in: Proc. of the Sixth Int. Conf. on Path Integrals from peV to TeV, Florence 1998, R. Casalbuoni, R. Giachetti, V. Tognetti, R. Vaia, P. Verrucchi, eds., World Scientific (Singapore1999), pp.: 407-409.

# Reaction Rates when Barriers Fluctuate: A Path Integral Approach

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Models of noise activated and diffusion controlled rate processes with *fluctuating* energy barriers are discussed. In doing so, newly developed path integral formalisms that account for *correlated* Gaussian and non-Gaussian environmental forces are presented. A common feature is the non-monotonic dependence of the escape time scale on the characteristic time scale of barrier fluctuations. We discuss this phenomenon of *Resonant Activation* and investigate whether this mechanism is at work for gated reaction processes proposed for binding ligands in proteins, and/or for ion transport in membranes. Finally, we elaborate on the connection with other timely topics, including noise driven directed transport in *Brownian motors* and *Stochastic Resonance*.

## 1 Surmounting Fluctating Barriers: Its scope

The thermally activated escape of a Brownian particle over a potential barrier plays an important role in a wide variety of physical, chemical, and biological contexts [1]. Correspondingly, with the word 'Brownian particle' one may refer either to a true physical particle but also to a chemical reaction coordinate, or some other relevant state variable or collective coordinate of the problem under investigation. In many cases, the potential experienced by the Brownian particle cannot be regarded as static but as subjected to random fluctuations with a characteristic time scale that is comparable with one of the time scales governing the escape problem itself. An example is the escape of a $O_2$ or $CO$ ligand molecule out of a myoglobin 'pocket' after photodissociation [2]. Further, a model for the ion channel kinetics in the lipid cell membrane based on fluctuations in the activation energy barriers has been proposed in [3]. In a new paradigm for the intracellular motion of a molecular motor along a microtubule put forward in Ref.[4], the binding of ATP and the release of ADP serve to randomly modulate the potential experienced by the motor protein as it travels along the biopolymer backbone. Also in other strongly coupled chemical systems [5,6], the dynamics of dye lasers [7], and even for some aspects of protein folding and relaxation in glasses, fluctuating potentials are likely to be of relevance[2,8,9]. In all those examples one has in mind the picture that the potential fluctuations experienced by the Brownian particle are controlled by some collective motion of the environment with a much larger real or effective mass, such that back-coupling effects can be neglected. On top of that, this collective environmental fluctuations must be *far from thermal equilibrium* since otherwise they would be negligibly small due to their large (effective) mass. In the abovementioned example of a ligand escaping from the ('heavy') myoglobin the far from equilibrium situation is created by the sudden photodissociation, while in the ion channel kinetics and the molecular motors it is maintained by permanent chemical reactions which are themselves far from thermal equilibrium. Finally, besides those examples of complex nonequilibrium systems, potential fluctuations without back-coupling, as we will study them here, can obviously be realized also by means of external noise imposed on a suitably designed experiment [10,11].

Note that a somewhat related phenomenon occurring for deterministic, time-*periodic* potential oscillations is presently much discussed under the label of 'stochastic resonance' [12]. While such periodic oscillations might in first priority be of interest in technical applications, random fluctuations may be more typical in natural or laboratory systems. Potential fluctuations mediating between the purely random and periodic cases (aperiodic stochastic resonance) have been studied in Refs.[13]. It is not surprising that in all these models many qualitatively similar features are observed.

By now, the literature on the fluctuating barrier problem is substantiual – especially since its application to the function of Brownian machinery [14,15] and molecular motors[16], and we refer the interested reader to a recent review[17].

In this proceedings article we shall not develop the detailed theory any further. The state of the art of a theoretical approach which uses path integration for systems not obeying detailed balance (because we are far from thermal equilibrium) in combination with singular pertubation theory has recently been reported already by the authors in Ref.[18].

## References


1. For a review see: P. Hänggi, P. Talkner, and M. Borkovec, Rev. Mod. Phys. **62**, 251 (1990).
2. D. Beece et al., Biochemistry **19**, 5147 (1980).
3. T. L. Croxton, Biochim. Biophys. Acta **946**, 19 (1988); A. Fuliński, Phys. Lett. A **193**, 267 (1994).
4. R. D. Astumian and M. Bier, Biophys. J. **70**, 637 (1996).
5. J. Maddox, Nature **359**, 771 (1992).
6. N. Agmon and J. J. Hopfield, J. Chem. Phys. **78**, 6947 (1983); **80**, 592 (1984); P. Pechukas and J. Ankerhold, J. Chem. Phys **107**, 2444 (1997).
7. R. F. Fox and R. Roy, Phys. Rev. A **35**, 1838 (1987); P. Jung, Th.

Leiber, and H. Risken, Z. Phys. **B66**, 397 (1987); **B68**, 123 (1987).
8. J. Wang and P. Wolynes, Chem. Phys. **180**, 141 (1994).
9. D. L. Stein, R. G. Palmer, J. L. van Hemmen, and C. R. Doering, Phys. Lett. **136A**, 353 (1989).
10. P. Hänggi, Phys. Lett. **78A**, 304 (1980).
11. P. D. Astumian, P. B. Chock, T. Y. Tsong, and H. V. Westerhoff, Phys. Rev. A **39**, 6416 (1989).
12. L. Gammaitoni, P. Hänggi, F. Marchesoni, and P. Jung, Rev. Mod. Phys. **70**, 223 (1998).
13. P. Jung and P. Hänggi, Phys. Rev. A **44**, 8032 (1991); A. Neiman and L. Schimansky-Geier, Phys. Rev. Lett.**72**, 2988 (1994); C. Henneghan, C. C. Chow, J. J. Collins, T. T. Imhoff, S. B. Lowen, and M. C. Teich, Phys. Rev. E **54**, R2228 (1996).
14. P. Hänggi and R. Bartussek, in: *Nonlinear Physics of Complex Systems, Brownian Rectifiers: How to Convert Brownian Motion into Directed Transport*, Lecture Notes in Physics, Vol. 476, J. Parisi *et al.* (eds.), Springer, Berlin 1996; pp: 294 - 308.
15. R. D. Astumian, Science **276**, 917 (1997).
16. F. Jülicher, A. Ajdari, and J. Prost, Rev. Mod. Phys. **69**, 1269 (1997).
17. P. Reimann and P. Hänggi, in: *Stochastic Dynamics*, *Surmounting Fluctuating Barriers: Basic Concepts and Results*, Lecture Notes in Physics, Vol. 484, L. Schimansky-Geier and Th. Pöschel (eds.), Springer, Berlin 1997; pp 127-139.
18. P. Reimann, R. Bartussek, and P. Hänggi, Chem. Phys. **235**,11 (1998).