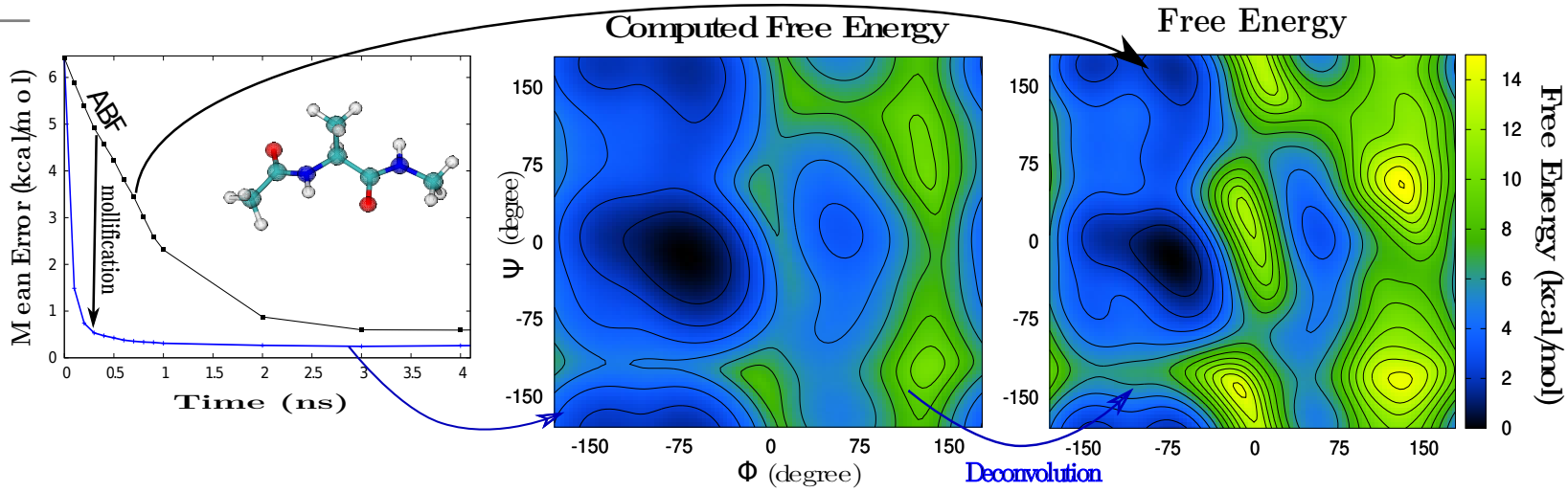
Free energy calculations: An efficient adaptive biasing potential method

P. Fleurat-Lessard - B. Dickson
F. Legoll - T. Lelièvre - G. Stoltz

ENS Lyon - ENPC

Abstract



We have recently introduced an efficient sampling and free energy calculation technique within the adaptive biasing potential (ABP) framework. The adaptive bias potential is computed from the population along the reaction coordinate:

$$e^{-\beta A_\alpha(\xi^*)} \propto \int \exp\left(-\frac{|\xi(x)-\xi^*|^2}{\alpha^2}\right) e^{-\beta V(x)}\, dx$$

This approximation introduces two parameters: strength of mollification and the zero of energy of the bias potential. We present here two extensions to deal with complex systems. The first extension consists in using a local and adaptive Gaussian height. In particular, adapting the height with the bias evolution rate prevents getting trapped in narrow but deep wells.

Introduction

- Rare events
- Bias to enhance sampling
- Reaction coordinate: ξ
- Adaptive Bias:
  - Adaptive Biasing Potential (or DoS): $A(\xi)$ is constructed
  - Adaptive Biasing Force: only $\frac{\partial A(\xi)}{\partial \xi}$ is constructed

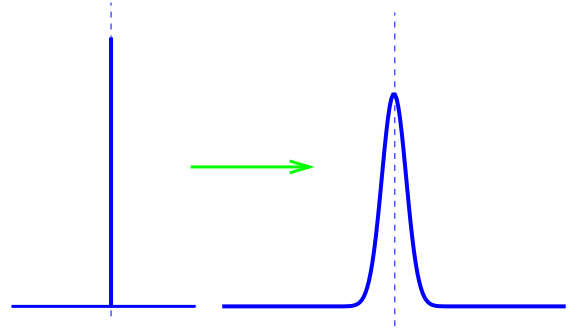
Our approach: mDoS

- We bias DoS:

$$e^{-\beta A(\xi^*)} = Z^{-1} \int_{\mathcal{X}} \delta(\xi(x) - \xi^*)\, e^{-\beta V(x)}\, dx$$

- Main idea:

$$\delta(\xi) \to \delta_\alpha(\xi) = \frac{1}{\alpha\sqrt{\pi}} \exp\left(-\frac{\xi^2}{\alpha^2}\right)$$



- mollified Density of States (mDoS):

$$e^{-\beta A_\alpha(\xi^*)} = Z^{-1} \int_{\mathcal{X}} \delta_\alpha(\xi(x) - \xi^*)\, e^{-\beta V(x)}\, dx$$

mDoS advantages

- Non-locality
- Derivatives easy to compute:

$$\frac{\partial A_\alpha(\xi^*)}{\partial \xi^*} = -k_B T \frac{\int_{\mathcal{X}} \partial_{\xi^*} \delta_\alpha(\xi(x) - \xi^*)\, e^{-\beta V(x)}\, dx}{\int_{\mathcal{X}} \delta_\alpha(\xi(x) - \xi^*)\, e^{-\beta V(x)}\, dx}$$

  with $\partial_{\xi_j^*} \delta_\alpha(\xi_j(x) - \xi^*) = \frac{2}{\alpha^2}(\xi_j(x) - \xi_j^*)\delta_\alpha(\xi(x) - \xi^*)$

- No derivatives of ξ !
- Icing on the cake: $e^{-\beta A_\alpha(\xi)} = e^{-\beta A(\xi)} * \delta_\alpha(\xi)$
  $\Rightarrow$ Error can be greatly reduced by deconvolution.

The bias $V_b(\xi)$

- $V_b(\xi, t) = -A_\alpha(\xi, t)$ does not converge
- Normalizing $A_\alpha(\xi, t) \rightarrow \Delta A_\alpha(\xi, t)$ with:

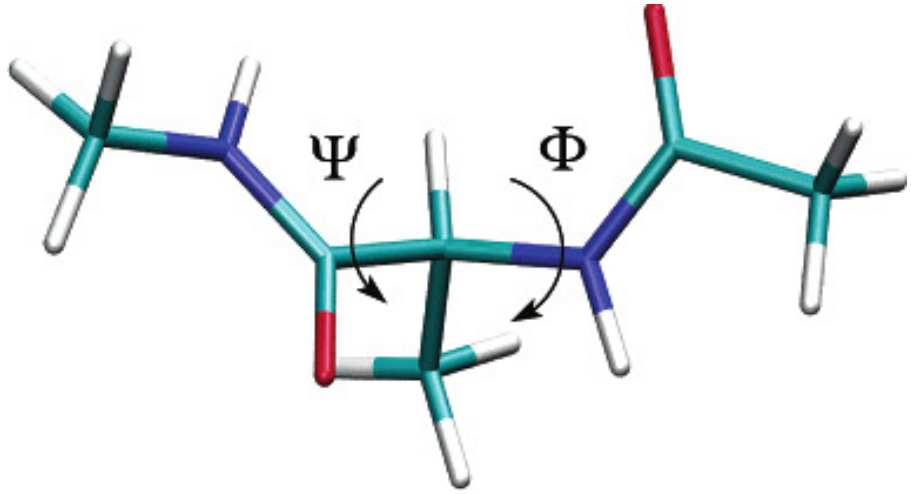
$$\Delta A_\alpha(\xi, t) = A_\alpha(\xi, t) - \min_{\xi^*} \left[A_\alpha(\xi^*, t)\right]$$

- Convergence boost:

$$e^{\beta V_b(\xi,t)} = e^{-\beta \Delta A_\alpha(\xi,t)}\, e^{\beta c},$$

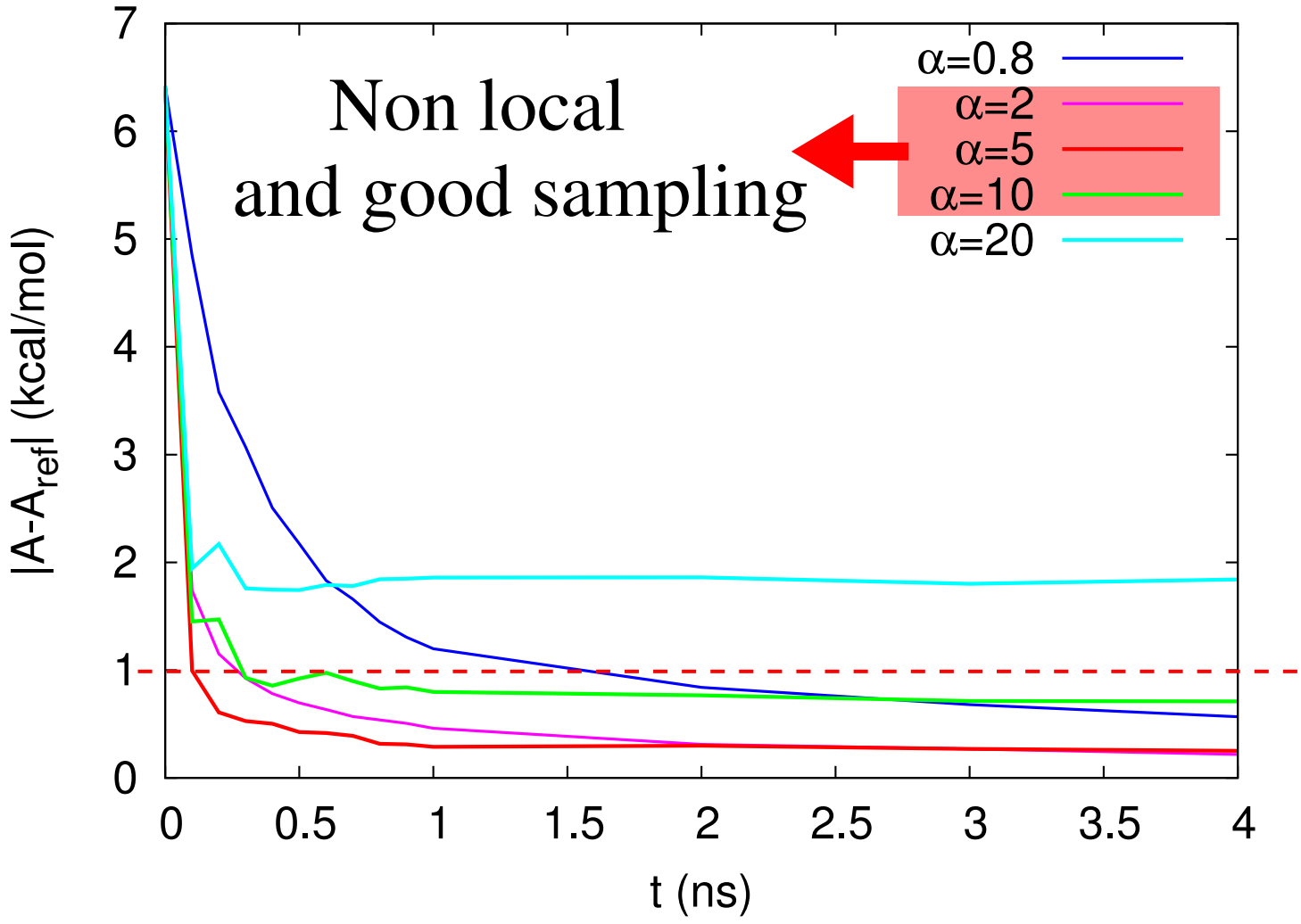
$e^{\beta c}$ can be seen as the Gaussians height

Application: alanine dipeptide

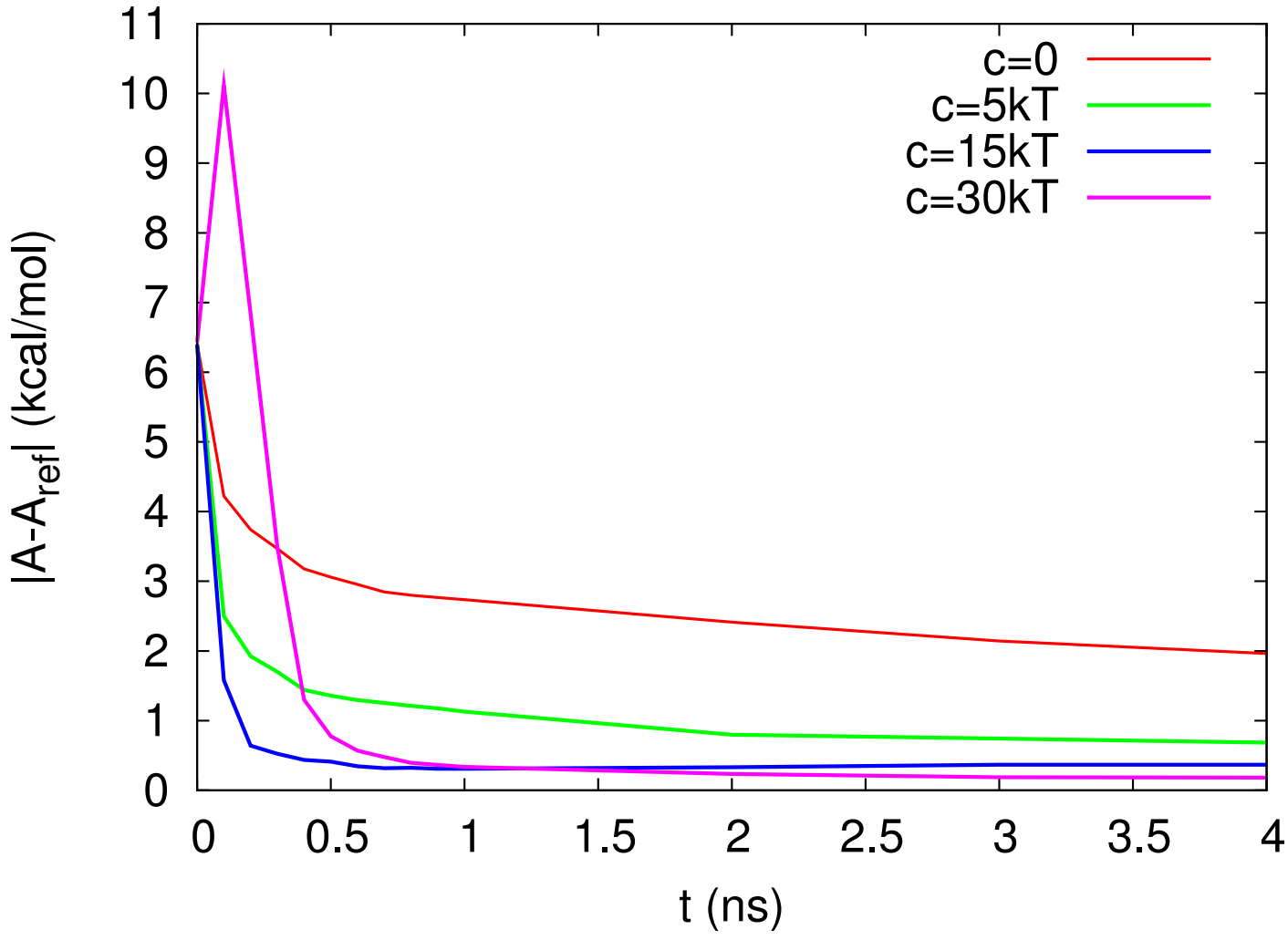


- AMBER ff94
- T=300K: Langevin
- Implicit solvent: Generalized-Born model
- RC: $(\xi_1, \xi_2) = (\Psi, \Phi)$
- $A_{ref}(\xi_1, \xi_2)$: 120ns of unbiased trajectory.

Influence of α



Influence of c



Other approaches: Metadynamics

- Well-tempered metadynamics
  Barducci, Bussi and Parrinello *PRL* **100**, 020603 (2008)

$$V_b^{\mathrm{meta}}(\xi,\tau) = \sum_{t'\leq\tau} h(\xi,t') \exp\left(-\frac{(\xi-\xi_{t'})^2}{2w^2}\right)$$

with $h(\xi,t) = \omega \exp[-V_b^{\mathrm{meta}}(\xi,t)/k_B\Delta T]\tau_G$.

but Gaussians add up to $A(\xi)$

Other approaches: ABF

- Adaptive Biasing Force
  - Darve, Rodriguez-Gomez, Pohorille *J. Chem. Phys.* 2008, **128**, 144120.

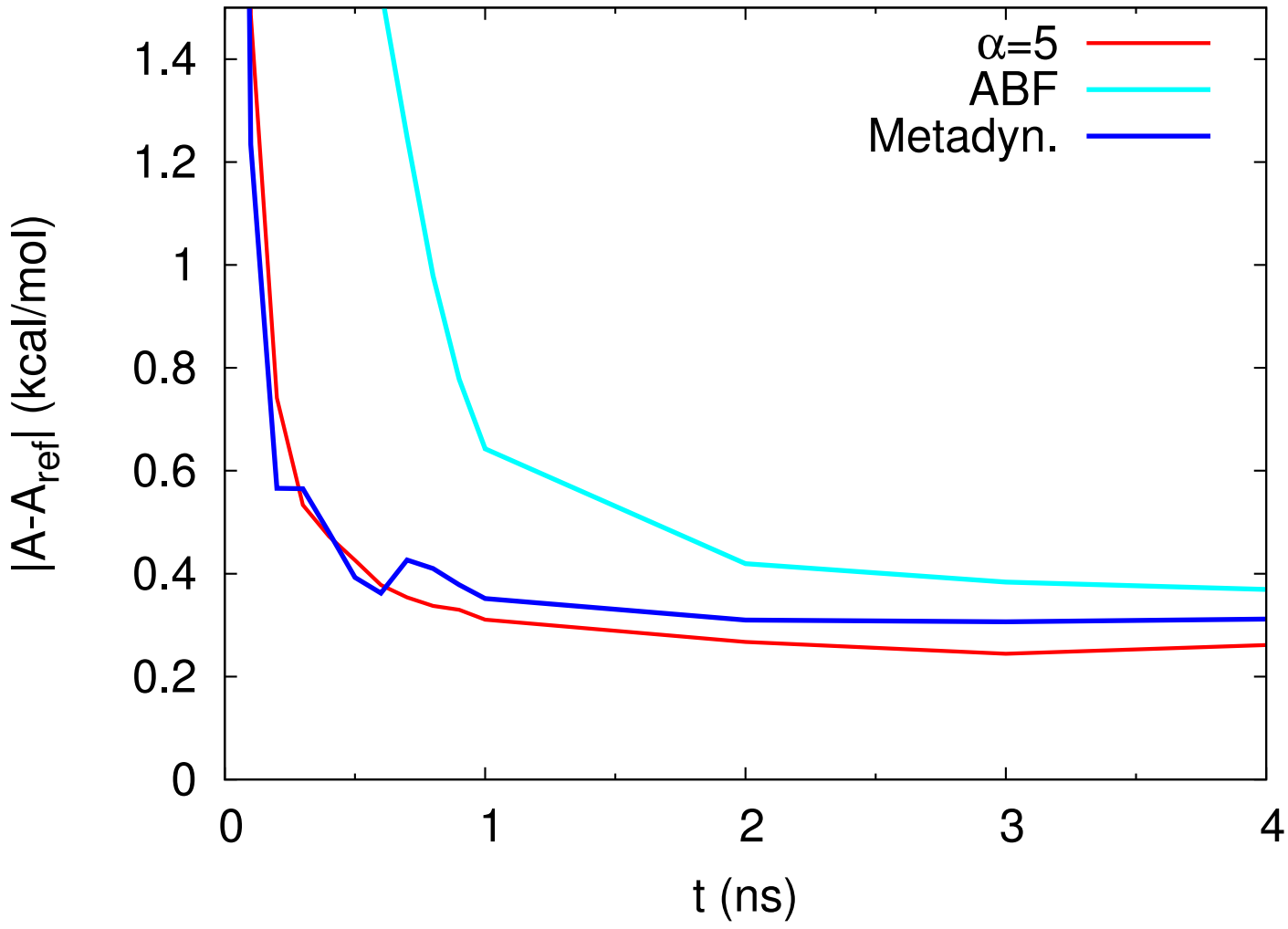
$$ABF(\xi^*) = -\left\langle \frac{d}{dt}\left(M_\xi \frac{d\xi}{dt}\right)\right\rangle_{\xi^*},$$

  - More standard:

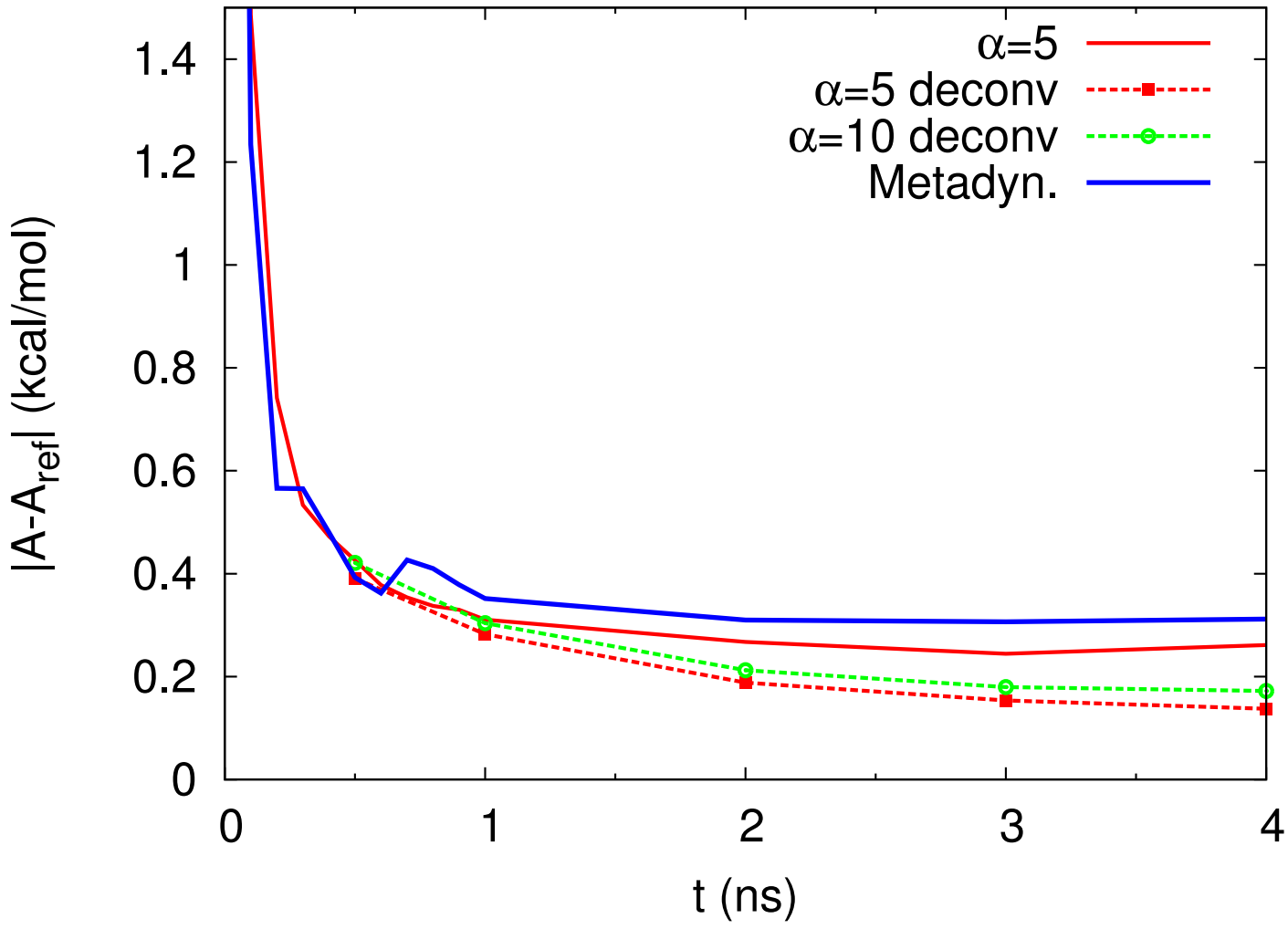
$$F_j(\xi^*) = \left\langle \sum_{i=1}^{N} \nabla V \cdot G_{ji}^{-1}\nabla\xi_i - \beta^{-1}\nabla\cdot(G_{ji}^{-1}\nabla\xi_i)\right\rangle_{\xi^*},$$

  - Parameter free
  - $\lim_{t\to\infty}$ ABF $= \dfrac{\partial A(\xi)}{\partial\xi}$

Comparison



Comparison: deconvolution



Conclusion and Perspectives

- mDos is a new method:
  - Very efficient
  - Easy to implement
- Perspectives:
  - Multi-replica with selection
  - Chemical reactions (high barriers)
  - Going to nD, n>2
  - Put it in PLUMED !

Dickson et al. *J. Phys. Chem. B* **2010**, 114, 5823-5830.