Quantum tunneling in closely coupled *N*-particle systems affects protein critical nuclei formation

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We show that for a system consisting of *n* arrangements of *N* closely coupled particles, in the asymptotically limiting case of very small *n* and not excessive $N < k$ and assuming a simplified muffin-tin potential within the WKB approximation, quantum tunneling probabilities *prob*(*Tn*|*n*,*N*) exist that contribute significantly to free nucleation energy ΔG_n and must be included in a modern protein nucleation theory.

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I. INTRODUCTION

Successful protein crystallization requires three key conditions to be fulfilled: (i) The protein itself must not possess any qualities that prevent the long-range ordered assembly of the molecules into a periodic crystal lattice; (ii) the macroscopic thermodynamic conditions for the formation of an ordered and stable condensed phase from a metastable, supersaturated protein solution must be met (McPherson, 1999), and (iii) the kinetics and underlying microscopic processes must enable the realization of the thermodynamically possible scenario, as reviewed in (Rupp, 2015). While the macroscopic thermodynamic parameters such as chemical composition, pressure, and temperature are easily controlled in an experiment, the microscopic kinetic parameters such as nucleation, transport, and growth processes enabling the thermodynamically possible scenario to develop are much harder to control and to understand. A fundamental role in the chain of events takes the process of nucleation (Garcia-Ruiz, 2003) into whose dynamics in-situ light scattering experiments have provided fascinating insights (Meyer et al., 2012).

The pre-nucleation of protein molecules and the actual formation of critical nuclei have been studied in great detail and revealed that the critical nucleus size is in essence determined (Garcia-Ruiz, 2003) by the competition of a volume dependent stabilizing term and a surface dependent destabilizing term dependent on supersaturation β and free interface energy γ

$$\Delta G_n = -\frac{4}{3}\pi r^3 kT \ln\beta + 4\pi r^2\gamma \,. \qquad (1)$$

It has been shown that such nuclei as well as pre-nucleation aggregates can consist of very few molecules, which allows a quantum-dynamic reevaluation of nucleation dynamics.

II. QUANTUM TUNNELING IN SYSTEMS WITH LARGE *N* AND SMALL *n*

In the following we will show that in a system consisting of *n* arrangements of *N* closely coupled particles, in the asymptotically limiting case of very small *n* and not excessive $N < k$ quantum tunneling probabilities exist that can contribute significantly to free nucleation energy ΔG_n.

We assume a standard muffin-tin potential wall (Atkins & de Paula, 2006) for each of the *n*, *N* particle systems whose height is of the order of ΔG. The de Broglie wavelength of each species *i* of *n*, *N* necessary to develop the tunneling coefficient *Tn* as a conditional joint probability density *prob*(*Tn*|*n*,*N*) can be readily computed from first principles from energy and momentum

$$E = h\nu \;\text{ and }\; p = E/c = h/\lambda \,. \qquad (2a,b)$$

As we are at this point only interested in the potential wall height and not its time development, we use a time independent Schrödinger equation and apply instead of a Liouville-Green approximation the Wentzel–Kramers–Brillouin method to derive *Tn* in the muffin-tin case as

$$Tn = \exp[-2\sqrt{2m/\hbar(V_0 - E)}(x_2 - x_1)] \,. \qquad (3)$$

The function in relation to its potential walls $[x_1,x_2]$ is shown in FIG.1, from which we can clearly see that the contribution of *Tn* is of the order of observed critical ΔG_n. As a consequence, the contri-

