



Multi-layered, Iterative Protocols for Quantum Chemical Calculations

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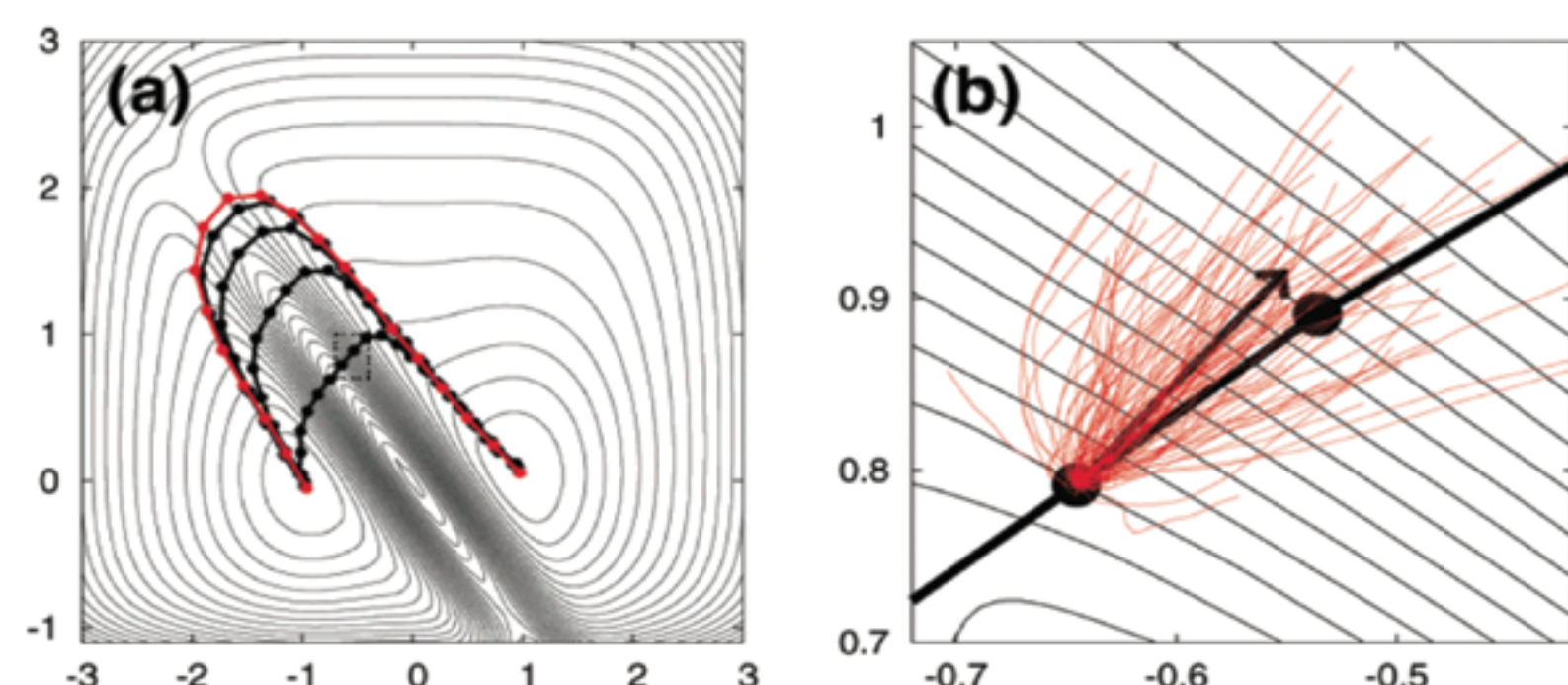
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Abstract

A common strategy in quantum chemical calculations is to start by modeling a system with a low level of theory and to progress to the desired (high) level of theory. While this seems intuitively reasonable, there is no formal reason that such a sequence is guaranteed to converge to the optimum for the desired level of theory. In fact, in cases in which the low and high levels of theory favor very different solutions, this approach could lead to local traps and slow down convergence. Here, we propose a theoretical framework for how one force field can be used to precondition another, so as to seamlessly accelerate convergence of the latter. We demonstrate this idea by applying it to reaction path discovery. Speedups of up to 3-5 fold are obtained.

String method: Path refinement via swarms of trajectories

Rare events can be efficiently sampled via specialized tools, such as the **string method**. Here, gradient is estimated via **swarms of short, dynamics trajectories**. These are released from multiple different instances of the system (images) along an initial guess of a reactive pathway. The path is typically projected onto a small set of slowly varying degrees of freedom, a.k.a. collective variables (CVs).



From [Pan, Sezer, Roux, *J. Phys. Chem. B* (2008)]: a) iterative path relaxation along a hypothetical model surface, b) zoom-in view on a swarm of trajectories released from a single image (black dot). Average drift is indicated with an arrow. Orthogonal component of the drift to the path provides an estimate of the gradient.

Multi-level (ML) preconditioning

Preconditioning is a standard technique in numerical optimization; it can be viewed as a variable transformation that enables a **root-finding problem** converge in fewer number of steps. We recently introduced a scheme [Tempkin *et al*, *J. Chem. Phys.* (2014)] that applies preconditioning ideas in iterative molecular calculations.

Given a reference (**R**) level of theory, and a corresponding string operator S_R on a reactive path φ , we iteratively refine a path as

$$S_R(\varphi_m) = \varphi_{m+1} \quad \text{until} \quad \varphi_{m+1} = \varphi_m$$

A change of variable of type $g(\varphi) = \varphi - S_P(\varphi)$ (**P** for preconditioning) permits us to rewrite the string equation as

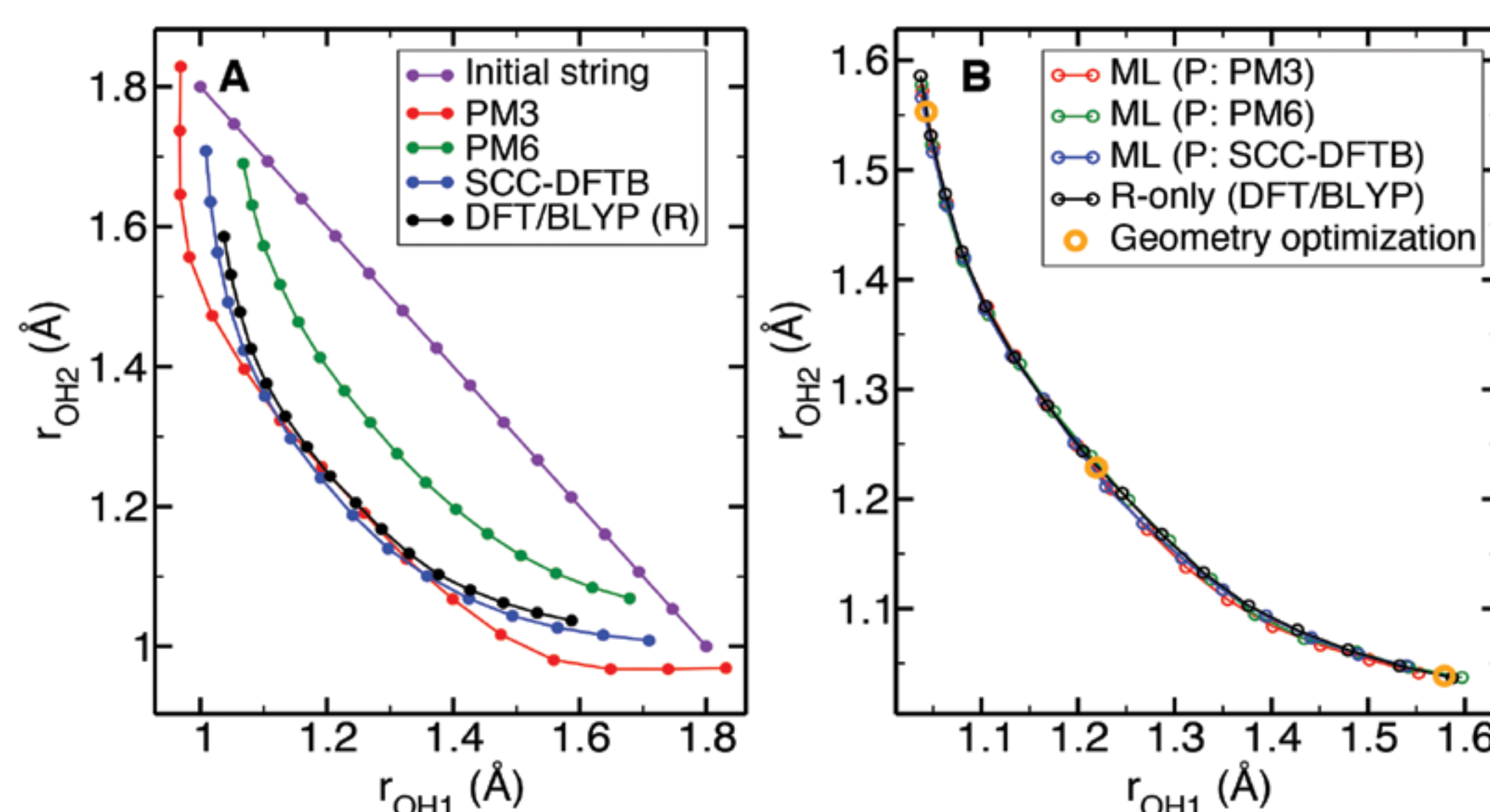
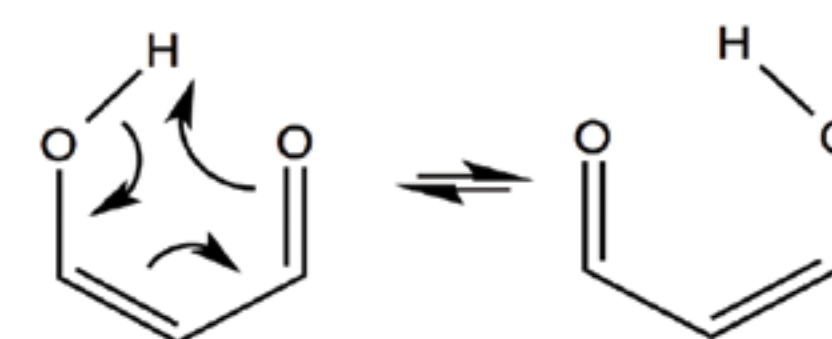
$$\varphi_{m+1} = S_P(\varphi_{m+1}) + S_R(\varphi_m) - S_P(\varphi_m)$$

In practice, this equation is solved again iteratively, only requiring S_P calls:

$$\varphi_{m+1}^{k+1} = S_P(\varphi_{m+1}^k) + \underbrace{[S_R(\varphi_m) - S_P(\varphi_m)]}_{\text{correction term}}$$

Tautomerization of Malonaldehyde near zero Kelvin

Cis-enol form of malonaldehyde can undergo **intramolecular proton transfers** (right). The reactant and product are equivalent which provides a suitable benchmark for a low temperature string protocol.

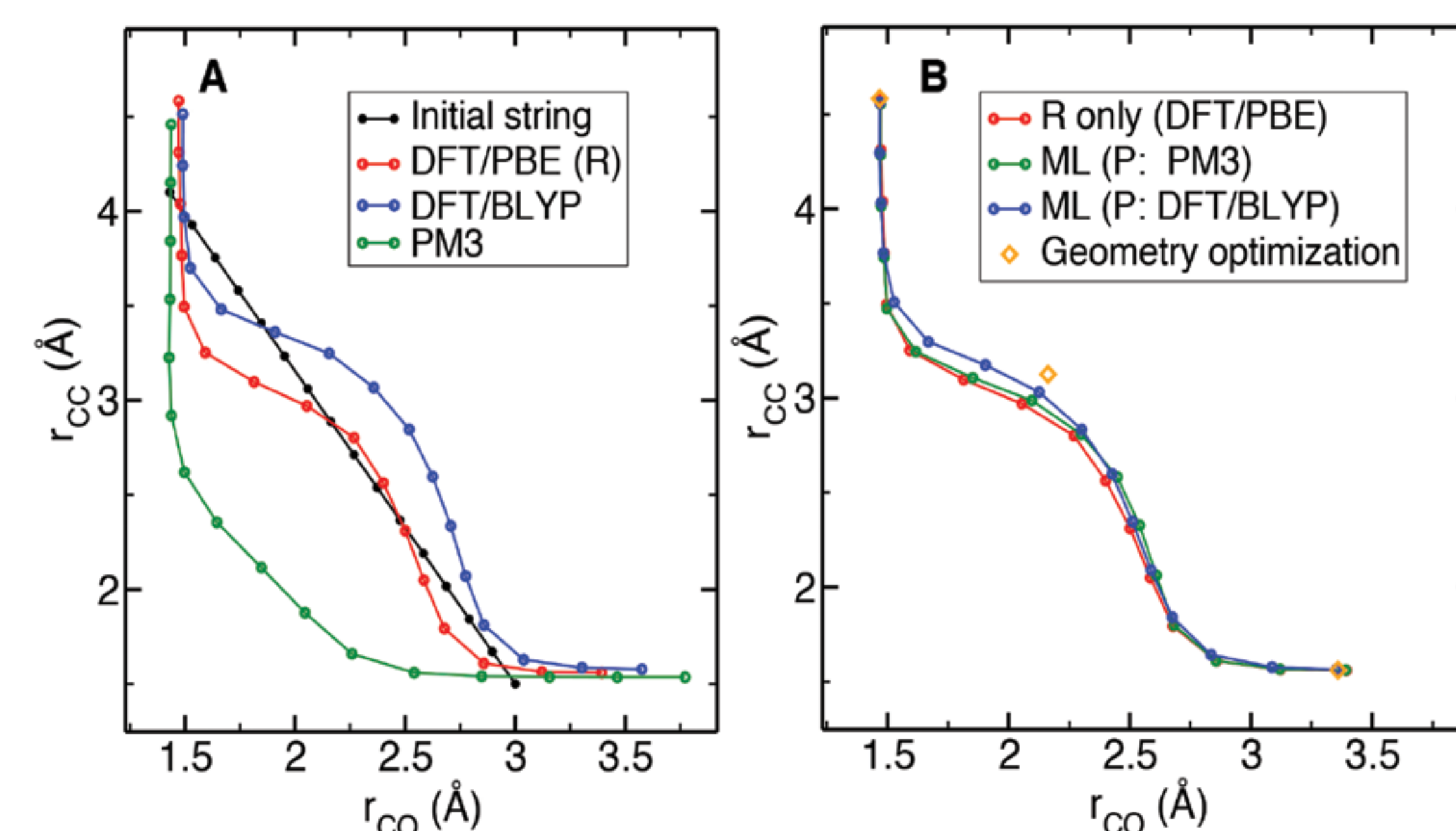
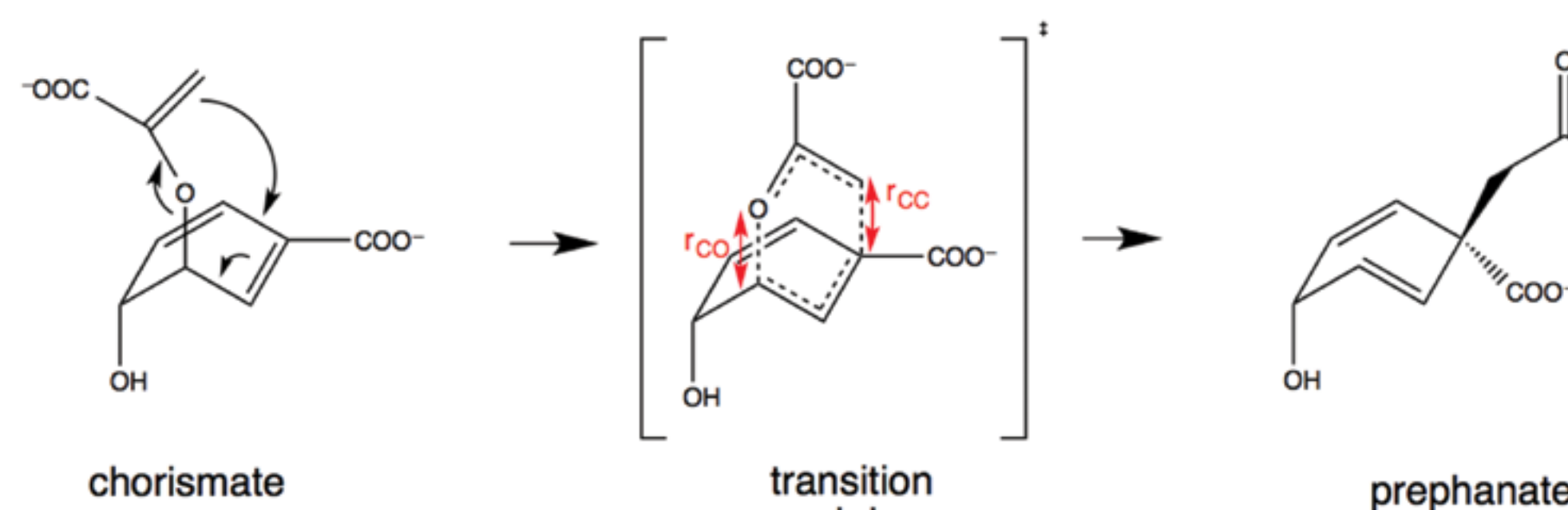


Left: Optimized tautomerization pathways as viewed from the CVs plane. **A)** R- and P- levels of theories alone, **B)** ML compared against R-only.

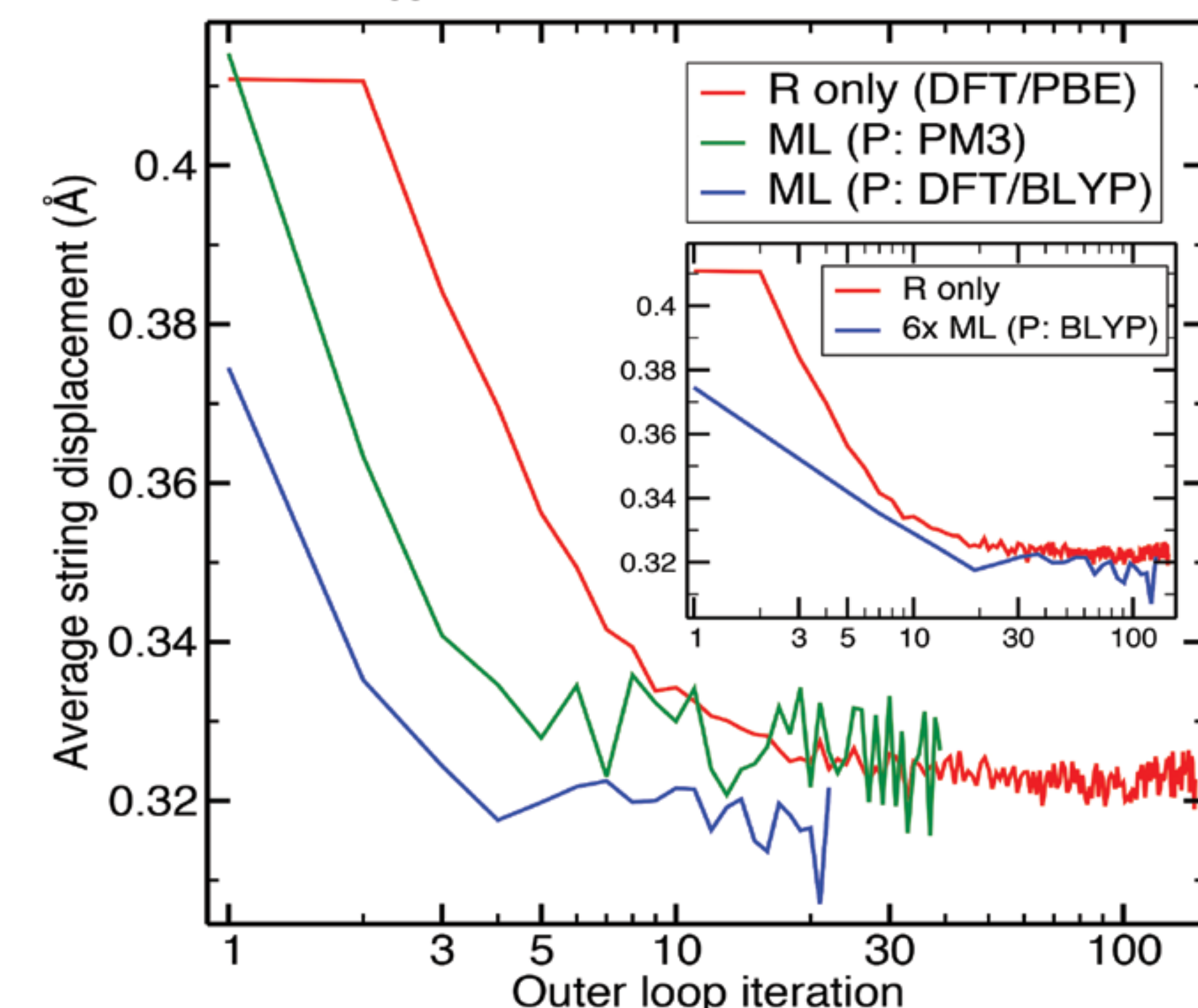
Bottom: ML runs converge in 3- to 5-fold fewer iterations compared to R-only refinement.

Pericyclic rearrangement of Chorismate to Prephenate

Chorismate (below, left) can convert to prephenate (below, right) via a pericyclic **Claissen rearrangement**. CVs are indicated in red.



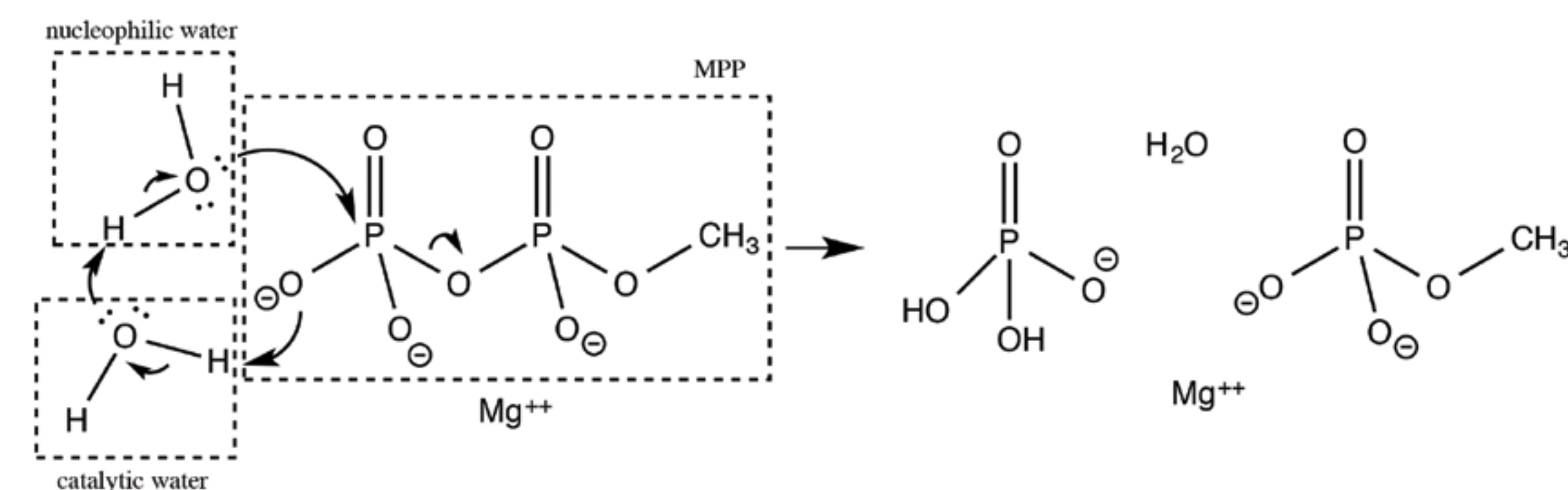
Left: Optimized reaction pathways as viewed from the CVs plane: **A)** **BLYP** and **PBE** predict more similar paths to each other than to **PM3**, **B)** ML paths agree with R-only refinement.



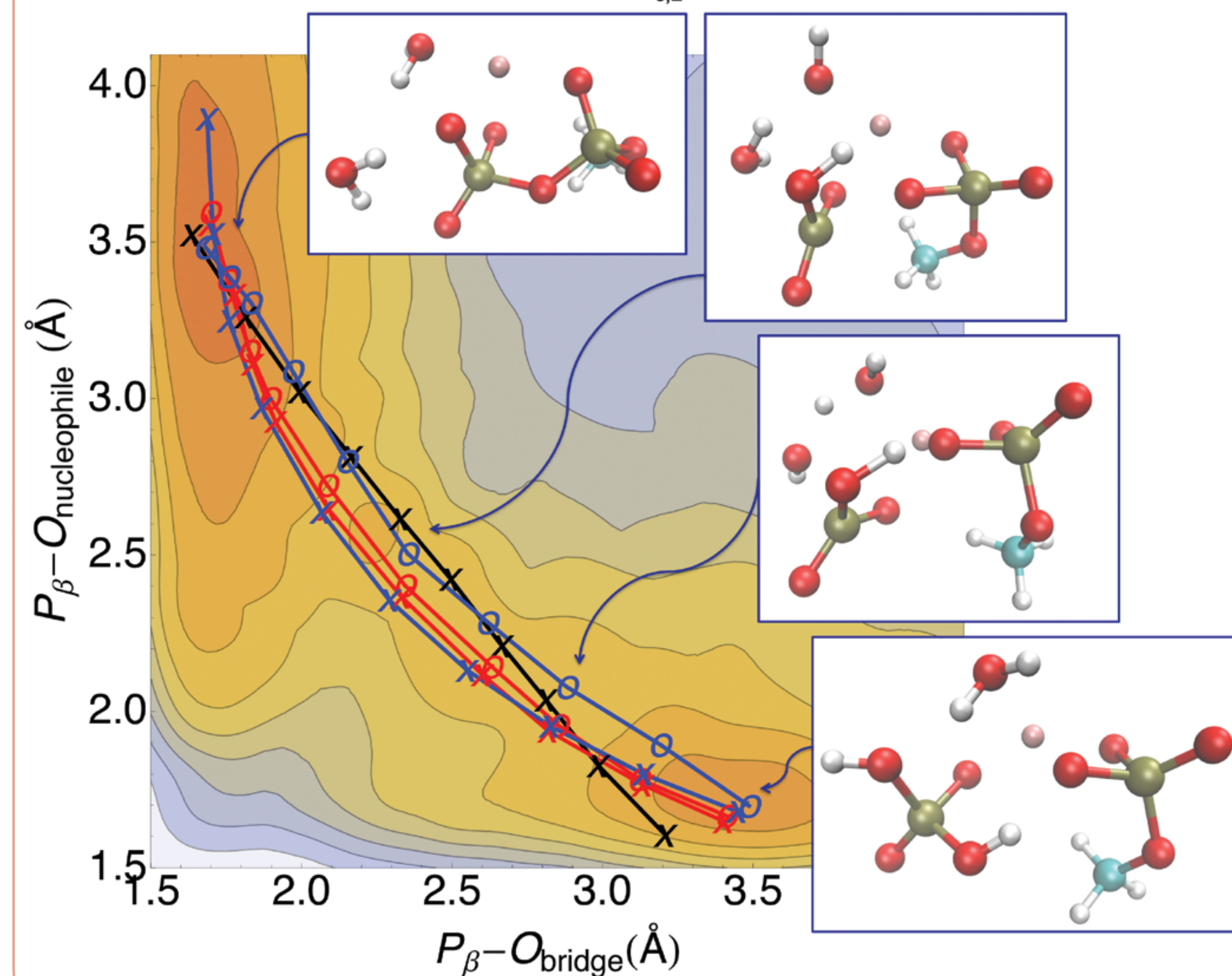
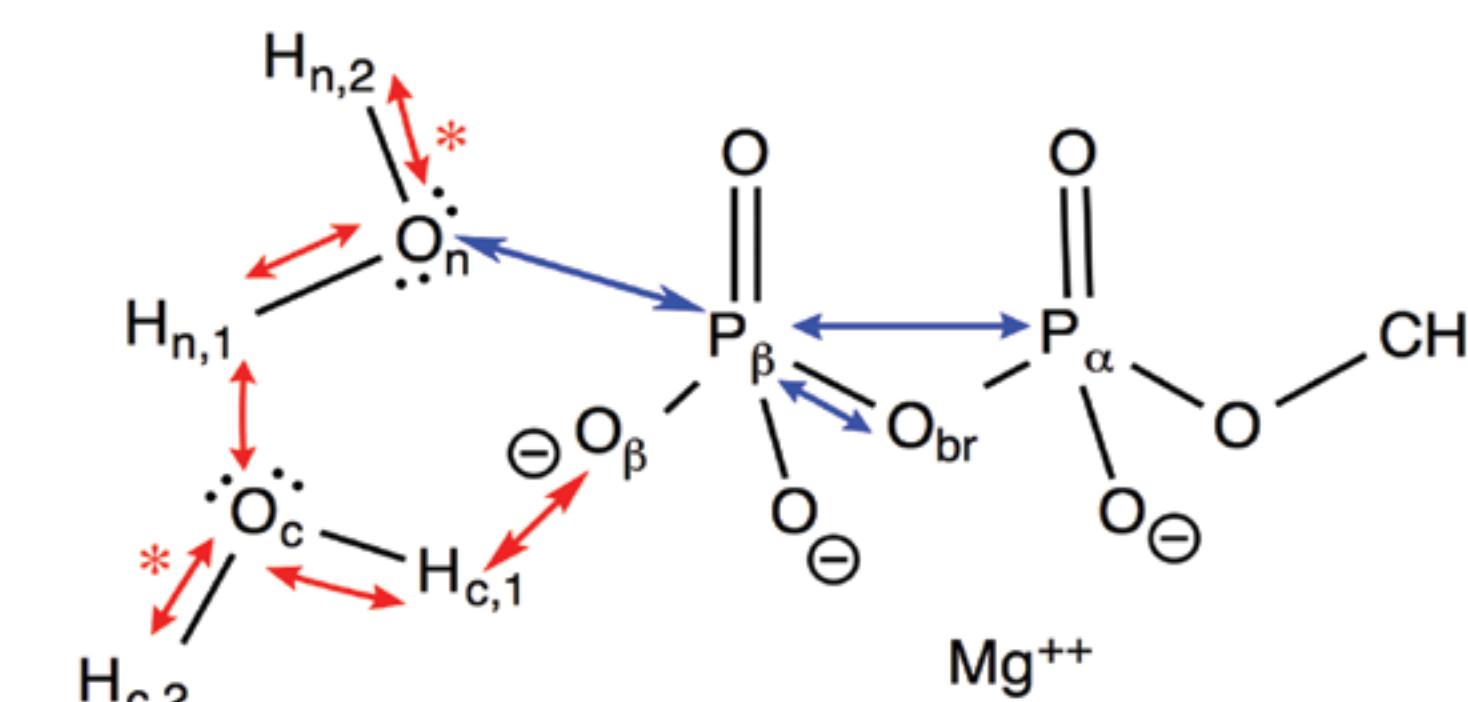
Convergence of R-only (**PBE**) and ML path refinements (**P=PM3** or **P=BLYP**). Convergence is given by the norm of the displacement vector projected over CVs. Inset shows a version of the **BLYP** ML curve in which the number of iterations is scaled by the number of energy evaluations per outer loop iteration.

Ambient hydrolysis of Methylpyrophosphate (MPP)

MPP is an ATP analog that can be hydrolyzed into methylmonophosphate and a phosphate ion.



Top: **Double-water catalyzed hydrolysis** diagram. Right: CVs used. Only non-protonic CVs (blue arrows) contribute to the ML correction term. Asterisk indicates a fixed bond.



MOFJ plot of MPP hydrolysis. **ML** and **R-only** paths extend over 30 and 72 R-iterations after convergence. ML run reaches convergence in ~3-fold fewer R-iterations. Contours are from metadynamics.

Conclusions

Preconditioning the string method provides convergence in up to 3- to 5-fold fewer number of iterations at the reference (R) level of theory.

Multi-level (ML) strings converge to the R-only solution even for when the preconditioning level of theory (P) predicts a qualitatively different solution.

Preconditioning with a P-model that better corresponds to the R-model, leads to a greater speedup. More work can be shifted to the P- iterations.

Achieving similar speedup at finite temperatures requires averaging the displacement and the correction term to control the noise, which preconditioning amplifies.