

# Enhancing the stability of the mollified impulse method

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## Acknowledgments

- Thanks to the organizers for their invitation, and you for attending.
- Work in collaboration with Dr. Robert D. Skeel, UIUC.
- Thanks to Jim Phillips for suggesting that H-bonds may be the cause of instability.
- Students: Qun Ma, Thierry Matthey, Jeremiah Willcock.
- Funding: NSF BIOCOMPLEXITY-PHY grant 0083653 and an University of Notre Dame grant. Part of this work was performed at UIUC with support from NIH and NSF.

## Overview

1. **Goal:** Lengthen time steps for stable molecular dynamics (MD) simulations, to get an asymptotic twofold speedup over Verlet-I/r-RESPA, and more scalable software when using fast electrostatics methods such as Particle Mesh Ewald (PME) or multigrid summations.
2. **This talk describes progress in:**
  - (a) Lengthening the longest time step using an H-bond mollified impulse method (Molly). The longest time step is 100% longer than Verlet-I/r-RESPA for a given drift, including no drift
  - (b) Understanding remaining challenges to enhance stability of MD, particularly nonlinear instabilities in Verlet-I/r-RESPA

## Outline

1. Background: multiple time stepping integrators and resonances
2. Mollified impulse method (Molly)
3. Analysis to motivate design of better algorithms
4. Numerical experiments to confirm insights from analysis
5. H-bond Molly
6. Future work

## Background

- Multiple time stepping integrators have been used to accelerate MD simulations. **Verlet-I/r-RESPA** partitions into fast and slow components of the force,  $-\nabla U^{\text{fast}}(x)$ ,  $-\nabla U^{\text{slow}}(x)$ , and incorporates them with different frequency,  $\delta^{-1}$  and  $\Delta^{-1}$ .
- Longest time steps of 3 or 4 fs are possible for unconstrained simulations of solvated proteins.
- There is **resonance** if the frequency of the slow force impulse coincides with a normal mode frequency of the system.
- There is also a problem for long time steps just smaller than *half* the period of the fastest normal mode.
- For example, with flexible water (fastest motion of 10 fs): analytical and empirical evidence that time steps greater than 5 fs are not possible for this method.

- Finally, we show evidence of nonlinear resonances if the time step is a *third* and even a *fourth* of the fastest period

## Mollified Impulse Method I

- Molly is a family of integrators that counteract the instabilities present in the Verlet-I/r-RESPA method. This is accomplished by:
  - Perturbing the potential at time averaged positions  $U^{\text{slow}}(x) \rightarrow U^{\text{slow}}(\mathcal{A}(x))$ ,
  - Defining the force as the gradient of this averaged potential,  $-\nabla U^{\text{slow}}(x) \rightarrow -\mathcal{A}_x(x)^T \nabla U^{\text{slow}}(\mathcal{A}(x))$ .
- Time averaging: takes into account high frequency vibrational motion
- Mollification: filter in frequency domain which damps high frequency components of  $-\nabla U^{\text{slow}}(x)$

## Mollified Impulse Method II

- García-Archilla, Sanz-Serna & Skeel (1996) proposed the following averaging:
  - Integrate for a time proportional to  $\Delta$  the system using only the fastest forces to compute auxiliary positions  $\tilde{X}(t)$
  - The averaged positions are defined as the weighted average of the positions  $\tilde{X}(t)$  using a weight function  $\phi(s)$  with local support, such as constant, linear, or quadratic:

$$\mathcal{A}(x) = \frac{1}{\Delta} \int_0^\infty \phi\left(\frac{t}{\Delta}\right) \tilde{X}(t) dt.$$

- The Jacobian matrix  $\mathcal{A}_x(x)$  is computed using the chain rule, and should be sparse.
- These methods were tested and they overcome the half period time step barrier: Skeel, Izaguirre, 1998; Izaguirre, Reich, Skeel, 1999

## Mollified Impulse Method III

Algorithm for MOLLY:

half a mollified kick

$$P^{n-1+\epsilon} = P^{n-1} + \frac{\Delta t}{2} F^{\text{slow},n-1}. \quad (1)$$

a vibration Propagate  $X^{n-1}$ ,  $P^{n-1+\epsilon}$  by integrating

$$\frac{d}{dt} X = M^{-1} P, \quad \frac{d}{dt} P = F^{\text{fast}}(X) \quad (2)$$

(e.g., Verlet/leapfrog with time step  $\delta t$ ) for an interval  $\Delta t$  to get  $X^n$  and  $P^{n-\epsilon}$ .

**a time averaging** Calculate a temporary vector of time-averaged positions  $\bar{X}^n = \mathcal{A}(X^n)$  and a Jacobian matrix  $J^n = \mathcal{A}_x(X^n)^T$ .

The time averaging function  $\mathcal{A}(x)$  uses only the fastest forces  $F^{\text{reduced}}(x)$ .

half a mollified kick

$$P^n = P^{n-\epsilon} + \frac{\Delta t}{2} F^{\text{slow},n} \quad (3)$$

Note that  $\bar{X}^n$  is used only for the purpose of evaluating  $F^{\text{slow}}$ , it does not replace the value of  $X^n$ .

## Mollified Impulse Method IV

Averaging and mollification:

$$\begin{aligned}
 P &:= P + \frac{1}{2}\delta t F^{\text{fastest}}(X), & P_x &:= P_x + \frac{1}{2}\delta t F_x^{\text{fastest}}(X)X_x, \\
 B &:= B + \frac{1}{2}\delta t X \phi(t/\Delta t), & B_x &:= B_x + \frac{1}{2}\delta t X_x \phi(t/\Delta t), \\
 X &:= X + \delta t M^{-1}P, & X_x &:= X_x + \delta t M^{-1}P_x, \\
 t &:= t + \delta t, \\
 B &:= B + \frac{1}{2}\delta t X \phi(t/\Delta t), & B_x &:= B_x + \frac{1}{2}\delta t X_x \phi(t/\Delta t), \\
 P &:= P + \frac{1}{2}\delta t F^{\text{fastest}}(X), & P_x &:= P_x + \frac{1}{2}\delta t F_x^{\text{fastest}}(X)X_x.
 \end{aligned}
 \tag{4}$$

## Analysis I

- **Goal:** compare stability of Verlet-I/r-RESPA and different Molly filters when applied to the simplest linear model problem, using information to guide development of new Molly methods

- **Model problem:**

Following T. Schlick and co-workers, we use the simple 1-d problem:

$$x' = p; p' = -(\lambda_1 + \lambda_2)x$$

that models a particle of unit mass at position  $x$ , connected to two springs with force constants  $\lambda_1 = \Omega^2$  and  $\lambda_2 = \omega^2$ , where  $\Omega^2 \geq \omega^2$ .

## Analysis II

- **Discretization using Verlet-I/r-RESPA and MOLLY** with a longest time step  $\Delta$ , and assuming analytical integration of the fast spring force associated with  $\Omega$ , can be written as

$$\begin{bmatrix} x_{n+1} \\ p_{n+1} \end{bmatrix} = \begin{bmatrix} 1 & 0 \\ -\omega^2 \frac{\Delta}{2} G^2 & 1 \end{bmatrix} \begin{bmatrix} x_n \\ p_n \end{bmatrix}$$

$$\begin{bmatrix} \cos \theta & \frac{\sin \theta}{\Omega} \\ -\Omega \sin \theta & \cos \theta \end{bmatrix} \begin{bmatrix} 1 & 0 \\ -\omega^2 \frac{\Delta}{2} G^2 & 1 \end{bmatrix} \begin{bmatrix} x_n \\ p_n \end{bmatrix}$$

where  $\theta = \Omega\Delta$ ,  $G$  is the Fourier transform of the averaging and mollification functions ( $G = 1$  for Verlet-I/r-RESPA).

## Analysis III

- **Stability:** Stability is given by analyzing the eigenvalues of the above propagation matrix.
- Because the scheme is symplectic, the determinant is one, and instability occurs when the eigenvalues become real and reciprocal of each other. Stability is insured if the value of the trace of this matrix

$$t(\theta) = -2\omega^2 \Delta G^2 \frac{\sin \theta}{\Omega} + 2 \cos \theta > -2,$$

or, the magnitude of the eigenvalues must be 1.

## Analysis IV

- The limit of interest is  $\Omega\delta \ll 1$ , assume analytical fast forces ( $\delta \rightarrow 0$ ).
- We also want  $\omega\Delta \leq 1$  to observe the stability condition of leapfrog,  $\omega\Delta < 2$ .
- For the purpose of giving numerical results, we assume  $\omega = \Omega/4$ .
- Finally, since the matrix  $BAB$  is similar to  $AB^2$ , we get

$$\begin{bmatrix} \cos \theta & \frac{\sin \theta}{\Omega} \\ -\Omega \sin \theta & \cos \theta \end{bmatrix} \begin{bmatrix} 1 & 0 \\ -\frac{1}{16}\Omega\theta G^2 & 1 \end{bmatrix}. \quad (5)$$

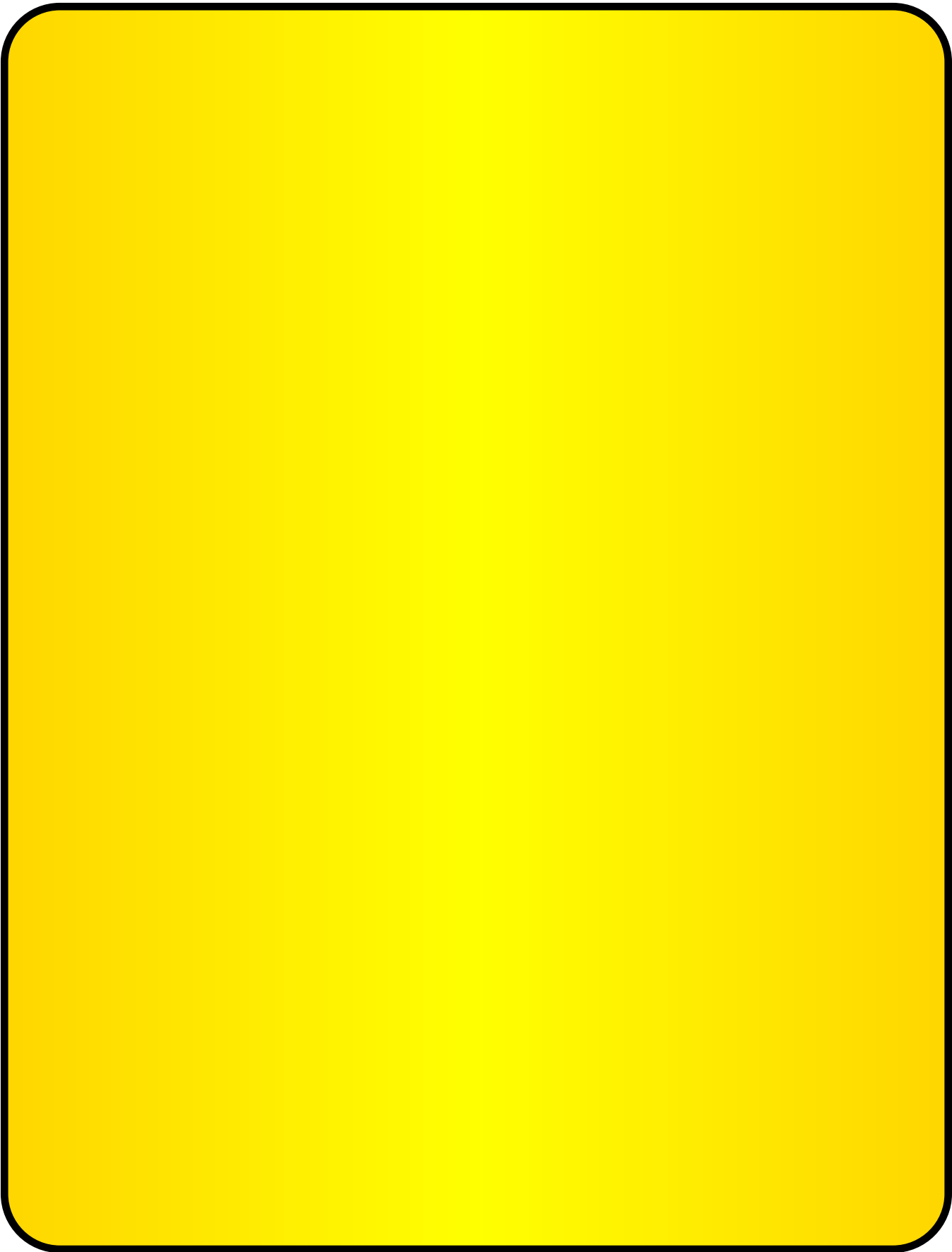
## Analysis V

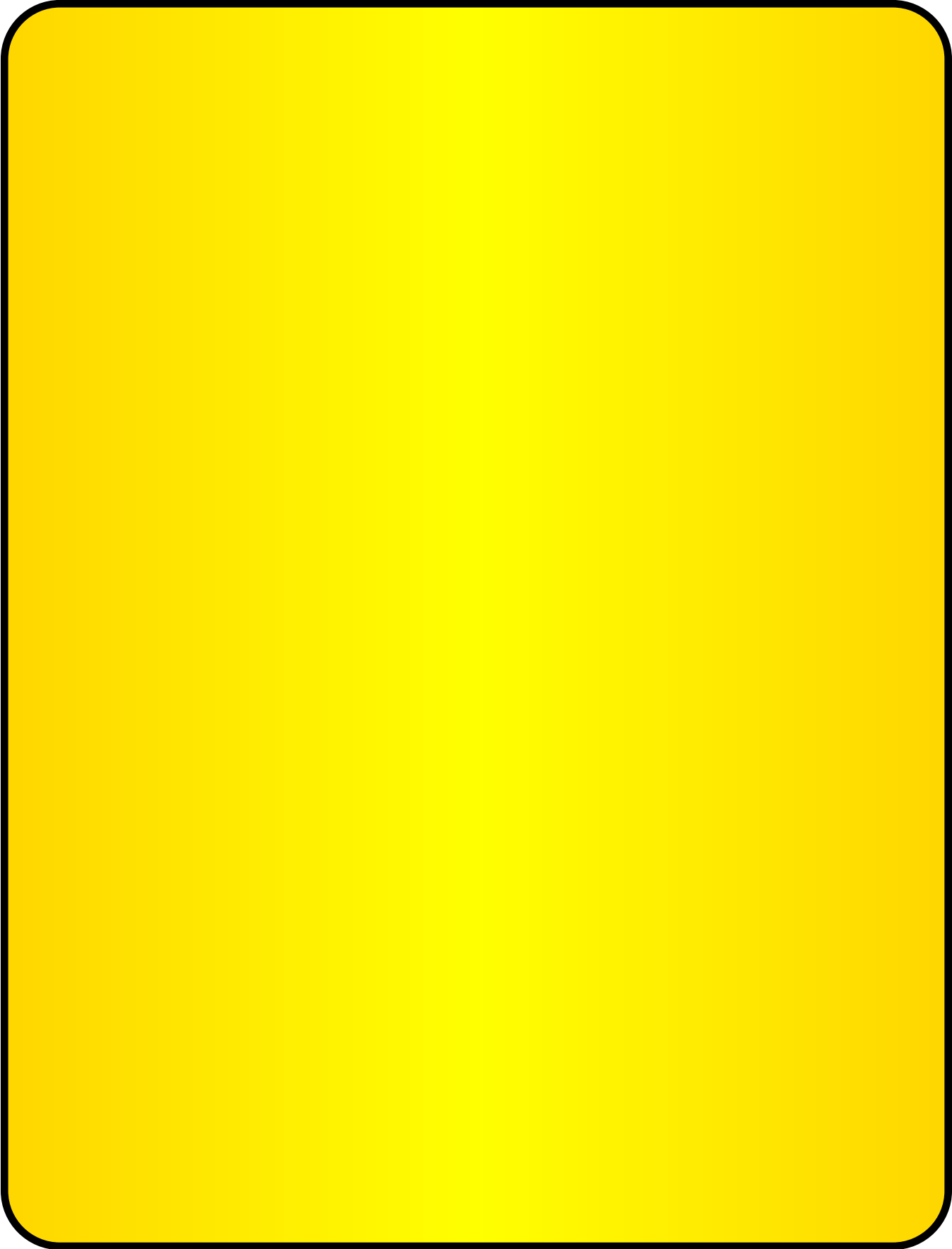
Long Average is stable at half the fastest period, whereas Verlet-I/r-RESPA and Short Average are not. This is confirmed by numerical experiments.

**Impulse method:**  $G = 1$

**Short average:**

$$G = \int_{-0.5}^{0.5} \exp(-i\theta x) \\ = \frac{2}{\theta} \sin . 5\theta .$$





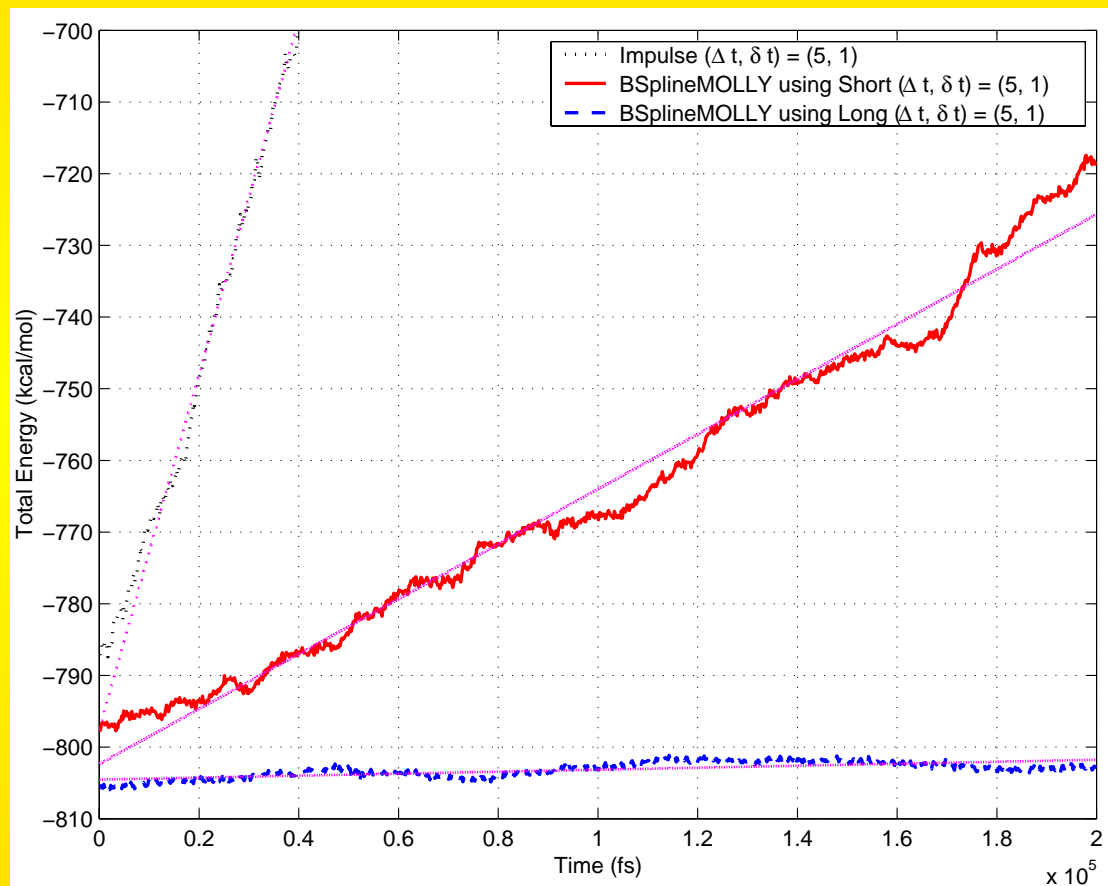
Long average:  $G = \int_{-1}^1 \frac{1}{2} \exp(-i\theta x) = \frac{\sin \theta}{\theta}$

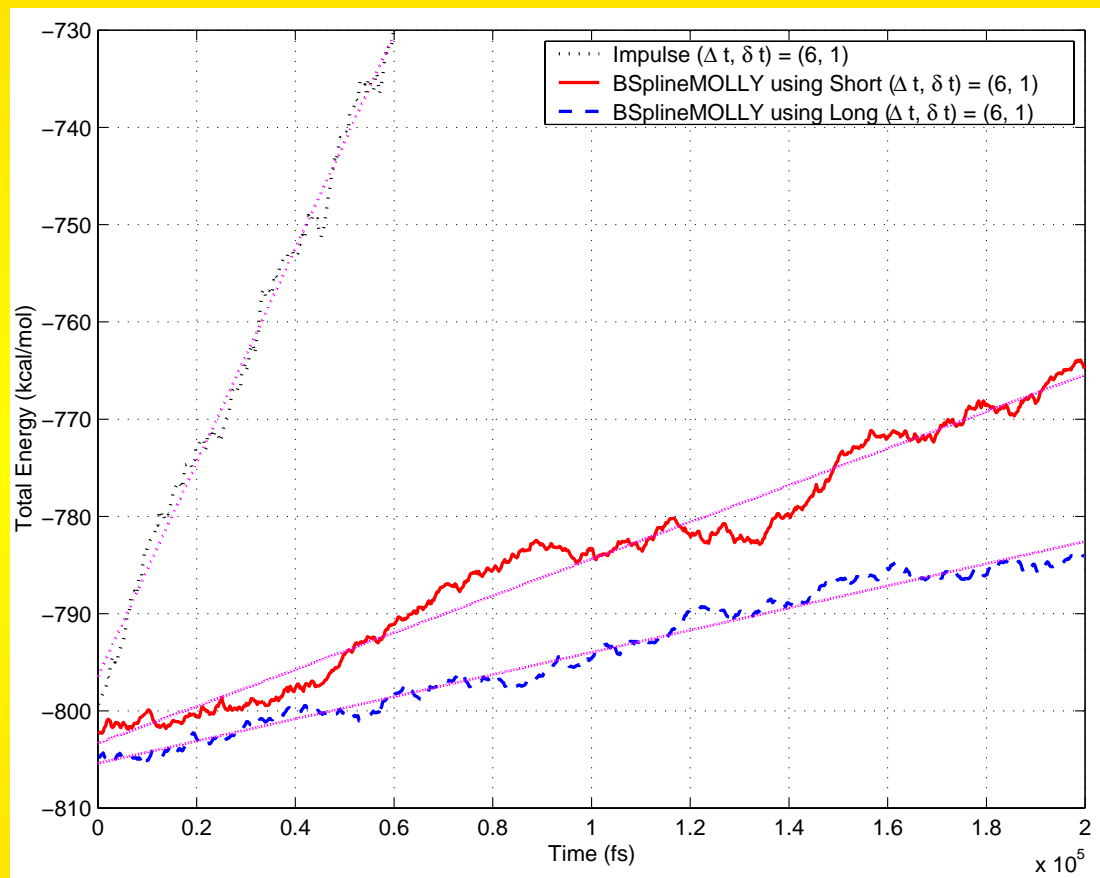
## Numerical Experiments I

- Evaluated with a box of flexible TIP3P waters (10 and 20 Å radius) and a solvated ER/ERF system.
- All the Molly methods are implemented in PROTO MOL, a framework for prototyping MD algorithms. PROTO MOL has been released and is available at <http://www.nd.edu/~1c1s/Protomol.html>.
- Implementation details of Molly, such as all the Hessians for the CHARMM force field, may be found in that web page.
- General result: *for a given drift, including zero drift, one can increase the size of the longest time step by 50% by using LongAverage Molly with only the fastest motions (bonds and angles).*
- In NAMMD 2.1, using Molly and 6 fs we got a 38% overall speedup for a 32000 atom system.

- The methods were validated by computing RDF and velocity auto-correlation functions and comparing against leapfrog with time step of 0.5 or 1 fs.

## Numerical Experiments II





## H-bond Molly I

- These Molly filters are not averaging the short range nonbonded forces. This is causing instabilities before the physical resonance  $\theta = 2\pi$ .
- We have included a subset of these forces, those due to H-bonds. Physical insight tells us H-bonds are the most important interaction in solvated biomolecules.
- We use a geometrical interpretation of H-bonds: interactions in the range of 2 – 4.5Å, and a planar angle of the acceptor and donor around 30 degrees.
- This keeps the number of nonzeros in the Jacobian for mollification relatively low (for  $N$  waters, about  $3N$ ).
- *For a given drift, including zero drift, one can increase the size of the longest time step over Verlet-I/ $r$ -RESPA by 100% by using H-bond Molly.*

# *H-bond Molly II*

## **Future Work**

- Optimization/specialization of H-bond Molly when working with biomolecules and water.
- There are mild instabilities remaining even after including H-bonds, we will remove 3:1 and 4:1 unstable nonlinear resonances. See plot of 3:1 instabilities.



- One possibility is to use a mild thermostat. For example, with damping of 0.2 /ps we are able to double the time steps possible with MOLLY.
- This mild thermostat has been validated through the computation of velocity autocorrelation functions and diffusion coefficients for the slightly damped and the Newtonian equilibrium. It allows a *fourfold* speedup over Verlet-I/r-RESPA, cf. Izaguirre, Catarella, Wozniak, and Skeel, 2001.