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Car-Parrinello
simulation of the RNA catalytic cleavage

Catalytic RNA modules

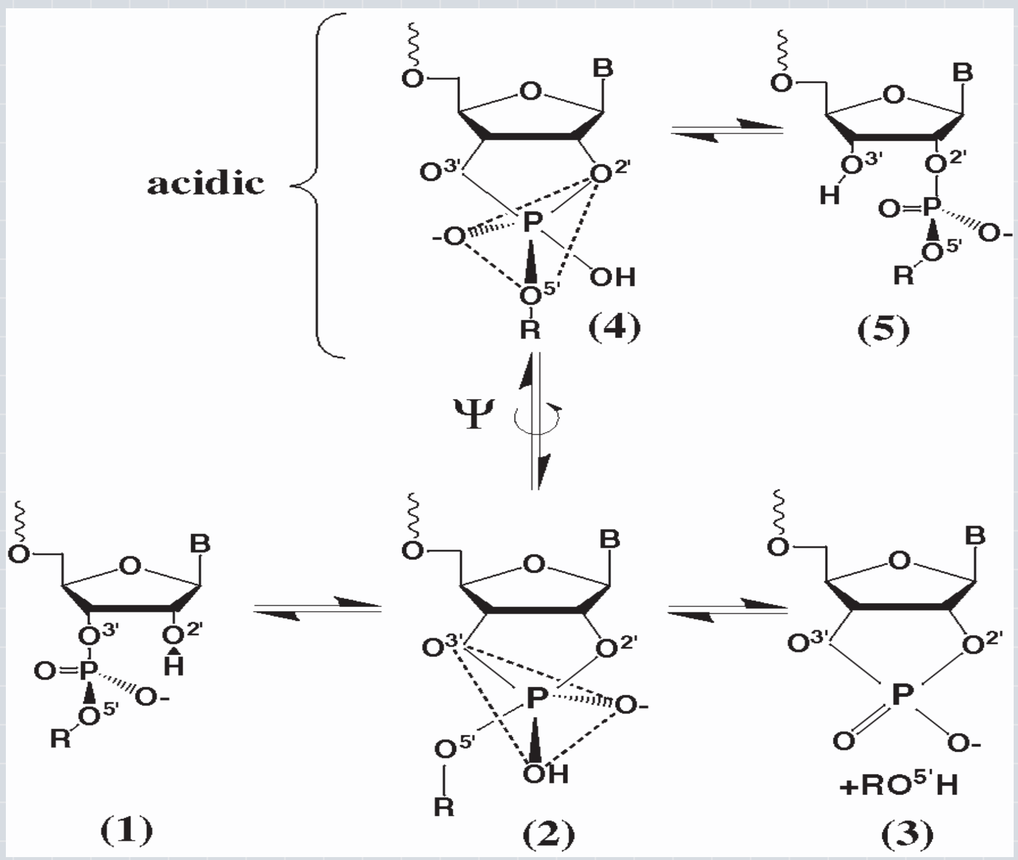

Fig.1 - The reaction scheme.

- Catalytic RNA molecules (ribozvmes) can catalyze the transformations of other RNA molecules and can be engineered to become potential therapeutic agents able to inhibit gene expression in cancer gene therapy. Yet, the reaction mechanism is still escaping accurate experimental determination.
- In this work, we used first principles molecular dynamics simulations as a tool to study the RNA catalytic reaction in an unbiased way as in a *virtual laboratory*.
- Panels from (1) to (3) represent the *right* reaction path, while (4), (5) are an alternative *wrong* channel.

- The simulations have shown that the water plays and active role in mediating the proton transfer and the metal catalyst (Mg^{2+}) is crucial in promoting both the proton abstraction and the RNA cleavage, lowering significantly the energy barrier and driving the reaction toward the right pathway.
- The blue and red lines represent the total and free energy, respectively.
- The atomic structures refer to the main reaction steps.

Details in: *J.Am. Chem.Soc.124*, 8949 (2002).

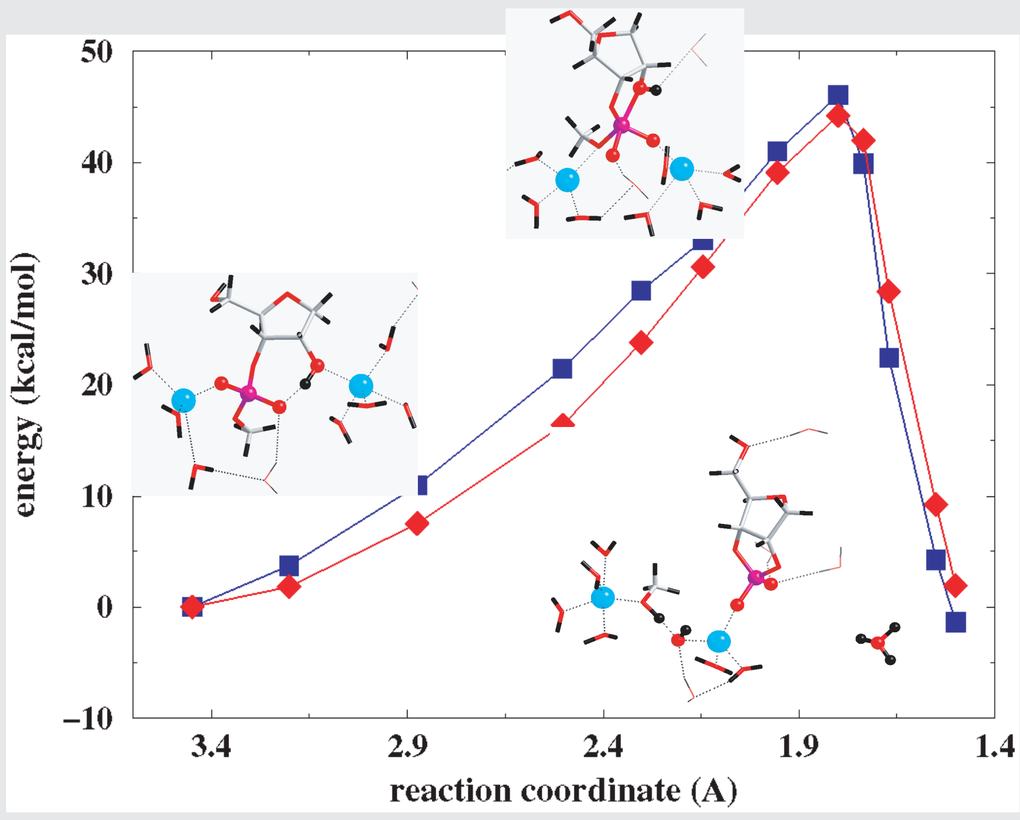

Fig.2 - The simulated RNA cleavage.

Color code :
red = O, black = H, purple = P, light blue = Mg^{2+}