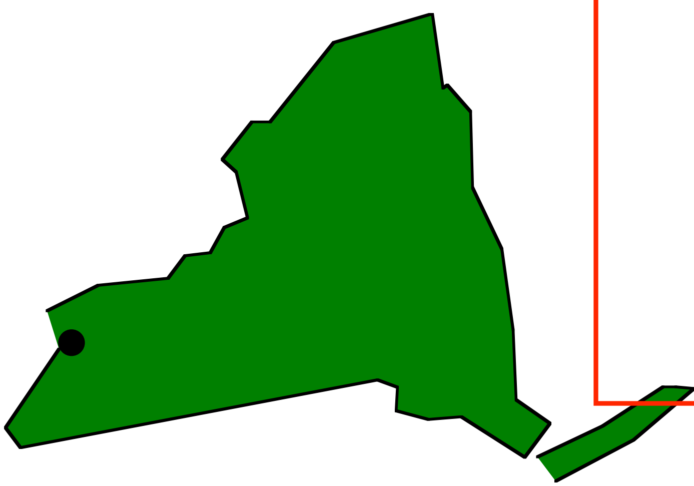
On bias in free-energy calculations, and some free-energy methods for crystalline phases



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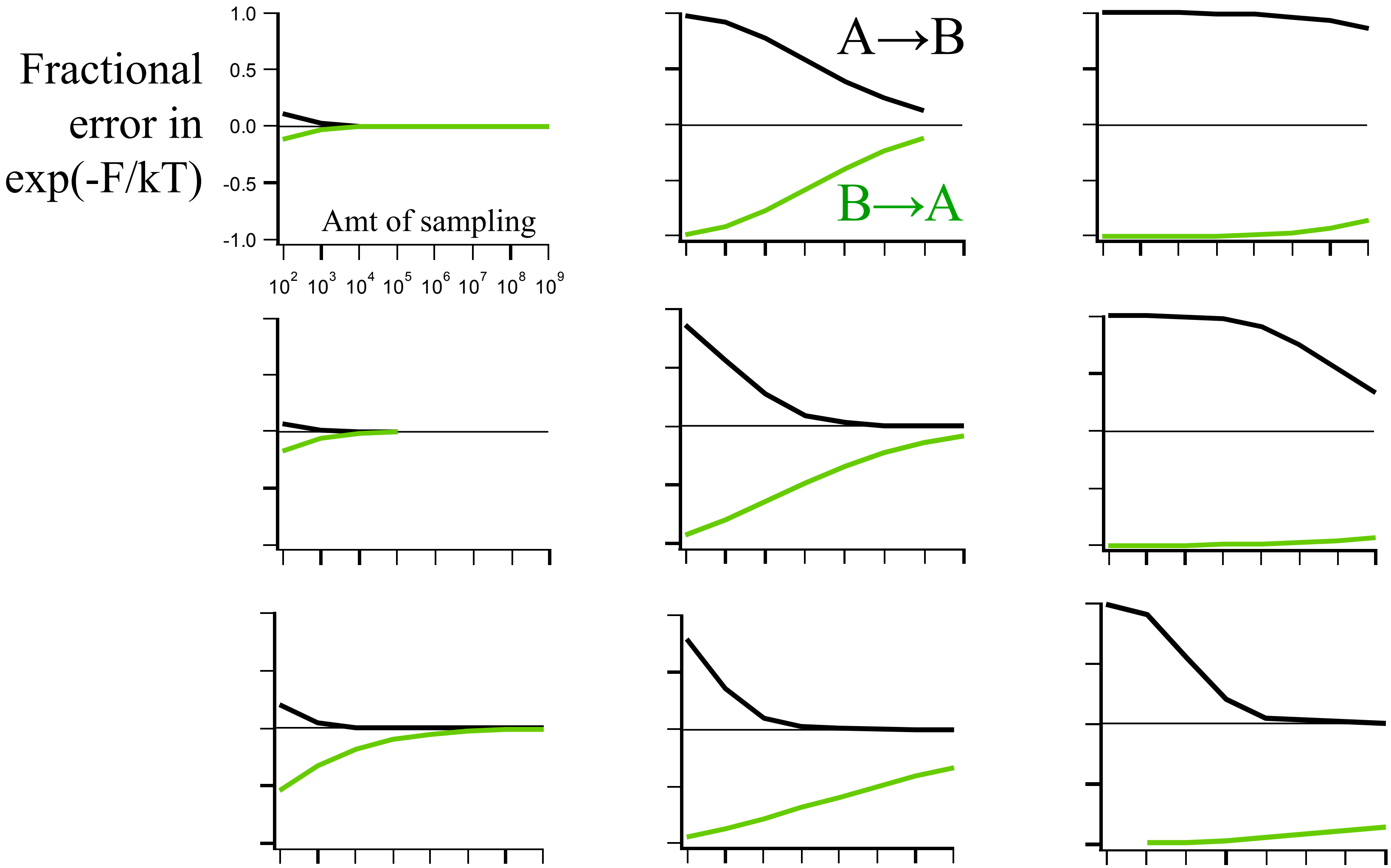
Outline

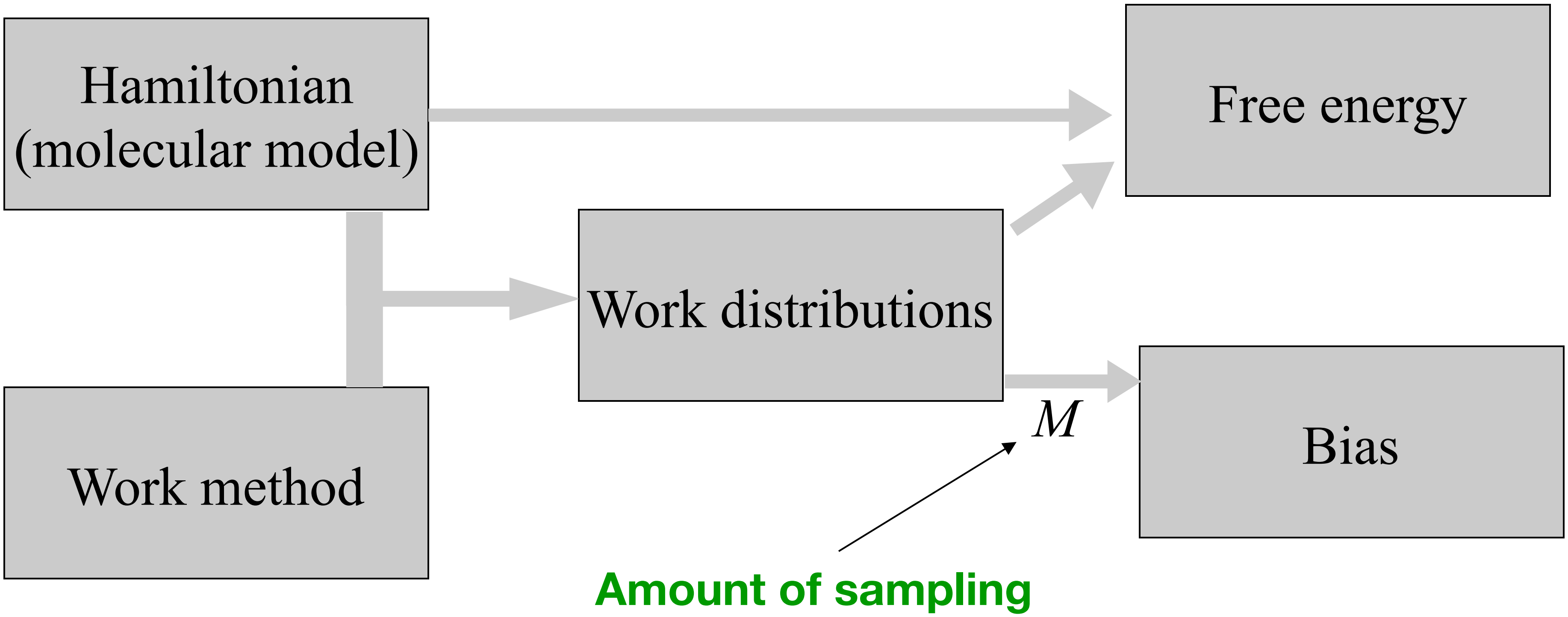
- Bias in free-energy calculations
  - Neglected-tail bias model
  - Neglected-sample bias model
  - Overlap sampling (BAR) and work distributions
- Some methods for solid phases
  - Harmonically-targeted temperature perturbation (HTTP)
  - NPT simulations

The Problem

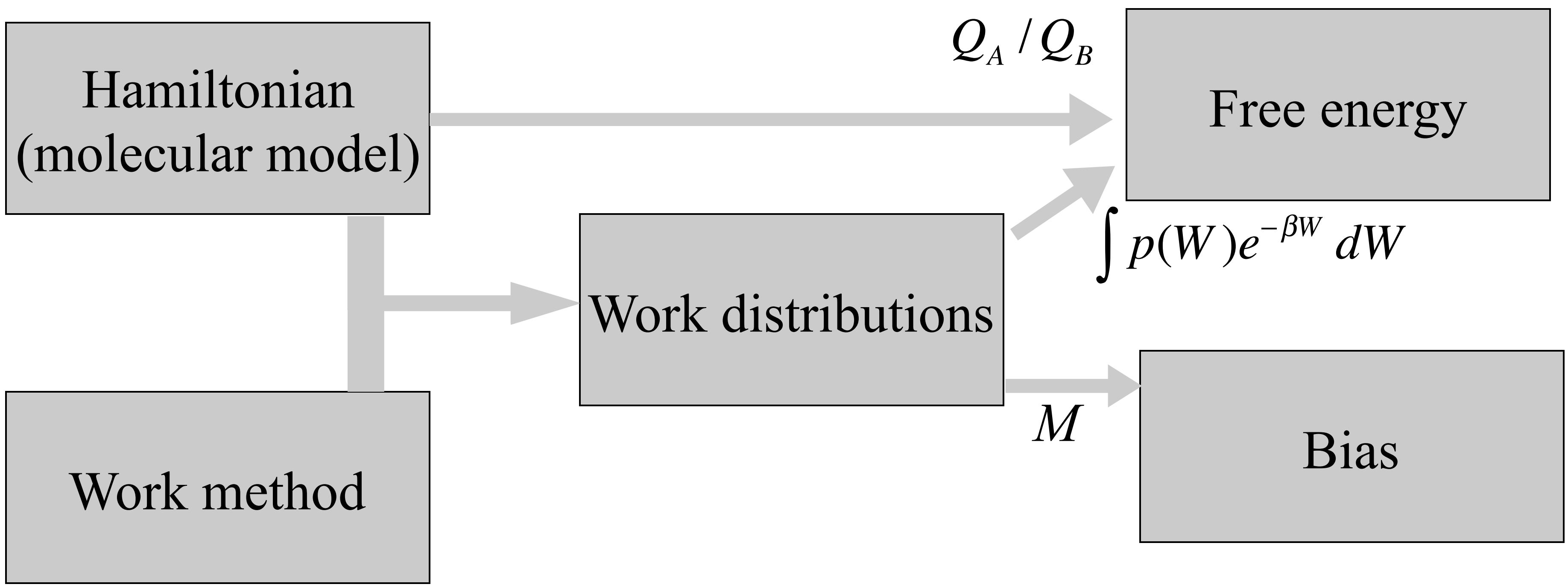
- Bias in work-based free energy calculations
  - Asymmetric, hard to detect, many different cases can be found



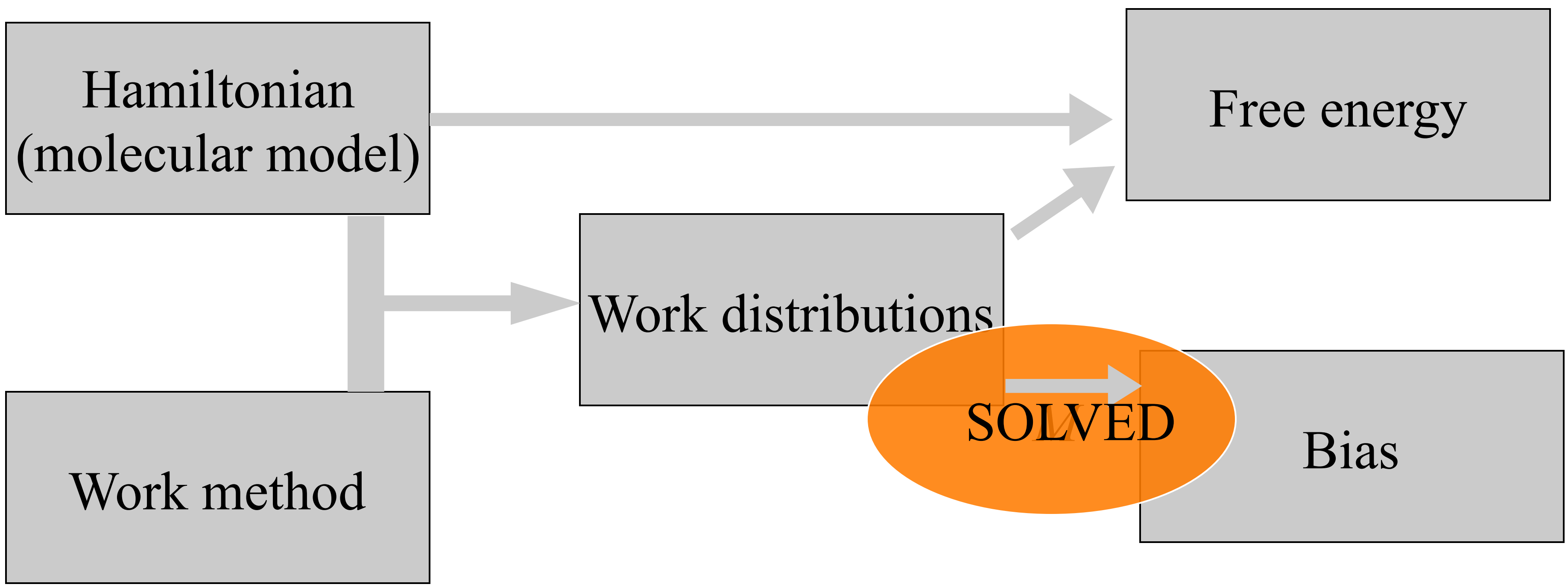
Modeling of Bias



Modeling of Bias

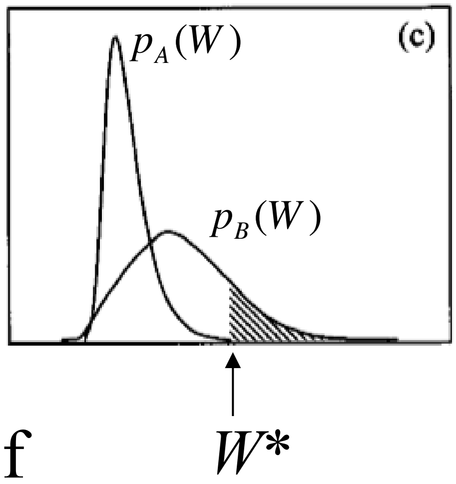


Modeling of Bias



Neglected-Tail Bias Model

- Begins with work distributions
- Assumes all error results from failure to sample tail past a specific point
  - Otherwise perfect sampling
- Tail cutoff determined by maximization of probability expression
  - Value depends on amount of sampling, *M*
- Care taken to be effective in both small- and large-sampling regimes
  - Many models apply only to large-sampling regimes

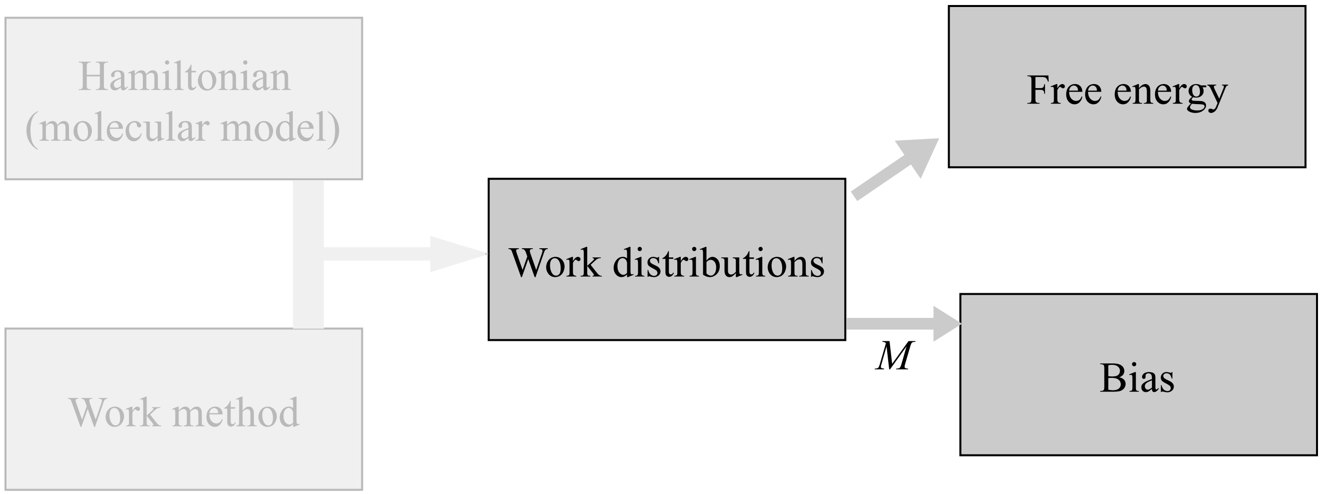


$$P_A(W^*) = Mp_A(W^*)\left[C_A(W^*)\right]^{M-1}$$

N. Lu & DAK, *JCP*, **114**, 7303 (2001)
D. Wu & DAK, *PRE*, **69**, 057702 (2004)

Example: Weibul work distribution

- Models work distribution directly



$$p_A(W) = \frac{q}{\Omega^\delta} \left| W - W_c \right|^{\delta - 1} \exp\left[- \frac{(W - W_c)^\delta}{\Omega^\delta} \right]$$

PRL **107**, 060601(2011)

"It is important to have a quantitative estimate of the bias…but no reliable analytical theory exists"

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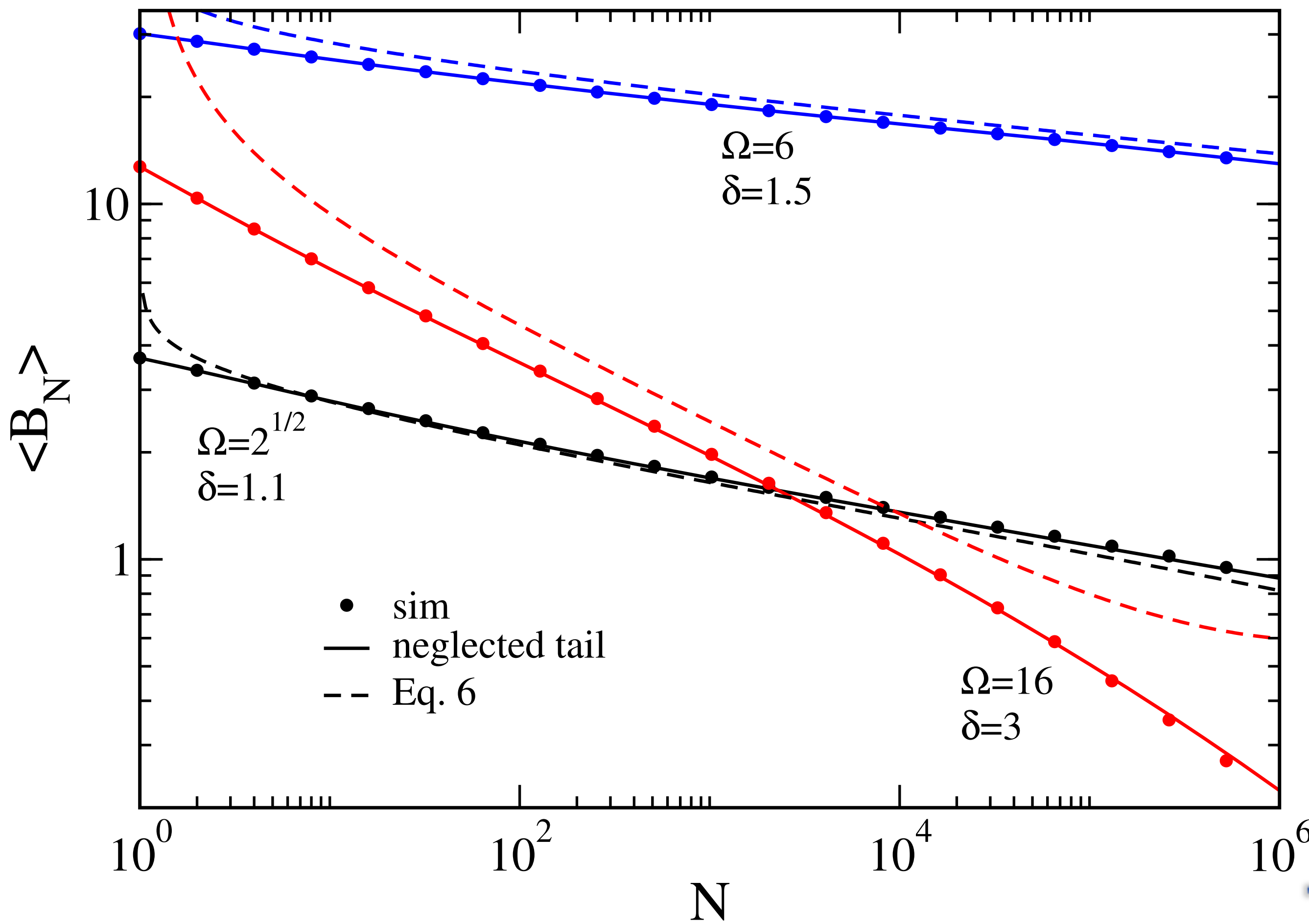
Example: Weibul work distribution

- Predicting the bias

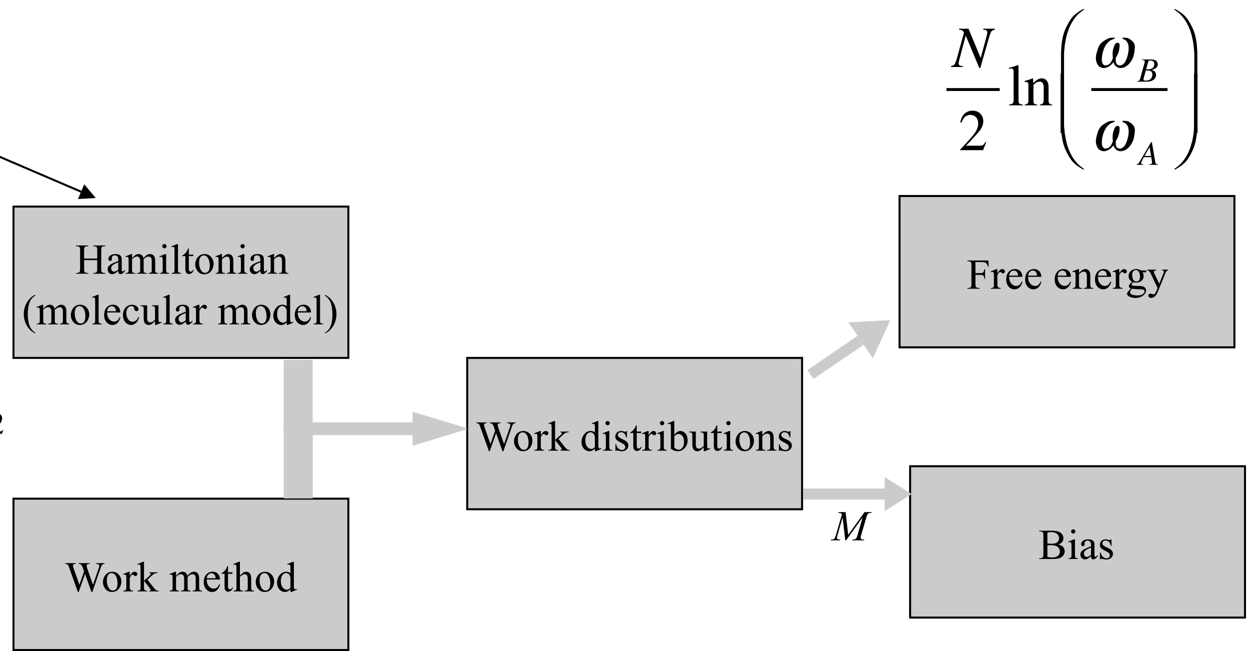


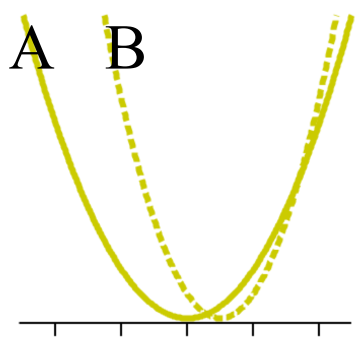
Independent Harmonic Oscillators (IHO)

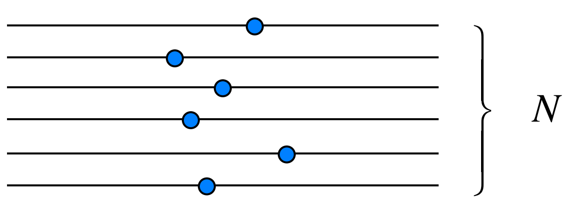
N independent harmonic oscillators

$$U_A(\Gamma) = \omega_A \sum_{j=1}^{N} x_j^2$$

$$U_B(\Gamma) = \omega_B \sum_{j=1}^{N} (x_j - x_o)^2$$







Single-stage free energy perturbation

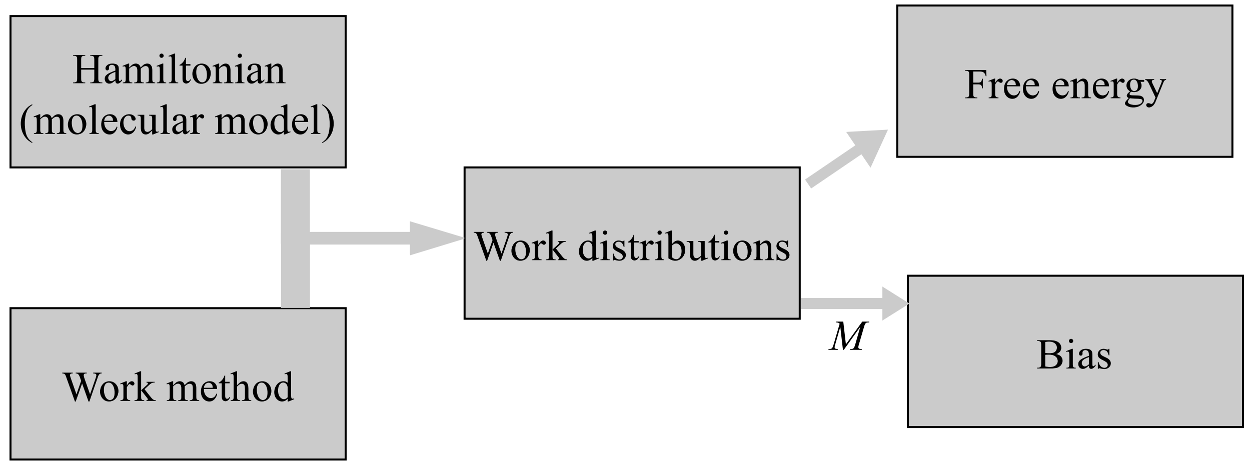
- Many properties analytically tractable
- Very easy to sample uncorrelated configurations

IHO - Work Distributions

$$U_A(\Gamma) = \omega_A \sum_{j=1}^{N} x_j^2$$

$$U_B(\Gamma) = \omega_B \sum_{j=1}^{N} (x_j - x_o)^2$$

FEP



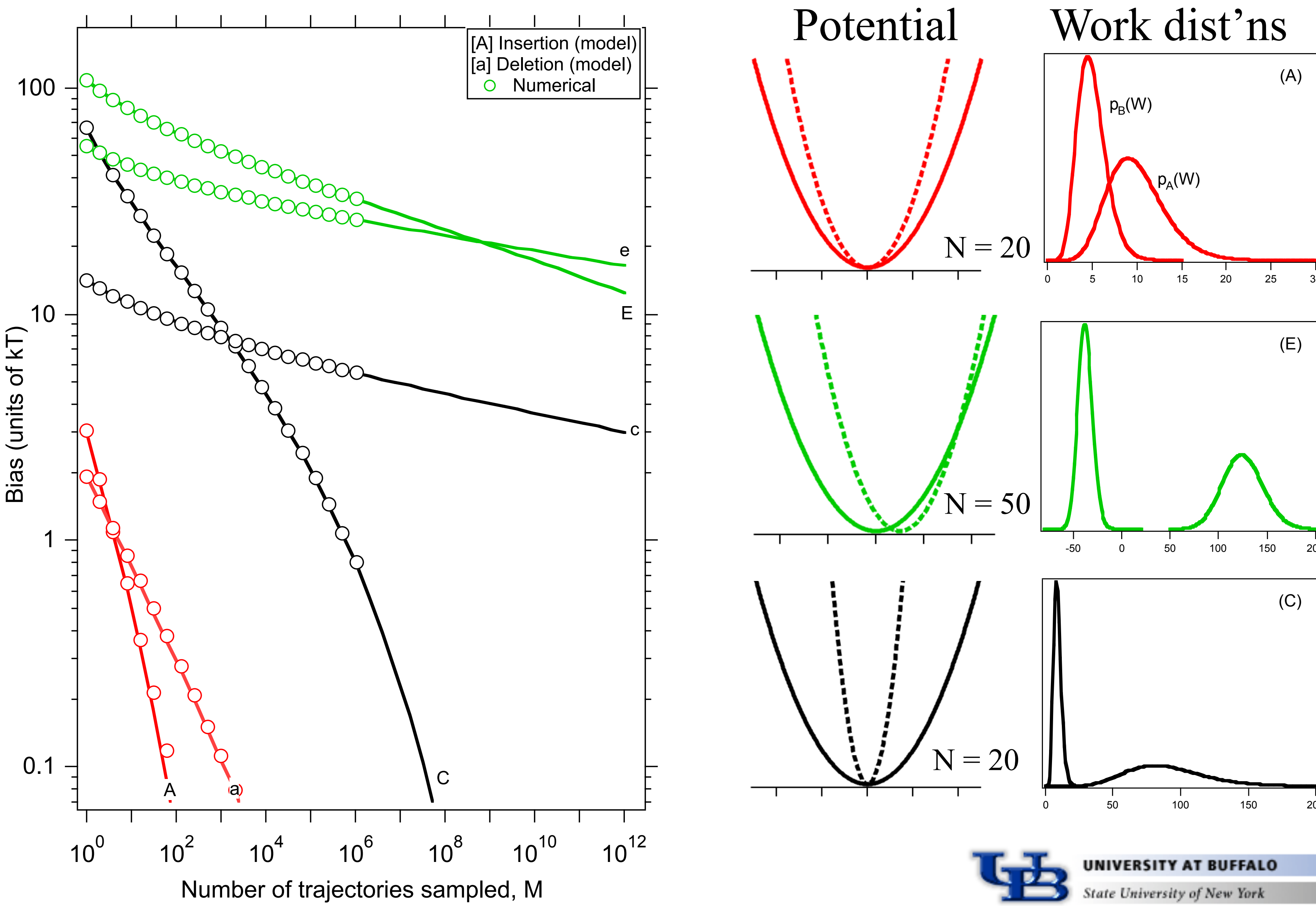
$$p_A(W) = \frac{\beta\omega_A/\omega_B}{1-\omega_A/\omega_B}\left[D(W)\right]^{\frac{N-2}{4}} \exp\left(-\frac{\beta\omega_A N x_o^2\left(1+D(W)\right)}{\left(1-\omega_A/\omega_B\right)^2}\right) I_{\frac{N}{2}-1}\left(\frac{2\beta\omega_A N x_o^2\sqrt{D(W)}}{\left(1-\omega_A/\omega_B\right)^2}\right)$$

$$p_B(W) = \exp\left(-\beta W + \beta\Delta F\right) p_A(W)$$

$$D(W) \equiv \frac{\omega_A}{\omega_B} + \frac{W}{\omega_B N x_o^2}\left(1-\frac{\omega_A}{\omega_B}\right)$$

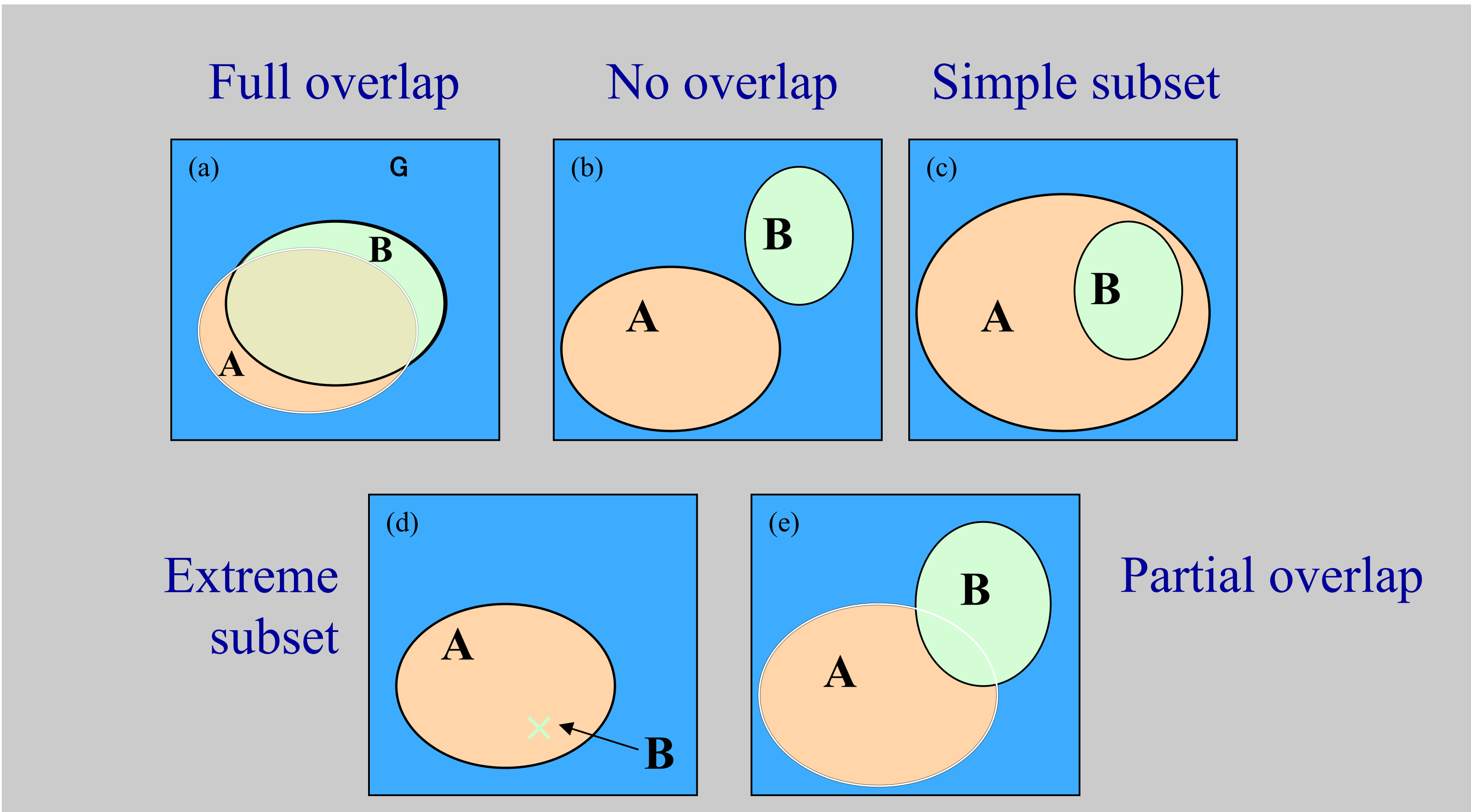
D. Wu & DAK, *PRE* **70**, 066702 (2004)

IHO - Bias


[A] Insertion (model)
[a] Deletion (model)
Numerical
Bias (units of kT)
100
10
1
0.1
10^0
10^2
10^4
10^6
10^8
10^{10}
10^{12}
Number of trajectories sampled, M
e
E
c
C
A
a
Potential
Work dist'ns
N = 20
N = 50
N = 20
(A)
$p_B(W)$
$p_A(W)$
(E)
(C)

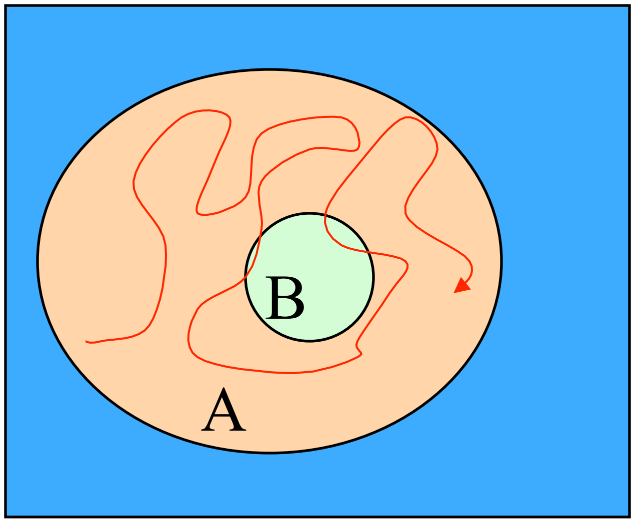
Phase-space Relations

- Two phase spaces relevant to free-energy calculations
  - Possible relations for systems "A" and "B"
  - "Typical" and "dominant" trajectories in NEW calculations



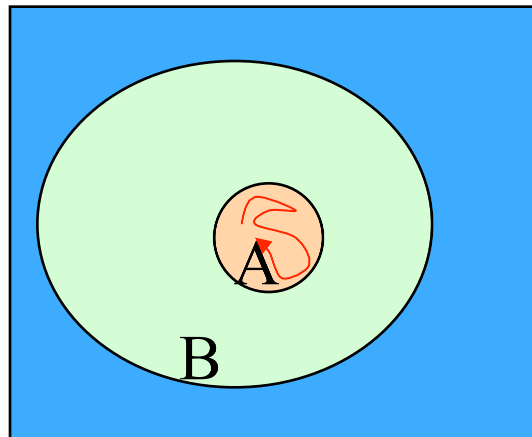
Origin of the Asymmetric Bias

- Asymmetry in phase space relations connects to asymmetry in bias
- Both spaces must be sampled at once
- Possible if subset

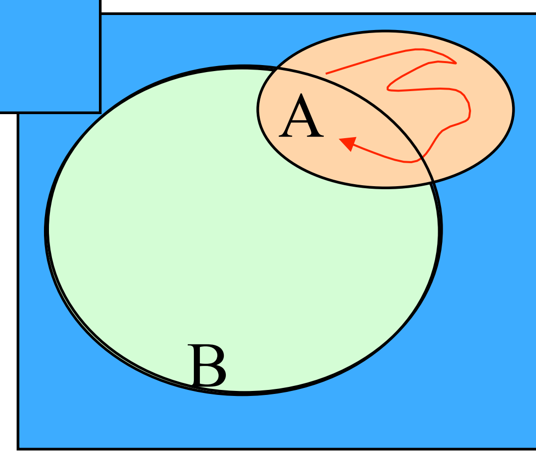


- Must have subset relation!

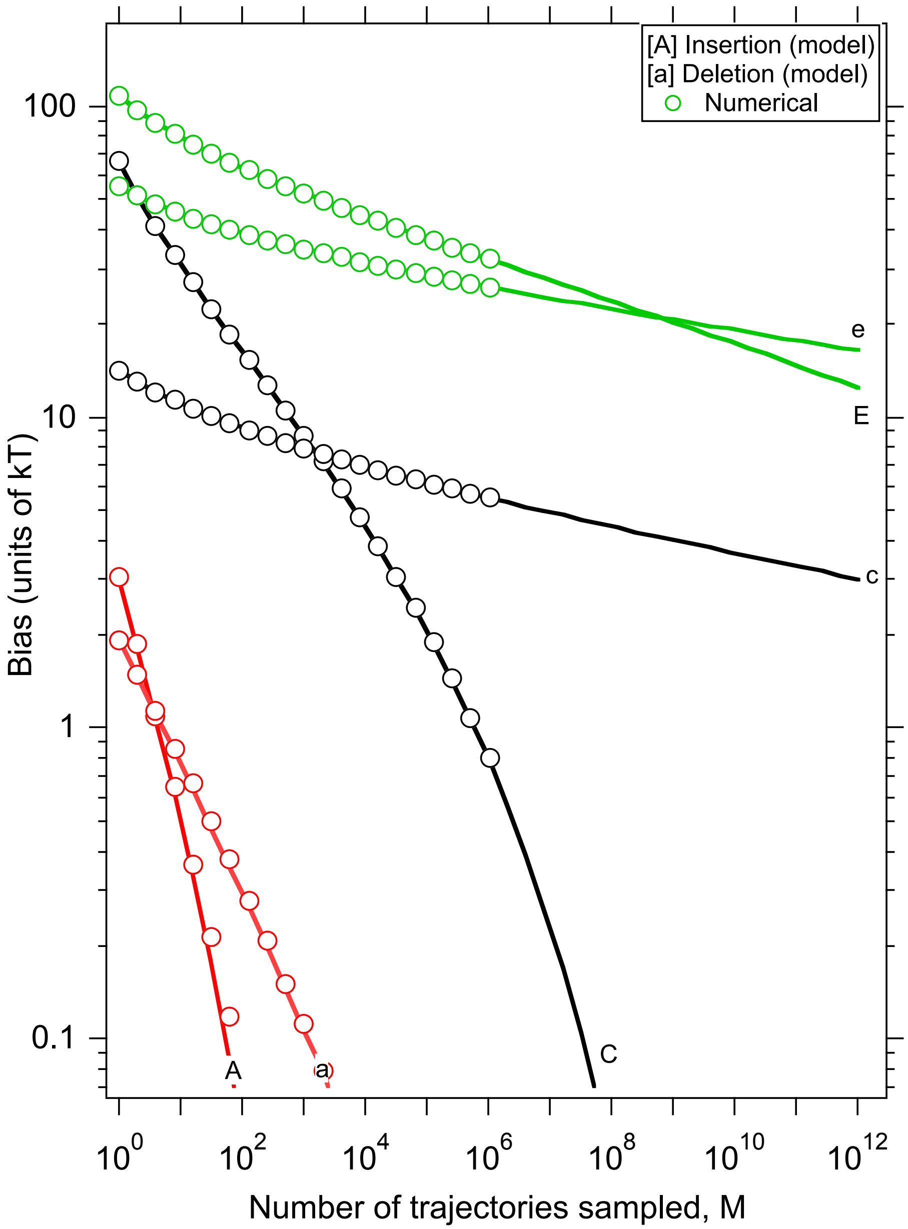
- Fails if non-subset

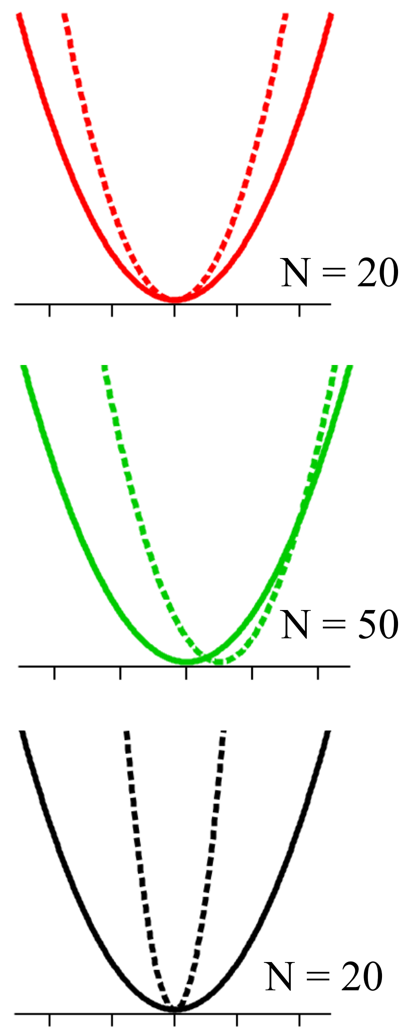


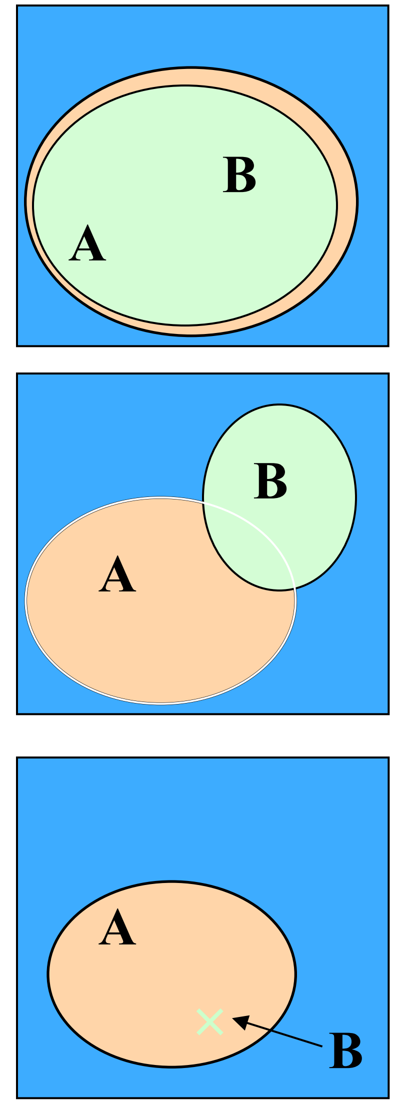
- Overlap is not enough!



IHO - Phase Space







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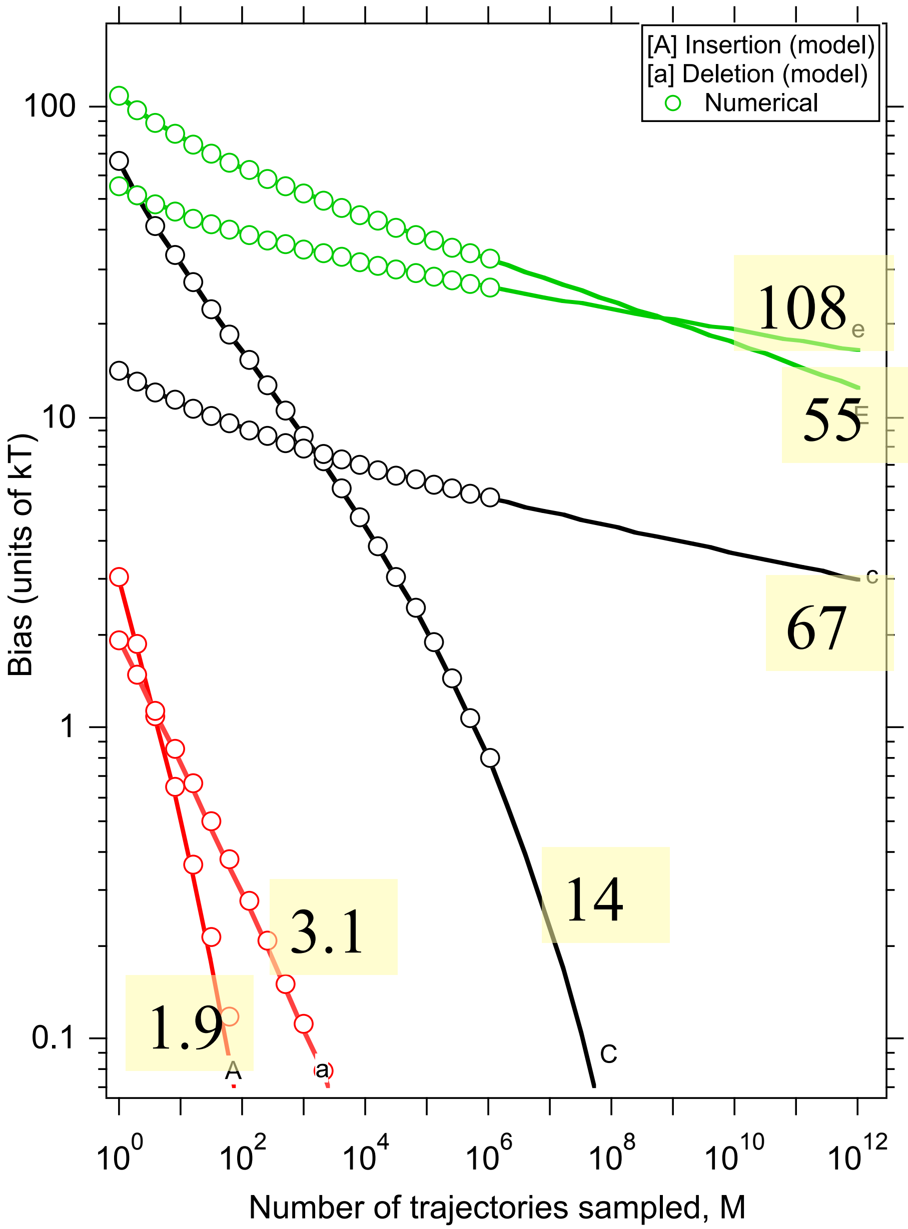
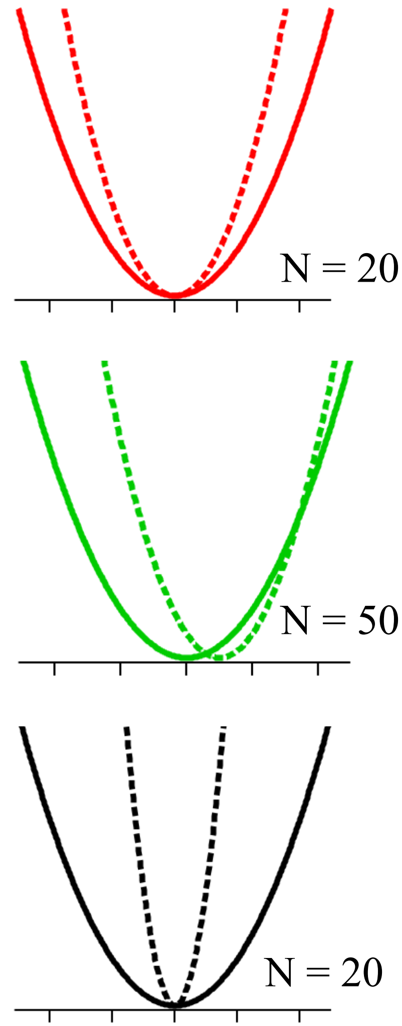
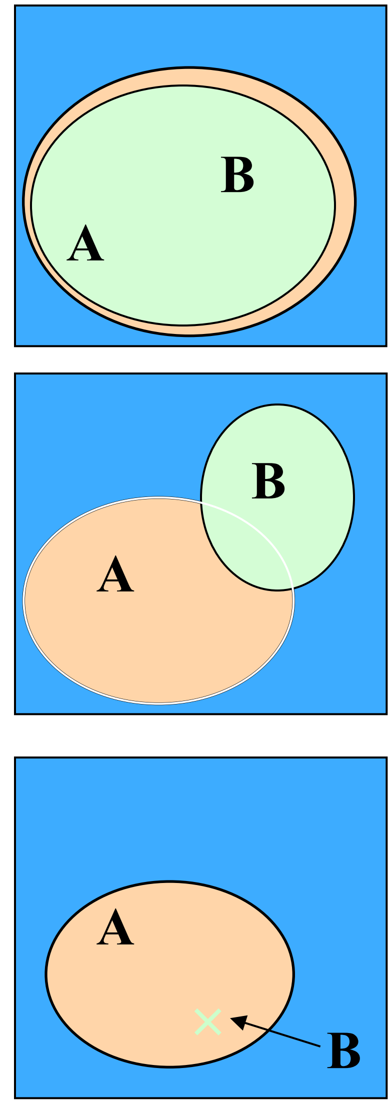
IHO - Relative Entropy







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Bias Estimation

- Neglected-tail model requires knowledge of work distributions
- Can we use neglected-tail concept to estimate bias in practice?

$$e^{-\beta(F_B-F_A)} = \int_{-\infty}^{\infty} dW\, e^{-\beta W} p_A(W)$$

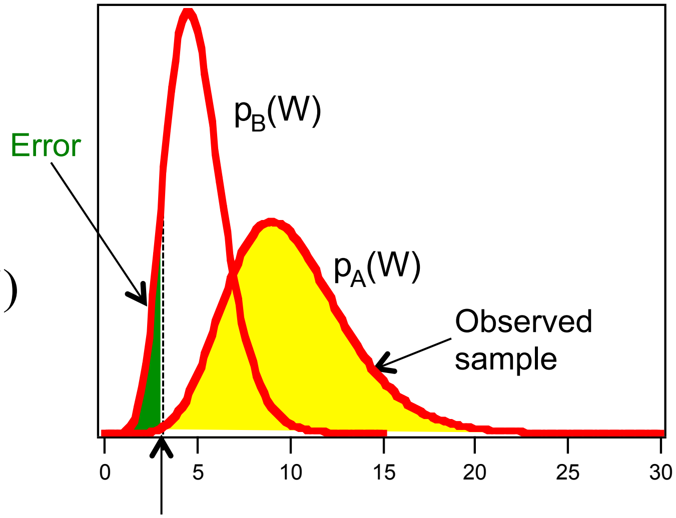
$$= \int_{-\infty}^{W_A^*} dW\, e^{-\beta W} p_A(W) + \int_{W_A^*}^{\infty} dW\, e^{-\beta W} p_A(W)$$

$$= e^{-\beta \Delta F} \int_{-\infty}^{W_A^*} dW p_B(W) + \left\langle e^{-\beta W} \right\rangle_A$$

$$e^{-\beta \Delta F} \left(1 - C_B(W_A^*)\right) = \left\langle e^{-\beta W} \right\rangle_A$$

$$e^{-\beta \Delta F} = \left\langle e^{-\beta W} \right\rangle_A \Big/ \left(1 - C_B(W_A^*)\right)$$

Biased average   Correction



W_A^*

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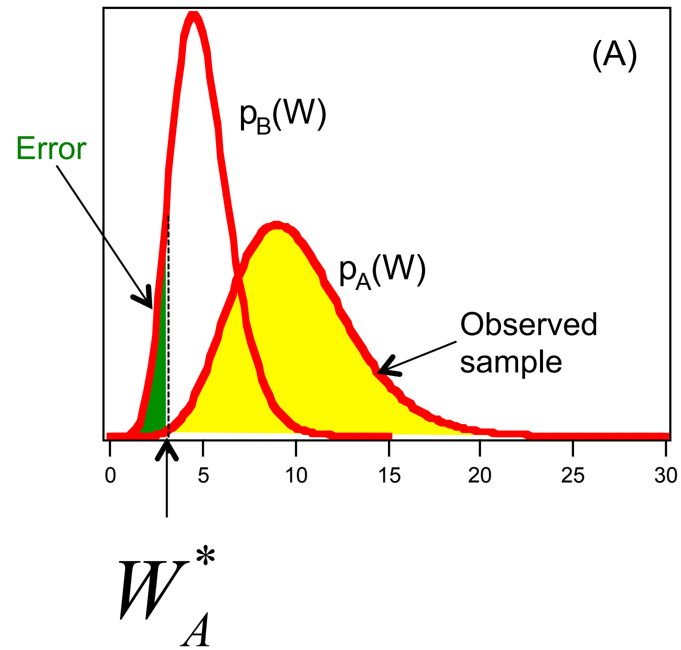
Bias Correction

- Measure perturbation average,

$$\left\langle e^{-\beta W} \right\rangle_A$$

…which may be biased

- Note the lowest work value observed, $W_A{}^*$
- Perform perturbations in opposite direction
- Note fraction of work values that are less than $W_A{}^*$, C_B
- Estimate unbiased average via



$$e^{-\beta(F_B - F_A)} = \left\langle e^{-\beta W} \right\rangle_A \Big/ \left(1 - C_B(W_A^*)\right)$$

Bias Correction - More General

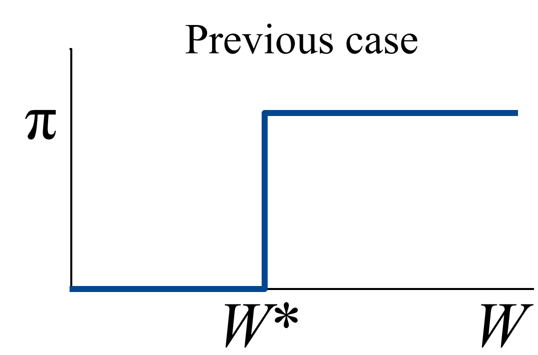
- General weight function

$$e^{-\beta\Delta F} = \int_{-\infty}^{\infty} dW\, e^{-\beta W} p_A(W)$$

$$= \int_{-\infty}^{\infty} dW\, e^{-\beta W} p_A(W)\big(1-\pi(W)\big) + \int_{-\infty}^{\infty} dW\, e^{-\beta W} p_A(W)\pi(W)$$

$$= e^{-\beta\Delta F}\left\langle\big(1-\pi\big)\right\rangle_B + \left\langle \pi e^{-\beta W}\right\rangle_A$$

$$e^{-\beta\Delta F} = \left\langle \pi e^{-\beta W}\right\rangle_A \Big/ \left\langle \pi \right\rangle_B$$



- …leads to Bennett's method on optimizing π!

Neglected-Sample Bias Model

- Let a single sample represent bias due to neglect of tail
  - When performing perturbation, consider the most important configuration in the system being perturbed into
  - Calculate the free energy in the normal way, but also calculate the free energy assuming that you also sampled that most important configuration once.
  - Take the difference between those results as an estimate of the bias.

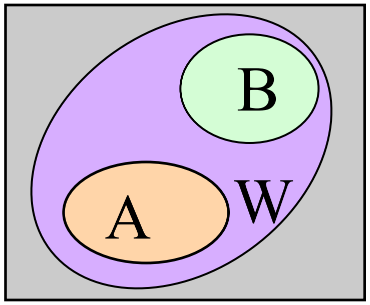
$$e^{-\beta(F_B - F_A)} = \frac{1}{M+1}\left[\sum_{i=1}^{M} e^{-\beta W_i} + e^{-\beta W_{\min}}\right]$$

Neglected-Sample Bias Model

- Does not rely on some characteristic of the calculation (distribution, rate of convergence, etc) to indicate "difficulty"
- When the calculation is abnormally unbiased, bias estimate will be small, or even negative
- Bias estimate will decay with 1/N
- Bias might persist after bias estimate vanishes due to very unlikely configurations with large contributions
- More on this later…

Staging Methods

- Optimal umbrella-sampling potential

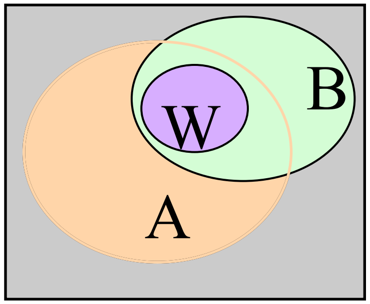


$$e^{-\beta U_W} = \left[e^{-\beta(U_A - F_A)} + e^{-\beta(U_B - F_B)} \right]$$

"Enveloping distribution"

$$e^{-\beta \Delta F} = \frac{\left\langle e^{-\beta(U_B - U_W)} \right\rangle_W}{\left\langle e^{-\beta(U_A - U_W)} \right\rangle_W}$$

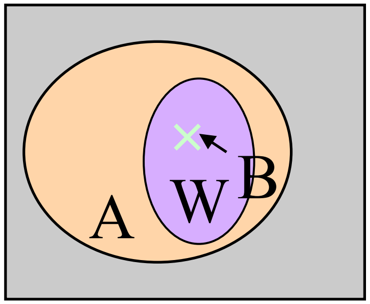
- Optimal overlap-sampling potential
  - Bennett's acceptance ratio



$$e^{-\beta U_W} = \left[e^{+\beta(U_A - F_A)} + e^{+\beta(U_B - F_B)} \right]^{-1}$$

$$e^{-\beta \Delta F} = \frac{\left\langle e^{-\beta(U_W - U_A)} \right\rangle_A}{\left\langle e^{-\beta(U_W - U_B)} \right\rangle_B}$$

- Optimal funnel-sampling potential
  - Optimal form impractical
    - involves solution to cubic polynomial
  - Useful nonetheless
    - non-optimally

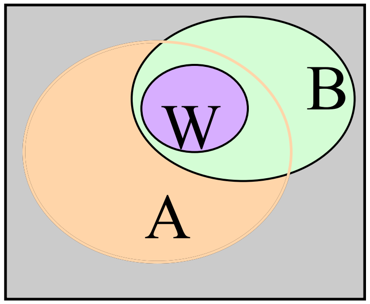


$$e^{-\beta \Delta F} = \left\langle e^{-\beta(U_W - U_A)} \right\rangle_A \left\langle e^{-\beta(U_B - U_W)} \right\rangle_W$$

Overlap Sampling

- Working equation

$$e = e^{-\beta U}$$

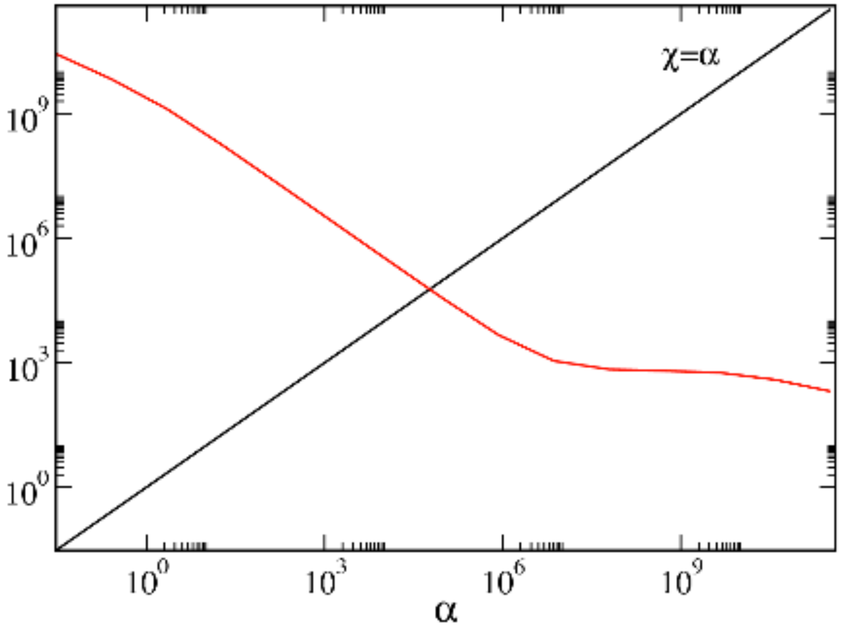


$$e^{-\beta \Delta F} \equiv \chi(\alpha) = \frac{\left\langle e_B / \left(e_A + \alpha e_B\right)\right\rangle_A}{\left\langle e_A / \left(e_A + \alpha e_B\right)\right\rangle_B}$$

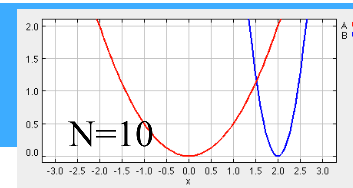
- Bennett's optimization of α:

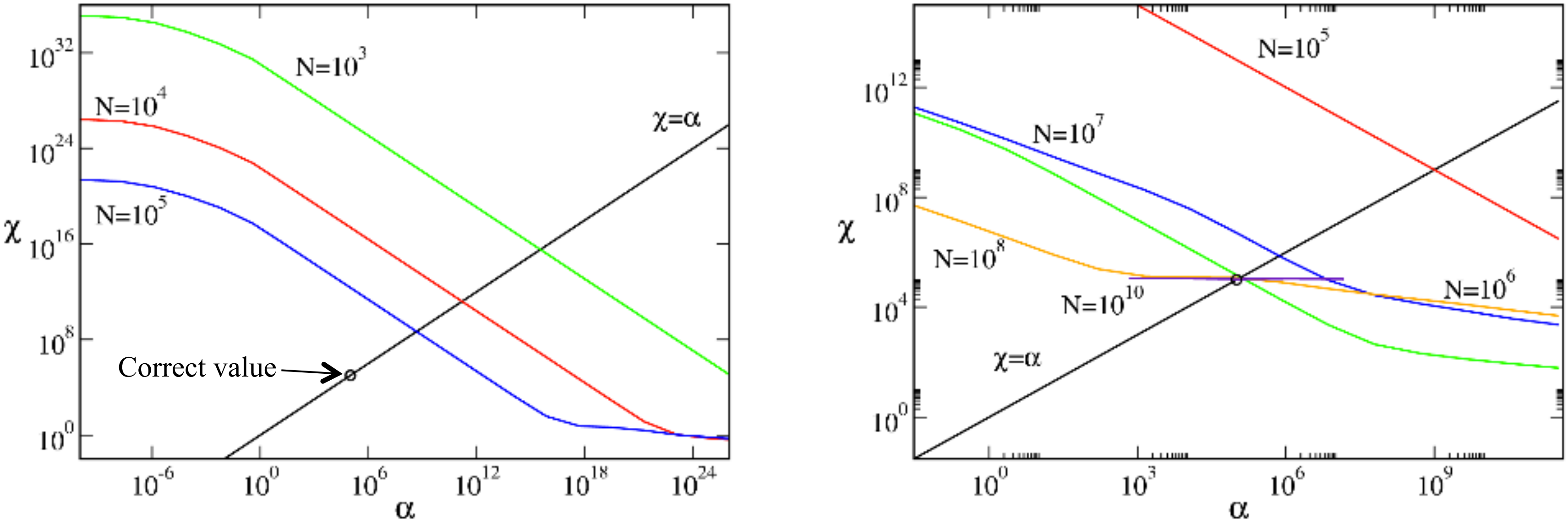
$$\alpha = \frac{n_B}{n_A}\chi$$

  – With enough samples, χ is independent of α, plot is flat

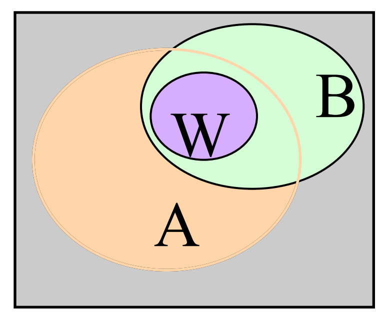


Overlap Sampling

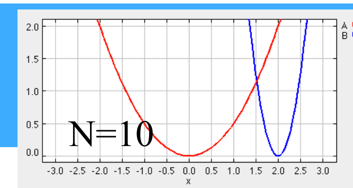




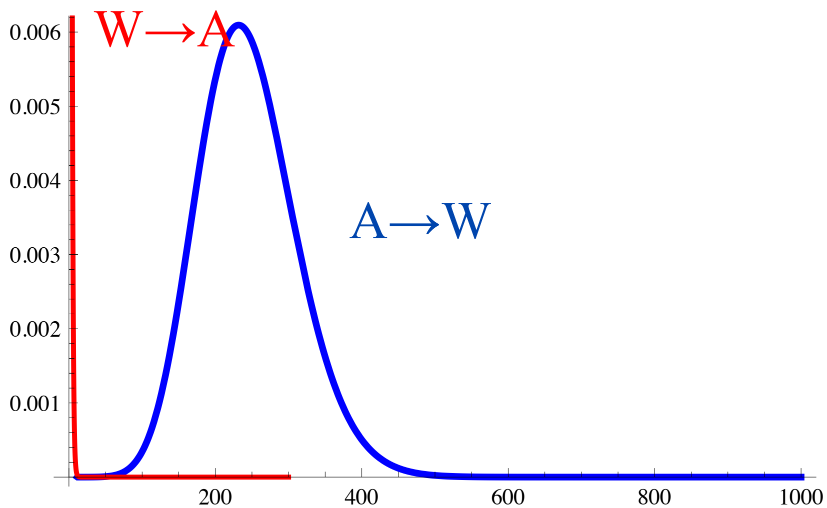
- For few samples, χ vs α is very straight line with slope -1
- With increasing samples, χ becomes flatter, but not yet flat even at 10^8 samples
- Flatness indicates that all parts of overlap region are properly sampled

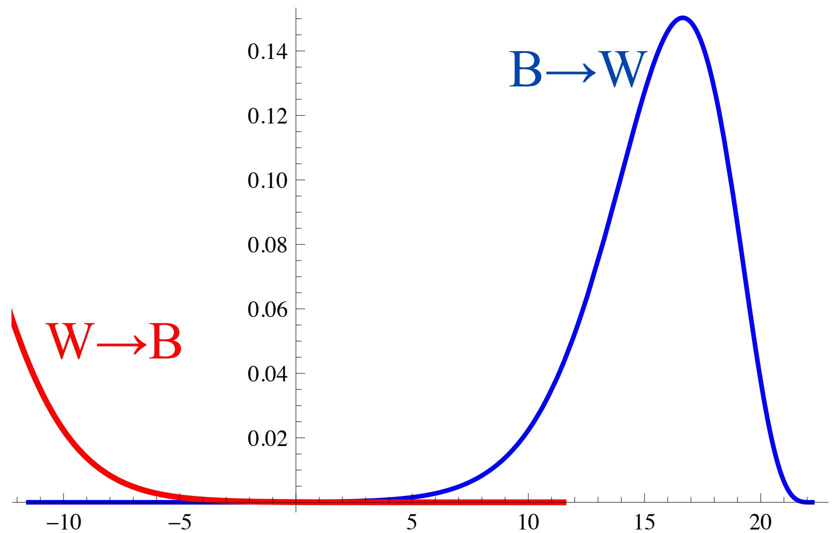


Overlap Sampling - Bias



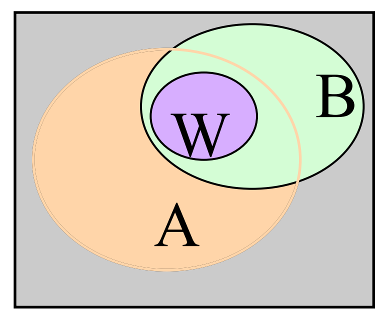
- Apply neglected-tail bias model to each stage
  - A→W and B→W work distributions evaluated analytically from A→B distribution





$$W_{AW}(W_{AB}) = kT\ln\left[1+\gamma e^{\beta W_{AB}}\right]$$

$$p_{AW}(W_{AW}) = p_{AB}\left(W_{AB}(W_{AW})\right)\frac{dW_{AB}}{dW_{AW}}$$



- Application is underway

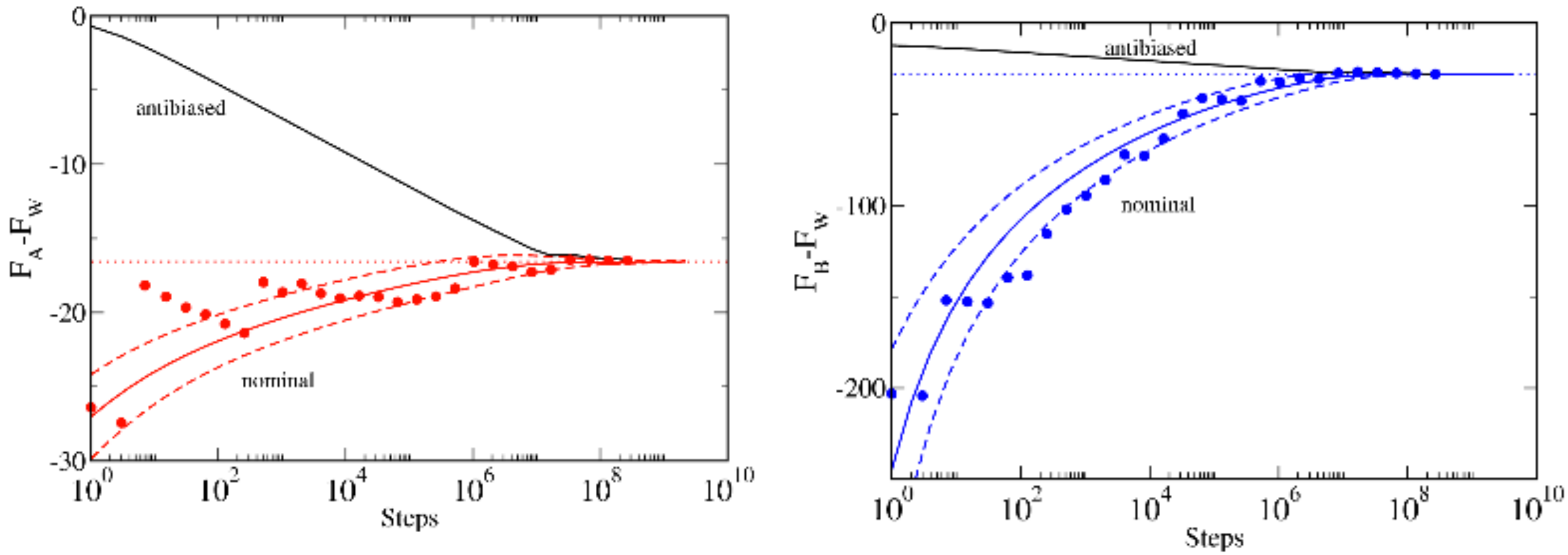
Overlap Sampling: Neglected-Sample

- For overlap sampling, it is easy to gauge the largest possible contribution to each average

$$e^{-\beta\Delta F} \equiv \chi(\alpha) = \frac{\left\langle e_B \big/ \left(e_A + \alpha e_B\right) \right\rangle_A}{\left\langle e_A \big/ \left(e_A + \alpha e_B\right) \right\rangle_B}$$

- A: $e_B / (e_B + \alpha e_A) \le 1$
- B: $e_A / (e_B + \alpha e_A) \le 1/\alpha$
- We will almost always overpredict the bias

Overlap Sampling: Neglected-Sample



- Neglected sample bias helps B perturbation quite a bit, although the correction is too large at first
- Neglected sample bias overcorrection is large for A, primarily because the largest contribution sample is very unlikely there.

Outline

- Bias in free-energy calculations
  - Neglected-tail bias model
  - Neglected-sample bias model
  - Overlap sampling (BAR) and work distributions
- Some methods for solid phases
  - Harmonically-targeted temperature perturbation (HTTP)
  - NPT simulations

Solid-Phase Free Energies, etc.

- Free-energy calculations can exploit the near-harmonic nature of the solid phase

$$A = A_{lat} + A_{harm} + A_{anharm}$$

- A_{lat} is just the sum energy for the perfect lattice
- A_{harm} can be obtained by lattice dynamics
- Free-energy calculation focuses on A_{anharm}
- Strategy
  - Integrate in temperature from T = 0 (where $A_{\mathrm{anharm}} \rightarrow 0$)
  - Use targeted perturbation to isolate contribution of A_{anharm} for increasing temperature

HTTP (Harmonically Targeted Temperature Perturbation)

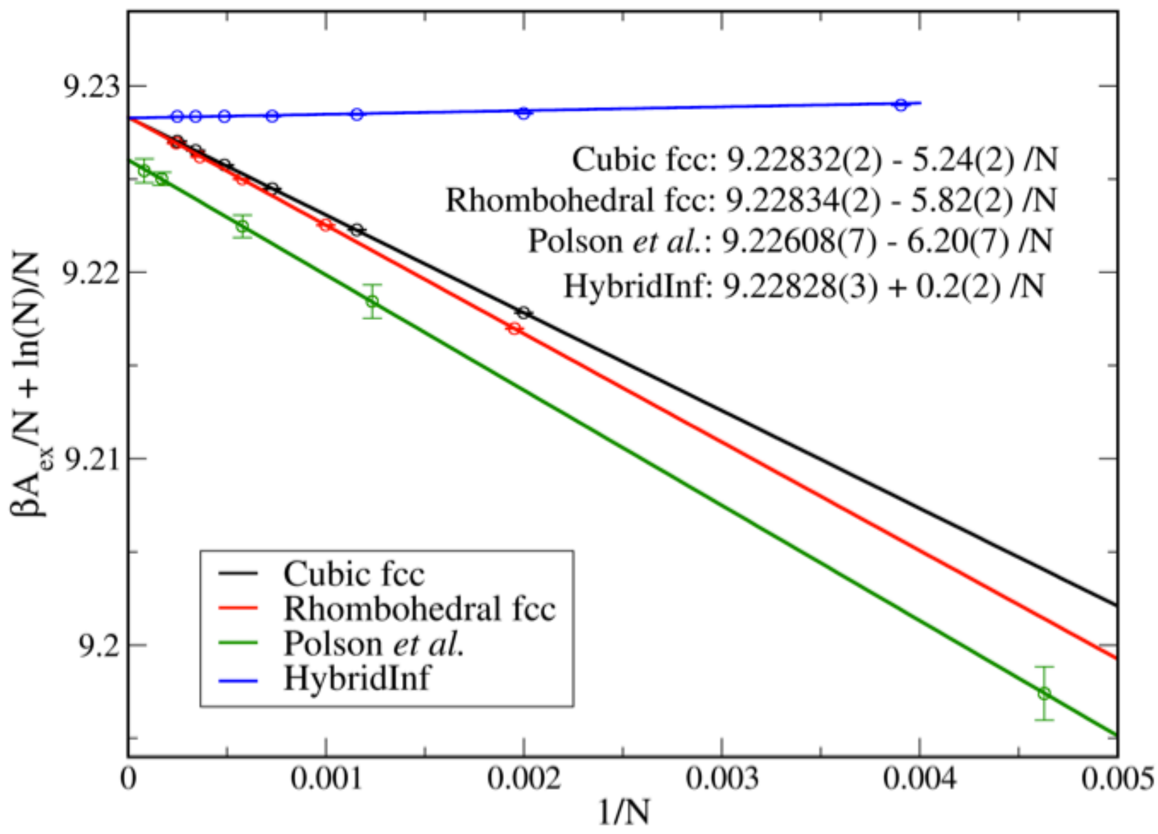
- Within the harmonic system, squared displacement is proportional to temperature
- When perturbing between temperatures T_1 and T_2, we scale coordinates (measured from lattice sites) as $x_2 = x_1(T_2/T_1)^{0.5}$
- Anharmonic contribution is given via exponential average of energy change after scaling of coordinates

$$e^{-\Delta(\beta A_{\text{anharm}})} = \left\langle e^{-\Delta(\beta U)} \right\rangle$$

- Use overlap sampling and perturb up and down in T
- Advantages
  - Smaller quantity to average
  - Precision increases to degree system is harmonic
    - Gives exact result (no noise) for perfectly harmonic system

Example - Soft Spheres

- Free energy at melting
  - $T = 1, \rho = 1.1964$
- Finite-size effects on A_{anharm} are very small!



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Solid-Phase NPT Simulation Algorithm

A.J. Schultz and D.A. Kofke,
Phys. Rev. E **84**, 046712 (2011)

- When proposing volume change trials, we use coordinate scaling to update molecule positions

$$\boldsymbol{r} = \boldsymbol{s}\left(\frac{1}{V} e^{\beta(PV + U_{\text{lat}}(\rho))}\right)^{1/(N-1)D}$$

- Accept or reject trial with probability

$$\chi = e^{-\beta(\Delta U - \Delta U_{\text{lat}})}$$

- Pressure doesn't appear in acceptance!
  - Its effect is felt instead in the coordinate scaling
- For hard spheres, if we can propose a volume change that does not cause overlaps, we will accept it
  - Expansion can lead to overlap

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Results: Hard Spheres

- Simulate 256 hard spheres at $P = 23.3$ for 10^9 steps

	Standard move	Improved move
$<\rho>$	1.1997(3)	1.200042(11)
step size	0.000336	0.0127
σ_V/V	0.00547	0.00549

- Densities agree, precision is improved by 33×
- Step is 38× larger
- Obtain more than twice the size of fluctuations in $\ln V$

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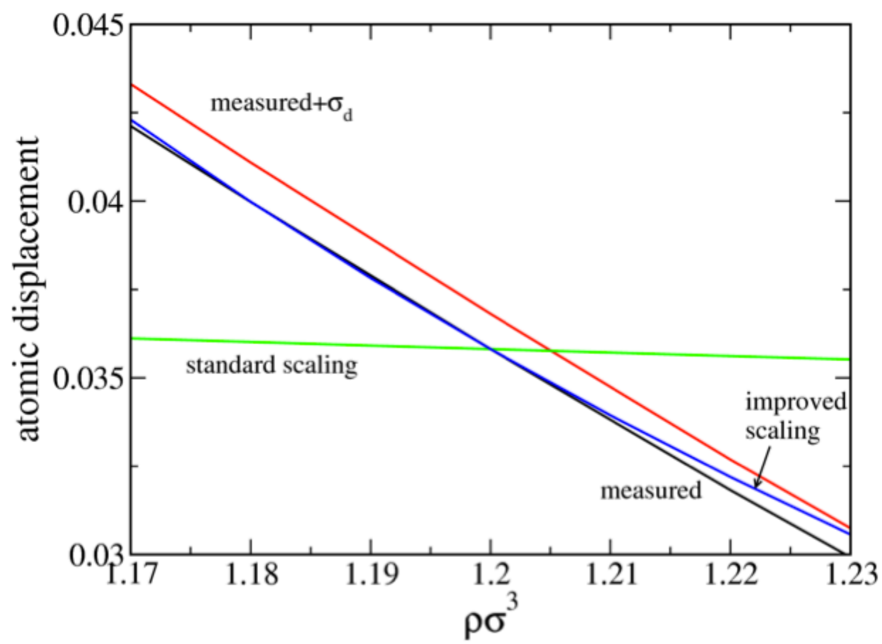
Results: Hard Spheres

- Calculate average atomic displacement



- Standard scaling leaves configuration with inappropriate atomic displacements
  - Translation MC moves must be used to relax configuration
- Excellent agreement between improved scaling and measured displacements

Two other applications

- Results are still very good in other applications
  - Albeit not as impressive as hard spheres
- Lennard-Jones spheres
  - Simulate 500 Lennard-Jones spheres at P =19.9 for 10^9 steps
  - Densities agree, precision is improved by 62%
  - Step size is 10% larger, more than double the fluctuations in lnV
- Hard dumbbell crystal
  - Scale rotational coordinates also
  - Simulate 144 hard dumbbells at P = 45 for 10^9 steps
  - Densities agree, precision improved by 3×
  - Step size is 6× larger, about 1/3 the size of fluctuations in lnV
    - Compare to < 1/15 for standard move

Outline

- Bias in free-energy calculations
  - Neglected-tail bias model
  - Neglected-sample bias model
  - Overlap sampling (BAR) and work distributions
- Some methods for solid phases
  - Harmonically-targeted temperature perturbation (HTTP)
  - NPT simulations