A statistical understanding of nucleation

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Abstract

In order to study a stochastic phenomenon such as nucleation it is necessary to collect a large enough set of nucleation data to obtain nucleation statistics. This is done by performing nucleation experiments with the same solution under exactly the same conditions many times \( N (N \sim 150–300) \). Such an experiment, based on simultaneous levitation of \( N \sim 150–300 \) identical microdroplets (1–20 \( \mu \)m in diameter) of supersaturated solutions in a solvent atmosphere, is possible by employing the linear quadrupole electrodynamic levitator trap (LQELT). The LQELT is supplemented with a special optical system which is based on scattering of monochromatic polarized light. This will enable fast observation of nucleation and, thus, induction times in each of the levitated microdroplets. The \( N \) different induction times, counted from the moment \( t_0 \) at which supersaturation is established are recorded. This data provides nucleation statistics (induction time statistics). The numerical and analytical studies of nucleation statistics and parameters provide an insight into statistical properties of the underlying nucleation phenomenon. © 1999 Elsevier Science B.V. All rights reserved.

\textit{PACS:} 81.10.A; 02.50

Keywords: Supersaturated Solution; Nucleation; Induction time; Statistics; Levitation; Microdroplet

1. Introduction

In this paper we address a fundamental problem in nucleation from a new direction: Induction time statistics (ITS). As it will be demonstrated, the determination of ITS will provide answers to important questions in nucleation phenomena:

(A) What is the nucleation rate \( \Omega \) and how it can be determined from the ITS.

(B) What is the energy functional of a metastable system and how it can be determined from the ITS.

(C) What are the vital parameters of nucleation such as the critical radius \( r_{cr} \) of subcritical solute clusters and the surface tension \( \eta \) between solution and new phase and how they can be determined by means of ITS.

In this paper we will suggest an experiment and its treatment which will allow determination of the energy functional of supersaturated solutions.
2. The essence of statistics in nucleation phenomenon

By its nature, a system in a metastable state must eventually pass into a stable state. This passage, known as the nucleation process, has a random nature [1–4]. For example, in the case of supersaturated solutions random fluctuations of solute concentration can trigger the nucleation onset. One of the most important characteristics of the nucleation process is its characteristic time, known as induction time needed to create a nucleus of thermodynamically stable phase. It is understandable that induction time is a random quantity. Therefore, in order to study nucleation and its characteristics it is necessary to obtain statistics of the phenomenon by performing multiple observations of nucleation in the same system and under precisely the same conditions, such as composition, supersaturation, including solution purity, temperature and thermal history. Knowledge of statistics in the study of random phenomena is absolutely essential. For example, in other areas such as spontaneous emission from excited atomic states the characteristic time is measured using multiple (temporal) experiments. Although in the atomic world this is possible due to the identical nature of excited atoms, in the world of nucleation it has only been in recent times that one could produce individual vessels which could be called identical [5]. This affords the possibility of nucleation experiments similar to those which are traditional for excited atomic states.

The passage into a thermodynamically stable state occurs through the spontaneous formation of solute embryo nuclei. This spontaneous formation which is intrinsically random in nature is known as the nucleation phenomenon. Any reasonable study of such a random phenomenon has always meant multiple “dice casting” performed under precisely the same conditions and by virtue of this, allowing one to collect enough information (statistics) to draw truthful conclusions. Therefore, in order to study nucleation it is absolutely vital to repeat nucleation experiment many times under precisely the same conditions. The experiment suggested in this paper is unique in the study of nucleation since it will produce enough statistical data for truthful conclusions to be drawn. Our study we will be capable of:

(A) simultaneous levitation in the same environment (atmosphere) \(N \sim 150–300\) identical microdroplets containing the same solution (see Section 7.2);
(B) simultaneous monitoring of nucleation events by recording randomly distributed induction times \(t_{\text{ind},j} (j = 1, 2, \ldots, N)\) in all \(N\) levitated microdroplets (see Section 7.3).

3. Probability density function for induction time

Simultaneous observation of \(N\) random nucleation events occurring inside of the identical microdroplets, containing supersaturated solution, under the same conditions will allow us to obtain enough information to get induction time statistics (ITS), i.e. the induction time (IT) probability density function \(\rho_N(t)\):

\[
\rho_N(t) = \frac{1}{2\pi} \int_{-\infty}^{\infty} du \ \theta_N(u)e^{-i(\omega-u)t_0},
\]

\[
\theta_N(u) = \exp \left( \sum_{n=1}^{\infty} \frac{(iu)^n}{n!} k_N(n), \right)
\]

where \(t\) is the current time variable, \(t_0\) is the time moment when supersaturation was established and \(k_N(n)\) \((n = 1, 2, \ldots, i)\) are cumulants (or semi-invariants) which are the experimentally determinable quantities. The subindex \(N\) stands to emphasize that the ITS is gained on the base of \(N\) observations of the same stochastic phenomenon. The cumulants \(k_N(n)\) can be expressed through the experimentally available moments \(M_N(n)\) of the ITS as follows [6,7]:

\[
k_N(1) = M_N(1) = \langle t - t_0 \rangle_N = \frac{1}{N} \sum_{j=1}^{N} (t_{\text{ind},j} - t_0),
\]

(2.1)

\[
k_N(2) = M_N(2) - M_N(1)^2 = \frac{1}{N} \sum_{j=1}^{N} (t_{\text{ind},j} - t_0)^2,
\]

(2.2)

\[
k_N(3) = M_N(3) - 3M_N(1)M_N(2) + 2M_N(1)^3 = \frac{1}{N} \sum_{j=1}^{N} (t_{\text{ind},j} - t_0)^3,
\]

(2.3)
The simplest continuous distribution which can describe positive random quantity – induction time is the gamma distribution [8]. This assumption about the distribution function \( \rho_N(t) \) allows its presentation in the form

\[
\rho_N(t) = \frac{t^{\lambda_N - 1} e^{-t / \lambda_N}}{\Gamma(\lambda_N)},
\]

where \( \lambda_N \) will be determined later.

4. Size distribution of subcritical solute clusters

As it was mentioned in the previous section, the probability density function of induction time \( \rho_N(t) \) will be completely determined in the result of ITS experiments. This function is related to the size distribution function \( \rho_N[r(t)] \) of the fluctuating radius \( r(t) \) of subcritical solute clusters through the following obvious relationship:

\[
\rho_N(t) = \rho_N(r_{st}; t) = \langle \rho_N[r(t)] \rangle, \quad r_{st} = \langle r(t) \rangle,
\]

where the symbol \( \langle \cdots \rangle \) means averaging over random fluctuations of the radius \( r(t) \) around its stationary value \( r_{st} \) and \( r_{ct} \) is the critical radius of solute clusters (for the sake of simplicity we assume that solute clusters are of spherical shape). The solute clusters with radius \( r(t) < r_{ct} \) are known as subcritical and do not have a tendency to grow whereas the protein clusters with radius \( r(t) \geq r_{ct} \) are known as critical or supercritical and have a tendency to grow into a new phase. It is known from numerous experiments that the size distribution of subcritical solute clusters \( \rho_N(r_{st}(t)) \) is usually established almost instantaneously compared to induction time since solution has been brought into a metastable state [3]. Therefore, the time-dependent probability density (distribution) function for the radii of subcritical solute clusters \( \rho_N(r_{st}(t)) \) describes statistics of random fluctuations of the radius \( r(t) \) around its stationary value \( r_{st} \). This corresponds to the physical situation where the existing size distribution \( \rho_N[r(t)] \) of subcritical solute clusters fluctuates around its stationary value \( \rho_N(r_{st}(t)) \) until a cluster with a radius \( r(t) \), close to the critical radius \( r_{ct} \), gets a few additional solute molecules attached and becomes critical or supercritical. From this moment the nucleation onset starts.

According to the classical theory of nucleation one can write the following expression for the function \( \rho_N[r(t)] \):

\[
\rho_N[r(t)] = A_N e^{-\frac{R_{\min,N}[r(t)]}{k_B T}}, \quad R_{\min,N}[r(t)]
\]

\[
= -\frac{8\pi\sigma_N r^3(t)}{3r_{ct}^2} + 4\pi\sigma_N r^2(t),
\]

where \( A_N \) is the pre-exponential factor, \( \sigma_N \) is the surface tension coefficient and \( R_{\min,N}[r(t)] \) is the minimum work required to create a subcritical solute cluster of radius \( r(t) \) [1–4]. This work, as usual, is a sum of volume and surface contributions. We are interested in fluctuations of the radii \( r(t) \) whose stationary values \( r_{st} \) are close to the critical radius \( r_{ct} \) \( r_{st} \approx r_{ct} \) since only these fluctuations contribute nucleation. Therefore, expression (5) for the work \( R_{\min,N}[r(t)] \) and size distribution function \( \rho_N[r(t)] \) can be simplified in the neighborhood of critical radius as follows:

\[
R_{\min,N}[r(t)] = \frac{4\pi\sigma_N r_{ct}^2}{3} - 4\pi\sigma_N [r(t) - r_{ct}]^2,
\]

\[
\rho_N[r(t)] = A_N e^{-\theta_N 1/3r_{ct}^2 - [r(t) - r_{ct}]^2},
\]

where \( \theta_N = 4\pi\sigma_N/(kT) \).

As it follows from the physics of nucleation, described briefly above, the fluctuating radius \( r(t) \) of subcritical solute cluster can be presented in the simple form

\[
r(t) = r_{st} + v \int_{t_0}^{t} dt' \zeta(t'),
\]

where \( \zeta(t) \) is a random function (white noise) describing fluctuations of the radius \( r(t) \) around its stationary value \( r_{st} \), \( v \) is the parameter characterizing strength (variance) of these fluctuations. Distinguishing of the time moment \( t_0 \) (the time moment when solution was brought into a metastable state (supersaturated state)) makes sense since the formation of solute clusters and their consequent fluctuations around stationary size are detectable only when solution is supersaturated.
Omitting cumbersome mathematical details of the averaging over fluctuations of the radius \( r(t) \) around its stationary value \( r_{\text{st}} \), i.e. over the white noise \( \xi(t) \), as prescribed by relationship (4), we present the final result for the stationary size distribution \( \rho_N(t) \) of subcritical solute clusters in the form

\[
\rho_N(t) = \frac{A_N}{[1 + 2\theta_N v^2(t - t_0)]^{1/2}} \times \exp - \theta_N \left[ \frac{1}{2} r_{\text{cr}}^2 - 2(r_{\text{st}} - r_{\text{cr}})^2 + (r_{\text{st}} - r_{\text{cr}})^2 [1 + 2\theta_N v^2(t - t_0)] \right].
\]

(8A)

Assuming that the maximum observable induction time \( t_{\text{ind,max}} = \max \{t_{\text{ind}} \} \) and \( t \) are known in terms of the following integral:

\[
\rho_N(t) \approx \frac{A_N}{[1 + 2\theta_N v^2(t - t_0)]^{1/2}} \times \exp - \theta_N \left[ \frac{1}{2} r_{\text{cr}}^2 - 2(r_{\text{st}} - r_{\text{cr}})^2 + (r_{\text{st}} - r_{\text{cr}})^2 [1 + 2\theta_N v^2(t - t_0)] \right].
\]

(8B)

Specifying the function \( f(\cdots) \) introduced in the definition of gamma distribution (3) as \( f(t - t_0) = 1 + 2\theta_N v^2(t - t_0) \) one can identify distribution (8B) as gamma distribution (3) with parameters \( \alpha = 1/2 \) and \( \beta = \theta_N (r_{\text{cr}} - r_{\text{st}})^2 \). The identification of the IT distribution function as the gamma distribution function allows the following specification of the pre-exponential factor \( A_N \):

\[
A_N = \sqrt{\frac{\theta_N}{\pi}} |r_{\text{st}} - r_{\text{cr}}| e^{-\theta_N [1/3 r_{\text{cr}}^2 - 2(r_{\text{st}} - r_{\text{cr}})^2 + (r_{\text{st}} - r_{\text{cr}})^2 [1 + 2\theta_N v^2(t - t_0)]]}.
\]

(9)

Given that the IT distribution function \( \rho_N(t) \) is gamma distribution one can derive the following remarkable relationships:

\[
\langle f^n(t - t_0) \rangle = \sum_{m=0}^{n} \frac{n!}{m!(n-m)!} (2\theta_N v^2)^{n-m} M_N(m) = \frac{\Gamma(n + 1/2)}{\Gamma(1/2)} \frac{1}{\lambda_N^m} \quad n = 0,1,2, \ldots,
\]

(10)

where

\[
\lambda_N = \theta_N (r_{\text{cr}} - r_{\text{st}})^2, \quad \Gamma(n + 1/2) = \frac{(2n - 1)!!}{2^n} I(1/2), \quad \Gamma(1/2) = \sqrt{\pi}.
\]

Rewriting expression (10) just for \( n = 1 \) and \( n = 2 \) allows immediate connections between physical parameters of the subcritical solute clusters such as \( 2\theta_N v^2 \) and \( \theta_N (r_{\text{cr}} - r_{\text{st}})^2 \) and experimentally measured quantities such as \( k_N(1) \) and \( k_N(2) \):

\[
\lambda_N = \theta_N (r_{\text{cr}} - r_{\text{st}})^2 = \frac{1}{2[1 + 2\theta_N v^2 k_N(1)]}, \quad n = 1,
\]

(11A)

\[
2\theta_N v^2 = 2k_N(1) + \sqrt{2k_N(2)}\frac{k_N(2) - 2k_N^2(1)},
\]

(11B)

\[
k_N(2) > 2k_N^2(1), \quad n = 2.
\]

Attraction of further identities corresponding to \( n = 3,4, \ldots \), will allow complete identification of all parameters of the supersaturated solution through the experimentally available ITS. Result (11B) allows interesting conclusion that the classical description of nucleation given by relationships (5) and (6) is consistent with the gamma distribution for induction times only when \( k_N(2) > 2k_N^2(1) \).

5. Nucleation rate

The meaning of function \( \rho_N(t) \) can be established in terms of the following integral:

\[
P_N(t_{\text{ind}} \leq t) = \int_{t_0}^{t} dt' \rho_N(t') = \frac{1}{2\theta_N v^2} \frac{1}{\sqrt{\pi}} \times \sum_{n=0}^{\infty} \frac{(-\lambda_N)^n}{n!(n + 1/2)} [1 + 2\theta_N v^2(t - t_0)]^{n + 1/2} - 1],
\]

(12)

where \( \lambda_N \) and \( 2\theta_N v^2 \) values are given by expressions (11A) and (11B). This integral gives the probability \( P_N(t_{\text{ind}} \leq t) \) that the induction time observed in a microdroplet, chosen at random from the set of \( N \) “identical” microdroplets, is less or equal to some time \( t \). The probability \( P_N(t_{\text{ind}} \leq t) \) is closely related to the time-dependent nucleation rate \( \Omega \):

\[
\Omega = \Omega_N(t) = -\frac{1}{V(t - t_0)\ln[P_N(t_{\text{ind}} \leq t)]},
\]

(13)

where \( V \) is the microdroplet volume. This expression gives the normalized number of nucleation events occurring within time \( t \). Investigation of the function \( \Omega_N(t) \) and its dependence on the solution properties is of paramount importance since it will
allow the knowledge of nucleation rate as a function of supersaturation, purity, temperature and thermal history at any time instant t.

6. Energy functional of subcritical solute clusters

The energy functional $H(t)$ of supersaturated solution is a function of time since solution is not in a state of thermodynamic equilibrium. According to the thermodynamic theory of fluctuations its knowledge allows an alternative representation for the IT probability density function $\rho(t)$:

$$\rho(t) = \frac{1}{A} e^{-\frac{H(t)}{k_BT}}, \quad A = \int_0^\infty dt \ e^{-\frac{H(t)}{k_BT}}. \quad (14)$$

This form of the function $\rho(t)$ is conditioned by the fact that any instantaneous state of a metastable system is in thermodynamic equilibrium with respect to infinitesimal fluctuations of the system entropy. Direct comparison of relationships (8B) and (14) is quite remarkable since it allows the expression of system energy functional $H(t)$ through the experimentally determinable cumulants $k_N(n)(n = 1,2, \ldots)$:

$$H(t) = H_N(t) = -k_BT \left[ \ln[\rho_N(t)] + \ln(A) \right]$$

$$= k_BT \left[ \frac{1}{2} \theta_N \tau_e^2 - \lambda_N + (2\lambda_N + 1)\nu^2(t - t_0) \right]$$

$$- k_BT \ln(A), \quad (15)$$

where expressions for $\theta_N$ and $\lambda_N$ through the cumulants $k_N(1)$ and $k_N(2)$ are given by relationships (11A) and (11B), respectively.

7. Experiment suggested to gain induction time statistics

7.1. History: spherical void electrodynamic levitator trap (SVELT)

The new paradigm in experiments involves microdroplets of supersaturated solutions [9–17]. The use of on-demand ink-jet-type devices enables one to produce microdroplets of virtually the same size (1 part in $10^4$). In addition, these microdroplets being levitated in the solvent atmosphere utilizing the spherical void electrodynamic levitator trap (SVELT) technique [18–22] serve as containerless vessels with supersaturated solutions [9–17]. Therefore, the SVELT technique allows the preparation of highly supersaturated solutions with the ability to observe homogeneous nucleation by suspending a microdroplet without a container, i.e. without the main source of heterogeneous nucleation.

Scattering of nucleation events because of its intrinsic stochastic nature is predictable as soon as we know a real nucleation rate, i.e. a mean number of nuclei which have to appear in 1 cm$^3$/s. However, density of macro-impurities may vary considerably causing the nucleation rate to be unpredictable and high. Modified molecular species also cause variations in the number of crystals nucleated at otherwise the very same conditions. Therefore, in order to reach a well-controlled nucleation rate one needs a protocol allowing elimination or control of the factors responsible for deviation from the “homogeneous nucleation rate”.

The SVELT-like technique allows one to eliminate foreign species, serving as centers of heterogeneous nucleation, up to 1 impurity ppb [23,24]. Therefore, the nucleation rates measured in the levitated microdroplets containing supersaturated solutions are not related to any heterogeneities like container walls or foreign particles. Validity of this statement has been proved experimentally [9–17]. However, the nucleation rates themselves will be measured by employing the next generation of the SVELT-like technique (see the next section).

7.2. Linear quadrupole electrodynamic levitator trap (LQELT)

A recent patent [5] will allow us to overcome the limitation of trapping devices such as SVELT [18–22] which works best for a single microdroplet. Although the SVELT produces a three-dimensional trap where a microdroplet nestles into the null point of the electrodynamic field, the device described in Ref. [5] produces a null line. Therefore, from the zero-dimensional trap we go to a one-dimensional trap, i.e. to linear quadrupole electrodynamic levitator trap (LQELT). Now it becomes possible to assemble a line of electrially
charged microdroplets very much like one-dimensional crystal. Our preliminary experiments show that the we can simultaneously levitate in an excess of 100 identical microdroplets particles within the same LQELT. These particles produce a periodic one-dimensional lattice.

The LQELT device which will be utilized in this research project consists of four electrically charged rods (see Fig. 1) which produce a time varying potential around the null-line \((0, 0, z)\):

\[
\varphi(x, y, z; t) = A(x^2 - y^2) \cos(\omega t) - By,
\]

where \(A\) is an amplitude of the alternating electromagnetic field and \(B\) is the strength of the constant electric field around the null-line \((0, 0, z)\). The alternating quadrupole filed is needed to trap the electrically charged microdroplets along the null-line \((0, 0, z)\). The gravity force pulls the microdroplet downward from this line. This force is compensated with the constant potential \(-By\) just as in Millikan’s famous levitator. The mutual repulsion between identically charged particles injected from one end of the LQELT produces a one-dimensional lattice. This lattice is compressed by using an electrode, at another end of the LQELT, charged with the same sign as the microdroplets.

Microdroplets injected are identical, i.e. they have almost the same size (1 part in \(10^4\)) and charge (1 part in \(10^3\)). The size is controlled by displacing a constant amount of liquid using a piezoelectric element in the injector head (picopipette). The charge is controlled by induction at the tip of the picopipette.

7.3. Determination of the ITS by employing the LQELT

In order to observe nucleation and to measure the ITS it is proposed to employ the LQELT technique. This technique allows simultaneous containerless suspension of \(N \sim 150-300\) electrically charged microdroplets of supersaturated solution in the solvent atmosphere (see Fig. 1). For stationary microdroplets trapped along the LQELT null-line their weight \(mg\) is balanced by the opposing electrostatic force \(qE_{dc} = qB\):

\[
mg = CqE_{dc},
\]

where \(q\) is the microdroplet electrical charge and \(C\) is the LQELT geometrical constant. The characteristic size (radius) of levitated microdroplets may vary in the range of 1–20 μm. The microdroplet charge remains unaltered during an experiment. This assumption of constant microdroplet charge \(q\) can be easily verified in each experiment [25]. In addition to that, numerous experiments with levitated microdroplets of various sizes [9–17] have allowed the following important conclusions:

\(\text{(A)}\) due to the screening effect of microdroplet surface charge there is no effect of external electrostatic and electro-magnetic fields on the processes occurring inside of a microdroplet;

\(\text{(B)}\) there is no effect of the microdroplet surface tension on the processes occurring inside of a microdroplet.

Therefore, the solute concentration \(n_{\text{sl}}\) inside of the microdroplet solution can be determined as follows:

\[
n_{\text{sl}}^{\text{high}} + n_{\text{sl}} = \frac{n_{\text{sl}}^{\text{low}} - n_{\text{sl}}^{\text{high}}}{1000 (\text{MW})^{\text{sl}} (V_{\text{low}}^{\text{dc}} - V_{\text{high}}^{\text{dc}})^{-1}} \quad \text{(in molal units). (18)}
\]

In this expression (MW)\(_{\text{sl}}\) is the solvent molecular weight ((MW)\(_{\text{water}}\) = 18), and \(V_{\text{low}}^{\text{dc}}\) and \(V_{\text{high}}^{\text{dc}}\) are the balancing voltages for the solution with the low \(n_{\text{sl}}^{\text{low}}\) and high \(n_{\text{sl}}^{\text{high}}\) solvent concentrations, respectively [12–17]. Therefore, the following two, experimentally justified, assumptions that:

\(\text{(A)}\) solute is nonvolatile, and
\(\text{(B)}\) the microdroplet solution is in the partial thermodynamic equilibrium with its solvent vapor, allow one to achieve the desired mean solute concentration \(n_{\text{sl}}\) inside of the microdroplet by adjusting pressure of the solvent vapor inside of the LQELT chamber.

Detection of nucleation is also simplified using the LQELT configuration. It is well known that a spherical particle illuminated with polarized light in the configuration shown in Fig. 1 do not depolarize the incident light. However, any slight asymmetry causes field components to be produced
parallel to the scattering plane making the scattering particles visible. Nucleation occurring inside of a levitated microdroplet containing supersaturated solution leads almost instantaneously to the microdroplet solidification. In its turn, solidification always causes asymmetry in the shape of solidified microdroplet (microparticle). Therefore, by viewing the microdroplets through a cross-polarizer the nucleation followed by instantaneous solidification can be detected by imaging the microdroplets in in-plane scattered light. At this point the induction time, counted from the moment of creation of supersaturation (metastable state) is recorded. The experiment is terminated when all microdroplets containing supersaturated protein solution, have nucleated.

8. Conclusions

8.1. General

We, thus, come to the conclusion that the technique of simultaneous levitation of identical microdroplets opens a way to identify the rates of homogeneous (containerless) nucleation and their dependence on solution supersaturation, purity, temperature and thermal history. Therefore, the LQELT based experiments provide the background for comparison with the nucleation rates obtained in experiments with conventional μl size droplets. This comparison will allow to elaborate tests in order to identify conditions under which it is most likely to have homogeneous nucleation.
Achievement of this goal will allow control of nucleation since due to the intrinsic stochastic nature of homogeneous nucleation all its characteristics such as size distribution of subcritical solute clusters, their critical size, etc. can be evaluated and predicted. This will result in understanding of the most likely conditions for the homogeneous nucleation. This knowledge will significantly increase the fraction of successful crystallization experiments and, thus, their efficiency.

8.2. Protein nucleation

The simultaneous containerless levitation of \( N \sim 150–300 \) identical microdroplets of buffered protein/precipitant solution in solvent atmosphere as well as simultaneous observation of the nucleation events in each of the levitated microdroplets will provide the ITS of protein solutions. The determination of ITS will provide an opportunity to study the size distribution of the subcritical protein clusters.

Repetition of the LQELT experiments supplemented with recording and treatment of the ITS in the different buffered protein/precipitant solutions by varying their characteristics such as:

(A) protein supersaturation, precipitant concentration and pH;
(B) purity, i.e. testing the well purified protein solutions and the ones without purification done;
(C) thermal history, etc;

will provide data to be compared with the data obtained in current experiments employing the “hanging or sitting droplets” technique. Statistical analysis of the two parallel sets of experiments:

(A) based on the simultaneous levitation of \( N \sim 150–300 \) identical microdroplets, and
(B) based on the conventional study of “hanging or sitting droplets”

of protein solutions will provide understanding of preparation protocols for protein solutions in order to achieve purely homogeneous and controlled protein nucleation.

Such a large-scale study will provide us with the following opportunities:

(A) to understand nucleation in protein solutions, its true dependence on protein supersaturation, precipitant concentration, pH, purity, specific impurities added, thermal history, etc.;
(B) to determine nucleation rate and its dependence on the factors mentioned above.

On the base of this knowledge we will gain an opportunity to discover the path to well controlled nucleation. Therefore, there is a unique opportunity to study the dependence of nucleation rate on protein supersaturation, precipitant concentration, pH, purity, thermal history and temperature in different buffered protein/precipitant solutions. This knowledge will ultimately contribute to control of protein nucleation which can be used to increase the fraction of successful crystallization experiments and, thus, their efficiency.

The successful levitation of the microdroplet of lysozyme solution has been recently performed in our laboratory.

Acknowledgements

The authors gratefully acknowledge the support of the National Science foundation (NSF Grant CTS-9625178) and NASA (NASA Grants NAG8-1370 and NAG8-1370). The authors thank A.A. Chernov and N. Wotherspoon for their help in useful remarks related to this work and in creating the experimental apparatus. The authors also are thankful to referees for their useful remarks concerning content of this paper.

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