Local hypergravity induced crystallization of biomaterials diffracting to ultrahigh resolution

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Using probabilistic Markov Chain Monte Carlo (MCMC) simulations implemented in PyMC (Davidson-Pilon, 2016) we designed a machineable device consisting of a tungsten bolus that generates a defined local, microscopic hypergravity field. We describe the theory, design, and practical results leading to protein-protein complex crystals diffracting to 0.8 Å resolution.

I. INTRODUCTION

Significant efforts have been extended to overcome the kinetic transport effects related to buoyancy-driven convection hampering the formation of high resolution crystals by conducting the experiments in microgravity ($g \leq 10^{-6}$ m·sec^{-2}).(DeLucas et al., 1989; McPherson & DeLucas, 2015). Despite the spectacular successes achieved in crystallization of selected proteins (DeLucas et al., 1989), the complexity and expense of the flight hardware and limited launch opportunities render microgravity experiments outside of routine use for laboratory crystallization trials (Rupp, 2009). The absence of gravitational influences effects the kinetics of the crystallization process (Garcia-Ruiz, 2003), while other requirements, such as the need for a suitable protein that does not possess any qualities that prevent the long-range ordered assembly of the molecules into a periodic crystal lattice; and the macroscopic thermodynamic conditions necessary for the formation of an ordered and stable condensed phase from a metastable, supersaturated protein solution, are not modified (Rupp, 2015).

Attempting to affect multiple parameters determining crystallization outcomes simultaneously, we have taken an inverse approach by utilizing enhanced local hypergravity to induce nucleation and ordering of macromolecules. Using probabilistic Markov Chain Monte Carlo (MCMC) simulations implemented in PyMC (Davidson-Pilon, 2016) we designed a machineable device consisting of a tungsten bolus that generates a defined local, microscopic hypergravity field. We describe the theory, design and practical results leading to protein-protein complex crystals diffracting to 0.8 Å resolution.

II. LOCAL GRAVITY FOCUSSING IN MULTIBODY SYSTEMS

In the design of a hypergravity device, the difficulties arise from two basic sources: (i) the simple fact that a general multibody system based on Newton's classical equations

$$F = g \cdot (m_1 \cdot m_2) / r^2 \tag{1}$$

cannot be generally solved for m_n with $n > 2$ whereupon it becomes chaotic (Aarseth, 2003); and (ii) the general theory of relativity (GTR) predicts (Einstein, 1915) that for the focusing of gravitational waves m has to approach truly galactic dimensions (Ligo Scientific Collaboration et al., 2016). In contrast to gravitational lens focusing, a glancing angle total reflection device of a sufficiently dense material should allow in the Schwarzschild approximation (Schwarzschild, 1916) to approach extreme gravitational densities, as soon as the Kretschman invariant

$$K = 48g^2m^2 / c^4r^6 \tag{2}$$

becomes singular at $r = 0$.

To keep m as high as reasonably achievable, we selected tungsten (W) as a material for designing a cone-shaped bolus of $m = 23$ kg (Figure 1) whose tip extends into the crystallization solution (cf. § III. for implementation of the probabilistic MCMC simulations). At the electro-etched focusing point measuring 2 -10 nm, the total reflection guided gravitational density reaches a point where $\lim(r \rightarrow 0)$, effectively creating a microscopic black hole, attracting the proximal protein molecules into an extremely densely packed nucleus. In successive steps, the next-shell protein molecules are