A semi-classical approach of the relationship between simple cells’ size and their living temperature limits based on number fluctuations of water coherence domains

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Abstract. Starting from the concepts of the quantum electrodynamics (QED) theory of coherence domains (CD) in water we propose a model aimed to evaluate the relationship between the size and the living temperature limits for simple, small cells. Cells are described as spherical potential wells with impenetrable walls, with CDs moving inside. The radius of the spherical potential well was estimated for physiological temperatures and the results match to bacteria and yeasts cells’ size. As a CD in the spherical cell exerts a force upon the membrane, a ‘gas’ formed by CDs bears a pressure on the walls. A classical statistical stability condition relates this pressure to cell volume and to the relative fluctuations of the CD number, allowing the evaluation of an upper temperature limit as a function of cellular volume. Assuming further that the CDs in the living cell form together a coherent state, the number-phase incertitude relationship (Heisenberg limit) applies. The maximum coherence between CDs is found in the ground state, a picture consistent also to Fröhlich’s postulate. For a given phase dispersion, a lower temperature limit as a function of the cell volume is found. Although we neglected the rod-like shape of certain bacteria and the presence of nucleus in yeasts, the biological data of volume and optimal living temperature intervals fit well to our model’s predictions. Moreover the larger the cell volume, the higher are the number of CDs and the coherence of their system. In addition we suggest a new classification criterion for small cells based on model’s parameters, which show discontinuities between Gram negative and positive microorganisms as well as between prokaryotes and the smallest eukaryotes.

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1. The problem of the cell size. An unexplained simple biological fact

Dimensions represent perhaps the most elementary characteristic of the living cells. They are apparently macroscopic objects, with typical sizes of 1 – 100 μm [1]. Smaller biological objects like viruses, proteins or nucleic acids are not actually living objects. Cells are far larger than objects of the microscopic, quantum world such as atoms and molecules, and also larger than nanoparticles, which define the mesoscopic scale (Figure 1).

The dimension of the cells is basically an empirical fact from the standpoint of traditional biology. Molecular biology sensibly postulates that a lower size limit is explained by a minimum number of $5 \times 10^2 – 5 \times 10^3$ different enzymes, while an upper size should be limited by the efficiency of metabolism, by the surface to volume ratio and by the dimensions of vacuoles. But this approach, though significant, is also based indirectly on certain empirical facts and therefore only displaces the problem, failing at least in part to look at the cell size as a basic feature of relevance for the phenomenon of life.

![Figure 1. Size scale of biological objects.](image)

2. Physical views on the cell size and the quantum biological approach

From the physical point of view, cell size is not a parameter reducible to the empirical data of molecular and cell biology, which in the large frame of Nature appear elementary, particular and casual, but instead it should be an essential feature of the living matter related to a specific kind of dynamics. Schrödinger [2] pointed out that in a living organism molecules must cooperate, and this condition requires a volume large enough to ensure the cooperation of a sufficient number of molecules against thermal agitation. Along this line the dissipative structures theory [3] is looking up to the cell as a giant density fluctuation and shows that its dimensions must exceed the Brownian diffusion which takes place during the lifetime of the cell. These two views look at the cell as a whole, without taking into account the molecular details inside the cell.

The same perspective is assumed by quantum biology, which proposes to understand the characteristics of the cell and multicellular organisms based on their integrative features, such as the emergence of self-organization and hierarchies of collective order above the molecular level (e.g., [4]). This approach tries to answer whether quantum mechanics plays a non-trivial role in understanding life or not, beyond the quantum chemistry calculations of molecular structure and properties. An answer based on quantum mechanics to the cell size problem was given in a model proposed by...
Demetrius [5], which connects size to metabolism, probably the most essential feature of life [6]. The model proved itself capable to derive the empirical allometric relationship, \( P = \alpha W^\beta \), where \( W \) is the weight of a cell or organism and \( P \) the metabolic rate, and \( \beta < 1 \) is a dimensionless scaling exponent which depends on the metabolic efficiency. The model applies Planck’s energy quantization rule and statistics for the electron and proton transfer taking place in the coupled cell respiration and oxidative phosphorylation according to the chemiosmotic theory.

However, the dependence of the cell size on metabolism in the quantum model of Demetrius leaves unanswered the question of the nature of metabolic rate (which may be interpreted as an observable of physical origin specific to the uniquely complex system which is the living cell or, alternately, a primary fact of the biological realm).

Another valuable physical approach of the cell size and geometry problem has been proposed recently ([7], to be published in this volume). These authors studied the oscillations of microtubules’ network in the dividing and non-dividing eukaryotic cell. The tubulin heterodimer was approximated as an elementary electric dipole performing coherent or quasi-coherent electromechanical longitudinal oscillations with low damping in the surrounding organized water. The size and shape of the cell was related to the electric field calculated around the oscillating microtubule network.

We do not intend to search here an answer to the question of the nature of metabolic rate, a challenge which is neither simple nor obvious. Rather, we propose here a new quantum model for the evaluation of cell size without any hypothesis on metabolism, along a line of attack related to our previous studies [8]. And while the microtubules continue to stimulate quantum mechanical models [9-11], our study is focused on the ubiquitous component of living cells, either prokaryotic or eukaryotic: water.

3. The QED theory of coherent domains of water
The philosophy of our approach finds support in a definition of life given by Del Giudice: “the protagonists of the biological process … [are] mesoscopic collectives characterized by millions of molecules acting in unison in wide regions of the space for long intervals” [12]. This view is in agreement to the theory of long-range coherence of dipole oscillations developed by Fröhlich [13-16] which helps understanding certain fundamental integrative features of living organisms. The very long-range character of this theory overcomes the fragmentary picture of molecular biology which admits information to be carried only by chemical messengers involved in short-range specific interactions and moving only at random. An active role for water in these long-range correlations within the cell, as opposed to its mere function of a cellular environment, is sustained by models of water collective dynamics based on \( \text{H}_2\text{O} \) molecule’s electrical properties. Moreover this role is related to inhomogeneous structures formed in water by self-organizing phenomena; we also proposed a model of ionic plasma oscillations accounting for density oscillations in liquid water [17]. As characterized by Ben-Jacob, water is „an active substance saturated with life-giving properties“ [18], in accordance to the quantum electrodynamics (QED) theory of coherence domains (CD) of water, described as clusters of electrical dipoles self-organized to oscillate in-phase with each other [19-24].

We note in this connection that quantum coherence is a theoretical concept describing a general property of living and non-living matter [24]. Most important, quantum coherence has been already demonstrated experimentally in plant photosynthesis, where light absorbing molecules capture and transfer energy according to quantum-mechanical laws at temperatures up to 180 K [25], and in a model system represented by a wet conjugated polymer where coherent intrachain energy migration takes place at room temperature [26]. Recent results obtained on the cryptophytae marine algae by 25
fs laser pulse irradiation and photoecho spectroscopy demonstrated that there exist long-lasting oscillations exciting a coherent superposition of antenna’s molecules vibrational-electronic eigenstates, with correlations across 5 nm long distances among dihydrobiliverdin pigments ‘entangled’ together by quantum coherence, even at 294 K [27]. In vitro studies on various water-containing systems evidenced experimentally a good number of phenomena consistent to the QED theory of CDs. These include among others the water bridge formed in ~15 kV static electric field [28], the long-lasting perturbations induced by weak extremely low frequency electromagnetic fields in solutions of glutamic acid [29], the ion cyclotron resonance (ICR) phenomenon in biological and biochemical systems [30, 31] and the sharp changes in conductivity for amino acids solutions exposed to ICR magnetic fields tuned to the q/m ratio of amino acid [32], the gel-state water extending up to ~1-10 μm at interfaces [33], and the phenomenon of autothixotropy evidencing the formation of fragile but truly macroscopic (~cm) structures in water by an ‘ephemeric polymerisation’ [34].

A low effective mass (excitation energy) of the water CDs was evaluated to about 12.1-13.6 eV, much lower than e.g. the electron mass [21, 24]. Accordingly, their wave-like properties are strongly enhanced because their de Broglie wavelength $\lambda = \hbar/mv$ will be much longer and comparable to the cell size. These properties together with the boson nature of the CDs, as well as with the capacity of CDs to interact with oscillating dipoles up to a few μm apart through the attractive $r^{-3}$ Fröhlich potential [35] endowed with resonant character of Askaryan forces’ type [36] sustain the view of a “supercoherence” state, a coherence spanning all the CDs throughout the cell water. Thus a supercoherent network of water CDs in the cell is postulated to play the role of command and control for the huge number of molecular interactions which take place at the right time and place through the life cycle of the cell. Long-range forces may provide an explanation for rouleaux formation [37] and anomalous light diffusion [38] of erythrocytes, dielectrophoresis of small dielectric particles by cells [39], and variations of the optical spectra of a nutrient in suspensions of yeast cells as a function of cell density [40]. A certain type of supercoherent state, or a Fröhlich condensate, has been unambiguously evidenced in living cells by a 8.085-MHz resonance by Pokorny’s group [41, 42], who identified microtubules’ network oscillations as a possible candidate.

4. Previous models and scope of the present study
Taking as a starting point the concept of water CD elaborated in the (relativistic) QED theory of the Milano group, we previously proposed a few different but related models explaining the size of the cell in the frame of non-relativistic quantum mechanics [8, 43]. To this purpose we postulated that the cell membrane is an impenetrable or semi-penetrable wall for the CDs and the shape and size of the cell selected during evolution are such as to represent a potential well or a resonant cavity imposing to the supercoherent CD system a specific type of dynamics, which is consistent to an integrated and unitary informational control of the molecular dynamics inside the living cell. With this heuristic approach and taking advantage of the low effective mass of CDs ($m_{\text{eff}} \approx 13.6$ eV $\approx 2.4 \times 10^{-35}$ kg) we evaluated the lower and higher cell size limits of spherical cells by models based on Bose-like condensation, on CD translation in a spherical well, and on an oscillator consisting of two interacting CDs [8, 43]. In our potential wells and harmonic oscillator models we assumed, for the sake of cell stability, the second energy level to be thermally inaccessible from the first (ground) level, where the system remains during cell life. The results matched well the size and shape of bacteria, yeast and erythrocytes, and explained also why the D$_2$O toxicity is higher for eukaryotes. For instance in a model
of water CDs moving in a spherical well (by analogy to the nucleons in the shell model of the atomic nucleus) the estimated upper limit for the cell radius $r_0$ is:

$$r_0 \leq \frac{\alpha \cdot h}{\sqrt{m_{\text{eff}} k_B T}}$$

where $\alpha = \pi = 3.1416$ for the cell with impenetrable walls (describing the cell membrane lipid bilayer with its highly hydrophobic inner region) and $\alpha < \pi$ for the cell with semipenetrable walls (which accounts also for the hydrophilic protein pores in the membrane), $h = h/2\pi = 1.05457 \times 10^{-34}$ J·s = 6.58212 × 10^{-16} eV·s is the reduced Planck’s constant, $k_B \approx 1.380 \times 10^{-23}$ J·K^{-1} = 8.617 × 10^{-5} eV·K^{-1} is the Boltzmann constant, and $T$ is the absolute temperature. For the model of two coupled water CDs forming a harmonic oscillator (with some particular assumptions) the maximum cell radius is given by:

$$r_0 \leq \frac{4}{\sqrt{3}} \cdot \frac{\hbar}{\sqrt{m_{\text{eff}} k_B T}}$$

(2)

Note that in relation (2) the numerical factor before $\hbar/(m_{\text{eff}} k_B T)^{1/2}$ changes from $4/3^{1/2} = 2.309$ to $(3^{1/2}/2 + 2^{1/2}) = 3.694$ when the assumptions in the harmonic oscillator model are slightly changed. In general, depending on the model, one obtains similar formulae for the maximum cell radius which differ only by a numerical factor. They all evidence a relationship between the maximum radius of spherical cells and the living temperature of the cell:

$$r_0 \leq \text{const} \, T^{1/2}$$

(3)

However, cells have various shapes, and in order to facilitate comparisons of various cells we may introduce the maximum cell volume as a function of temperature:

$$V \leq \text{const} \, T^{3/2}$$

(4)

Similarly, one may search for models expressing a relationship of minimum cell volume with temperature. Conversely, it is convenient to express the upper and lower living temperature limits in relation to the cell volume:

$$T \leq \text{const} \, V^{2/3}$$

(5a)

$$T \geq \text{const} \, V^{2/3}$$

(5b)

Here we search for such T-V relationships for the lower and upper limits of temperature which, together with temperatures close to the boiling and freezing points of water which restrict the living conditions of organisms:

$$T \leq 383 \, \text{K}$$

(6a)
define a close surface, where one can ideally expect to localize all living cells. To this purpose we
evaluate the cell size using the spherical potential well, and take advantage of the QED nature of the
water CDs due to which their instantaneous number $N$ in the cell is defined only as an average value
with associated incertitude $\Delta N$. Then we apply properties of particle number fluctuations derived from
classical statistical physics to the CDs’ number fluctuations to deduce an expression of the type of
equation (5a) of the upper temperature limit, and the number-phase incertitude relationship
(Heisenberg limit) which characterizes quantum relativistic systems of particles to derive the lower
temperature limit of the form of equation (5b). Because we use both quantum and classical concepts,
the present model may be considered a semi-classical one. The theoretical predictions are compared to
biological data. Our models are aimed mainly at prokaryote cells, due to their much simpler internal
structure which does not contain a nucleus; however, smaller simple eukaryotes are also considered.

5. Upper temperature limit vs. volume: A model based on CD number fluctuations and classical
stability conditions

We consider an average number $N$ of CDs in a spherical cell with an impenetrable plasmatic
membrane and combine this simple model which applies to each CD with a thermodynamic stability
condition for biphasic systems in equilibrium from classical statistical physics.

In the simplest case of a CD inside a spherical well of radius $r_0$ with impenetrable walls (namely,
infinite deep potential well, $U_0 \to \infty$, with the membrane described also as infinitely thick), the
translation energy of each CD is purely kinetic and quantized on an infinite number of discrete levels
$E_1, E_2, \ldots$:

$$E_n = \frac{\pi^2 \hbar^2}{2 m_{\text{eff}} r_0^2} \cdot n^2 \quad (n = 1, 2, \ldots)$$

(7)

In our previous model of a CD moving in a spherical potential well [8], we postulated $n = 1$; for $N$
coherence domains in the cell, this means that each CD occupies the same ground state, a situation
which is allowed due to the boson nature of the coherence domains of water which accordingly are
submitted to the Bose-Einstein statistics.

At the same time each CD in the spherical well collides the walls and such a single quasi-particle
exerts a force upon the walls given by [44]:

$$f = \frac{\partial H}{\partial r_0} = \frac{\partial E_n}{\partial r_0} = \frac{\pi^2 \hbar^2}{m_{\text{eff}} r_0^3} \cdot n^2$$

(8)

where $H$ is the Hamilton function of the CD in translation movement. The pressure exerted by a “gas”
formed by the $N$ CDs present in the average in the intracellular water on the walls of the spherical cell
of area $A = 4\pi r_0^2$, due exclusively to the water CDs, is therefore:
\[
p = -\frac{Nf}{A} = \frac{\pi \hbar^2 n^2 N}{4m_{\text{eff}} \left( \frac{3Nv}{4\pi} \right)^{\frac{5}{3}}}
\]

where we used the reduced volume per CD, namely \( v = V/N \).

We now turn back to the QED nature of CDs and to the \( N \) quasi-particles in the cell. Their instantaneous number is not precisely defined, and only their average number \( N \) is a real observable, which can be measured with an incertitude (standard deviation) \( \Delta N = (\langle N^2 \rangle - \langle N \rangle^2)^{1/2} \). In an intuitive view, the CDs number ‘flickers’ with a fluctuation \( \Delta N \) by annihilation in the ‘vacuum’ represented by the surrounding unordered water and by creation from the same environment. This allows an analogy with the situation described in the classical statistical physics for a liquid in thermodynamic equilibrium with its vapors in a closed vessel. The liquid phase corresponds to the ‘gas’ of CDs within the cell and the vapor phase to the ‘vacuum’ of disordered water molecules. The number \( N \) of molecules in the liquid phase (which now in the classical description is the instantaneous number, but this aspect is overlooked) undergoes fluctuations of size \( \Delta N \). The necessary and sufficient condition which ensures the stability of the system and keeps the system far of the critical point, comes up to [45]:

\[
\frac{\partial p}{\partial v} < 0
\]

We impose to the CDs gas this stability condition, which is immediately verified by the derivative \( \partial p/\partial v \) calculated using equation (9):

\[
\frac{\partial p}{\partial v} = -\frac{5\pi^2}{9} \left( \frac{4\pi}{3} \right)^{\frac{2}{3}} \frac{\hbar^2 n^2}{N^\frac{4}{3} v^{\frac{5}{3}}}
\]

In the classical statistical physics the relative fluctuation is given by [45]:

\[
\frac{\Delta N}{N} = \sqrt{\frac{\langle N^2 \rangle - \langle N \rangle^2}{N}} = \sqrt{\frac{k_B T}{v^2 \left( -\frac{\partial p}{\partial v} \right) N}}
\]

and substituting here the above result of equation (11) we get for the relative fluctuations of the CD number in the spherical cell:

\[
\frac{\Delta N}{N} = 3 \frac{\sqrt{m_{\text{eff}} k_B T}}{\pi \hbar} \frac{r_0}{n\sqrt{N}}
\]
where we impose \( n = 1 \) in numerical calculations. Note that implicitly \( \Delta N \sim r_o N^{3/2}/n \); this evidences an obvious conclusion, namely that a living cell must be always of finite size, as the absolute fluctuations may never be infinite. At the same time the relative fluctuations will decrease as \( N^{3/2} \), pointing that the larger the number of CDs in the cell the higher the degree of order in its dynamics; thus eq. (13) gives a quantitative expression to the assumption of more than one single CD synergically correlated in every living cell. More important, we obtained an expression which connects \( T \) and \( r_o \), and the relationship between these two observables depends on the choice of the relative fluctuation \( \Delta N/N \). For the stability of the CD system in the cell we impose a higher limit for the relative fluctuations:

\[
\frac{\Delta N}{N} < 1
\]  

(14)

and thus the maximum radius of the spherical cell \( r_o \) is defined for a given temperature \( T \). With the formula of the spherical cell volume, \( V = (4\pi/3)r_o^3 \), we obtain an upper limit for the living temperature of a cell as a function of its volume:

\[
T < 5 \left( \frac{\pi}{3} \right)^{8/3} \frac{4^4 h^2}{m_{eff} k_B} \frac{n^2 N}{V^3}
\]  

(15)

which is of the form of inequality (5a) as expected, i.e., of the form of results obtained by previous models (equations 1 and 2). For instance with \( n = 1 \) as used before and with \( N = 2 \) – which is the minimum number of CDs which may correlate themselves in a cell and thus the minimum number compatible with life – we get after substituting the numerical values:

\[
T < \frac{946.8}{V^{3/2}}
\]  

(16)

where \( V \) is in \( \mu m^3 \). The corresponding maximum radius of a cell living at 310 K (37 °C) is:

\[
r_0 < \frac{\sqrt{N}}{1.314}
\]  

(17)

and for \( N = 2 \) a maximum radius of 1.08 \( \mu m \) results, as observed for many bacteria. For the smallest eukaryotic cell, the baker’s yeast, one obtains \( r_0 < 1.87 \mu m \) with \( N = 6 \), and for larger eukaryotic cells with e.g. \( r_0 < 19 \mu m \), we find \( N = 25 \).

6. Lower temperature limit vs. volume: A model based on the number-phase incertitude relationship in the cell CD system

The CDs are bosons, therefore we may admit as a plausible approximation that they can form a Bose gas, a quantum ideal gas without interactions between the quasi-particles. Below a critical temperature \( T_c \) given by the Bose-Einstein equation:
a Bose-type condensate with all CDs in the same ground state can form, making possible the role of command and control of the CD system in the cell. Here \( h = 2\pi\hbar \) is Planck’s constant and \( \zeta(3/2) = 2.6124 \) is the Riemann zeta function. Due to the low effective mass of the CD, the critical temperature \( T_c \) is high. Assuming \( N = 2 \) as the minimum number of CDs compatible with life, \( T_c = 273 \) K (water freezing point) for \( r_0 = 0.50 \, \mu\text{m} \) and \( V = 0.51 \, \mu\text{m}^3 \); \( T_c = 310 \) K (which is the physiological temperature) for \( r_0 = 0.46 \, \mu\text{m} \) and \( V = 0.42 \, \mu\text{m}^3 \); and \( T_c = 373 \) K (water boiling point) for \( r_0 = 0.42 \, \mu\text{m} \) and \( V = 0.32 \, \mu\text{m}^3 \). Obviously for larger \( N \) values \( T_c \) can be even higher than \( 100 \) °C, and for the later critical temperature value the volume can be larger for larger \( N \) values. Such dimensions are indeed confirmed by the size of many prokaryotic cells. On the other hand, the condition of non-interacting bosons is probably only a rough approximation due to the Fröhlich long-range Coulombian attracting forces, and in such conditions the condensate is even more stable even when the number of bosons is small, as we assumed in all our models. Note that an accurate description of the state of the Bose-Einstein condensate is in terms of its wavefunction written as a solution of the Gross-Pitaevskii equation [46]. This is a non-linear Schrödinger equation postulated by treating the bosons within a mean field theory, and which takes into account the inter-particle interactions as well as an external potential. Also, the ‘internal’ degree of freedom associated to the coherent dipole oscillation is neglected in our picture.

In the Bose-type or Fröhlich condensate or supercoherence state, the instantaneous number of CDs is ‘ill-defined’, and one can measure only its average value \( N \) with an associated incertitude \( \Delta N \). Therefore the number fluctuations \( \Delta N \) will be subject to the number-phase realtionship or Heisenberg limit for systems with undetermined number of particles (like the number of electrons in a superconductor and the phase of its Ginzburg–Landau order parameter) [47]:

\[
\Delta N \cdot \Delta \phi \geq 1/2.
\] (19)

where \( \Delta \phi \) is the dispersion in the phase of the coherent oscillations which the \( N \) CDs perform together. It is obvious that the higher is \( \Delta \phi \), the lower is the coherence in the living cell.

From equation (13) – which was obtained by using both the quantum potential well and the fluctuations expression from classical statistical physics – we obtain the absolute value of fluctuations of \( N \):

\[
\Delta N = \frac{3}{\sqrt{5}} \left( \frac{m_{eff} k_B T}{h} \right)^{1/3} \frac{r_0 \sqrt{N}}{n}.
\] (20)

Substituting this formula in the incertitude relationship (19) one obtains several interesting results. In the first place, a relation giving the dispersion of phase is established. For simplicity, the phase dispersion in radians at \( T = 310 \) K is:
\[ \Delta \varphi \geq \frac{0.38 \, n}{r_0 \sqrt{N}}. \]  

(21)

One sees that the functioning of the cell reaches a maximum coherence (\( \Delta \varphi = \text{min} \)) in the ground state \((n = 1)\) of the CDs confined in the spherical potential well with impenetrable walls. So far we made arbitrarily the choice \(n = 1\), but this result sustains, at least indirectly, the postulate of Fröhlich theory that a driven set of oscillators can condense with nearly all of the supplied energy activating the vibrational mode of lowest frequency, i.e. the ground state.

The relationship (21) shows also the decrease of \(\Delta \varphi\) (the increase of coherence) with the size of the cell \(r_0\) and with the square root of \(N\). In fact, the highly specialized eukaryotic cells of higher organisms, which perform strongly specialized functions and thus require a higher coherence of the CDs system, are larger than the simpler prokaryotic cells.

At the same time, for a given value of the phase dispersion \(\Delta \varphi_0\), equation (20) defines the lower limit of the viability temperature of the cell as a function of its volume. For the ground state \((n = 1)\):

\[ T \geq \frac{8}{5 (\pi / 3)^{5/2}} \frac{\hbar^2}{m_{\text{eff}} k_B} \frac{N}{\Delta \varphi_0^5 V^{3/2}}. \]  

(22)

This relationship is of the same form as the inequality (5b) as expected. Together with (15) and with the limits imposed by the freezing and boiling points of water, it defines a closed surface in a V-T plot predicting the allowed values for the volume and temperature of the prokaryotic living cells.

7. Comparison of theoretical predictions with experimental data. Discussions

The dimensions and optimal temperature ranges for a number of prokaryotic microorganisms and of eukaryotic cells are shown in table 1 (after [1, 48, 49]). One notes the distinctive situation of \textit{Bacillus thermophillus}, which lives in the hot waters of geysers, in a temperature range drastically different of all considered cells. This bacterium is representative for the extremophilic microorganisms, which live in very harsh conditions. Other bacteria from the same taxum live in very cold waters. There is no evidence of clear-cut maximum or minimum temperatures for metabolism [50]. However, even if such organisms survive above the boiling point of water or below its freezing point, they may undergo spore formation in such conditions, and their metabolism would be profoundly changed. Therefore we will limit ourselves to a temperature range which is optimal for the functioning of these microorganisms, and the temperatures of the phase transitions of water as given by (6a) and (6b) will not be surpassed.

The temperature ranges of the considered cells are plotted against the cell volume in figure 2. The plot includes small and larger bacteria as well as two of the smallest unicellular eukaryotes. Remarkably, one can see that by appropriate choices of the parameters in inequalities (15) and (22), practically all the cells can be included in some of the distorted trapezes formed by the 4 curves according to their biological characteristics measured experimentally.
According to the values of the parameters of inequations (15) and (22) as synthesized in table 2, the prokaryotes plotted in figure 1 divide in three groups, and a fourth group is constituted by the small eukaryotic unicellular organisms (table 2). A constant trend is evidenced: the larger the cellular volume, the larger is the number \( N \) of CDs which co-ordinate the molecular dynamics in the cell and the stronger is the coherence within the CD system (the smaller is \( \Delta \phi \)).
Apparently, the group of the smallest cells shows the lowest degree of coherence between the two CDs inside. These bacteria are rather diverse structurally, biochemically and functionally. *Mycoplasma* does not have a cell wall, in contrast to most bacteria. It is Gram negative just as *Rickettsia*, *Salmonella*, *Pseudomonas* and *Prochlorococcus*, which have a thinner cell wall formed by an inner peptidoglycan layer covered with lipopolysaccharides. On the other hand *Staphylococcus* is Gram positive, with a thicker multilayered peptidoglycan cell wall. The *Rickettsia*, unlike all other bacteria, use the energetic metabolism of host cells for their multiplication; this feature is puzzling, because the pumping of metabolic energy is essential for the CD’s stability. The small size seems to be, perhaps, the most important common observable feature in this group with the lowest $N$ and highest $\Delta \phi$. The

**Figure 2.** Theoretically predicted upper and lower living temperature limits (solid and broken lines, respectively) vs. cell volume. The horizontal lines are placed slightly below and above the freezing and boiling points of water, respectively. According to the parameter values in equations (15) and (22), the cells group in four distinct clusters represented in different colors: small prokaryotes ($N = 2$, $\Delta \phi_0 \approx 0.90$ rad $\approx 2\pi/7$), medium-size prokaryotes ($N = 2$, $\Delta \phi_0 \approx 0.45$ rad $\approx \pi/7$), larger prokaryotes ($N = 3$, $\Delta \phi_0 \approx 0.35$ rad $\approx \pi/9$) and the smallest eukaryotes ($N = 6$, $\Delta \phi_0 \approx 0.17$ rad $\approx \pi/18$). Although the clusters of cells are generally well separated, there is some degree of overlapping due to the large spread in volume associated with the high individual variability of some species.
low degree of coherence in this group would mean a poor degree of co-ordination of the molecular
dynamics by the CDs.

Or it may point to another fundamental effect, and we would like to comment briefly on a possible
hypothesis. In our models based on the spherical well with impenetrable walls we neglected any
possible energy exchange between the “moving” CD clusters and the unstructured water around. This
is only a rough approximation, and consideration of possible friction of the CD with the “quantum
vacuum” constituted by the cytosol – which is a very complex aqueous environment containing
dissolved ions, small molecules and large biopolymers – while leaving the energy levels unchanged
in the average, would require a description based on the statistical density matrix and the Fokker-Plank
equation [51]. This would imply certain non-negligible corrections in the correlations between CDs.
But on the other hand, possible frictional effects might be much reduced in the smallest cells,
enhancing thus the coherence between CDs and compensating for the high dispersion of phase, due to
a property of water confined in very small spaces of up to 1 µm. Using AFM and SEM, Takahashi [52,
53] demonstrated the existence of a special state of water (“super-water”) in such spaces which
Correspond to a “minimum drop” of the liquid; this water looses completely its superficial tension and
behaves as an ideal lubricant. The biological significance of this finding was commented [54] starting
from the interest shown by Abdus Salam for the living cell and origin of life [55]. One may suppose
that in the case of very small cells the dynamics of water CDs may be better described by a frictionless
potential well model, in contrast to the larger cells, which would require density matrix treatment and
where some coherence might be lost due to dissipation and friction. Although speculative at this
moment, this possibility should be kept in mind for further developments.

The second group of cells including common and ubiquitous bacteria like E. coli and Proteus
contains also only two CDs similarly to the microorganisms of the first group, but their coherence is
twice better. These Gram negative bacteria have similar metabolism and cell wall and show increased
thermotolerance and resistance to putrefaction as compared to the microorganisms of the first group,
which are also Gram negative with the only two exceptions mentioned above.

The dispersion of the phase decreases (the coherence increases) even more in the third group of
prokaryotes; however, here the cells contain 3 CDs. The larger number of CDs and their increased
coherence may be associated to some evolutionary distance of the bacilli belonging to this group and
their more simple predecessors. The bacilli in this class, in contrast to the previous two classes of
smaller bacteria, are able to form spores, which enhances their resistance to the environment.

Finally, the two yeasts representative of small eukaryotic unicellular organisms contain 6 CDs
each, a significant jump from the 3 CDs in the previous class. Taking into account the hypothesis that
metabolism came first in the origin of life and that the nucleus appeared in the eukaryotes as a cell
internalized from outside [6], the fact that the nucleated cells seem to require a stepwise-increase in the
number of CDs may be of particular biological significance because it may indicate an evolutionary
discontinuity with their prokaryotic predecessors. Note also that the bacteria in the first and second
class are Gram negative with the only exception of Staphylococcus from the first group, while the
microorganisms of the third and fourth groups are all Gram positive. Moreover, the Gram-positive
Staphylococcus may change to Gram-negative when ageing. Therefore, the model appears to evidence
an evolutionary step by correlating the structural and functional differences between unicellular
organisms associated to negative and positive Gram staining of the cell wall, with values of the
parameters below and above certain critical values (N = 3, ∆φ = 0.35 rad). At the same time, this
correlation underlines the importance of the cell wall, ignored so far in our model.
Altogether, the present model may provide a new classification criterion for cells, able to evidence discontinuity points in the evolution of unicellular organisms. We note finally that our model may accommodate also larger eukaryotic cells if a sufficient number of CDs is included, e.g. some tens in the case of the erythrocyte.

The results of our theoretical model are encouraging beyond expectations. The model succeeds to find reasonable relationships between the upper and lower limits of the living temperatures vs. the cell volume which are consistent with the experimental data, in spite of all its approximations. For instance, the complex composition of cytosol and its properties different of those of pure water may require indeed the density matrix treatment as well as corrections to the classical equation (11). Such corrections may be needed to account also for the higher compressibility of the CDs boson gas as compared to an ideal gas [56]. Second, the interspersed classical and quantum character seems epistemologically uncomfortable; but this is not uncommon in many areas of physics and may be not only an expression of the emerging character of quantum biology. We may suppose also that this aspect could be related somehow also to decoherence theory. Considering the cell as a large complex quantum system that collapses to become a classical entity we can expect that the emergence of classicality will involve some quantum signatures that cannot be ignored [57] – and size and shape may be among them. Third, the specific numbers of CDs for the considered prokaryotic cells is low, although we use statistical concepts. But given the postulated command and control role of CDs in the cell, their small numbers involving very large relative fluctuations may play a key role in understanding the functioning of the cell.

Table 2. The number of water coherence domains and the phase dispersion of the CD system in relation to some biological characteristics in the four groups of cells discriminated according to the model’s predictions.

| Species          | Shape      | Gram staining¹ | N  | Δφ₀ (rad) | V (µm³) | T domain (°C) |
|------------------|------------|----------------|----|-----------|---------|---------------|
| *Mycoplasma*     | Spherical  | −              |    | 0.90      | 0.001-0.9 | 18-45         |
| *Prochlorococcus*| *ibid.*    | −              |    | 0.45      | 0.4-3.7  | 12-52         |
| *Staphylococcus* | *ibid.*    | +              | 2  | 0.35      | 0.3–17   | 10-100        |
| *Rikettia*       | Rod-like   | −              |    |           |         |               |
| *Salmonella*     | *ibid.*    | −              |    |           |         |               |
| *Pseudomonas*    | *ibid.*    | −              |    |           |         |               |
| *Proteus*        | Rod-like   | −              | 2  | 0.17      | 14–28    | 25-30         |
| *E. coli*        | *ibid.*    | +              |    |           |         |               |
| *B. thermophilus*| Rod-like   | +              | 3  | 0.35      | 0.3–17   | 10-100        |
| *B. subtilis*    | *ibid.*    | +              |    |           |         |               |
| *S. cerevisiae*  | Spherical  | +              | 6  | 0.17      | 14–28    | 25-30         |
| *Rhodotorulla*   | *ibid.*    | +              |    |           |         |               |

¹The Gram-positive bacterium *Staphylococcus* may change to Gram-negative when ageing.
Fourth and most important, here we did not take into account the shape of the cells except for the simplest spherical cells, and made no distinction between spherical and cylindrical cells (like the rod-like bacteria and the disk-like erythrocyte). A model of cylindrical potential well would lead to energy levels of a more complicated form than equation (7) involving the roots of Bessel functions and, therefore, the two curves given by inequalities (15) and (22) should be replaced by more complicated functions. At the same time, although the two smallest yeast cells may be fitted well by the model, we did not take into consideration the existence of the nuclear membrane, which is expected to divide the spherical potential well in two uneven concentric compartments. However, we expect that these corrections would affect only the ‘fine structure’ of the curves (15) and (22), and, therefore, to a first approximation we did not restrict the convergence of the theory with the microbiological data by ignoring the cylindrical shape of some bacteria as well as the nucleus in yeasts. This suggests that in our model the size of the cell is more important than shape. The same conclusion has been reached independently, by the completely different approach of [7] (in this volume), who related the cell size and shape to the power of electromagnetic field radiated by (quasi)coherent electromechanical longitudinal oscillations of the microtubules’ network in the dividing and non-dividing eukaryotic cell.

The satisfactory fit with microbiology data does not exclude the possibility that other factors be involved, such as decoherence mentioned above. For example one can consider an analogy with superconductors and suggest that the size of the cell is somehow connected to a coherence length $\xi$ describing the size of thermodynamic fluctuations [47]:

$$\xi = \frac{h}{\sqrt{2m_{\text{eff}} \alpha_c \left| T - T_c \right|}}$$

(23)

where $T_c$ should be evaluated by equation (18) to a first approximation. But to make operational such an approach one should perhaps adapt the Ginsburg-Landau theory of superconductors to describe the CD boson system in the cell water before one could define the meaning of the parameter $\alpha_o$ and establish its value. This may be a task for future examination.

8. Conclusions
Our semi-classical approach based on fluctuations of water CDs’ number inside cells with impenetrable walls succeeds to accommodate, by appropriate choices of the parameters, the experimentally measured values of biological observables for many typical unicellular organisms within the predicted limits of living temperature and cellular volume. According to the model, the cells cluster in distinct groups; the prokaryotes divide in three classes, and a fourth group is constituted by the small eukaryotic cells. The results suggest not only that the number of CDs which co-ordinate the molecular dynamics in the cell increase with the volume, but also that the coherence within the CD system is stronger in cells with larger volume. By establishing this rule, the model provides a new criterion for the classification cells which is sustained by biological criteria, most notably by evidencing discontinuities in the number of CDs and their coherence at the evolutionary boundary between prokaryotes and eukaryotes as well as between low- and medium-sized bacteria (mostly Gram negative) and larger unicellular organisms (Gram positive). Moreover, one may foresee plausible extensions of the model to larger eukaryotic cells by including a sufficient number of CDs. Finally, the occurrence of maximum coherence predicted in the ground state is consistent to the postulate of...
Fröhlich picture stating that a driven set of coupled oscillators can condense in the ground state mode of oscillation.

The convergence of the model with the biological data notwithstanding the present neglect of the geometry of cylindrical and nucleated cells in the model implies that the size of the cell is more important than its shape for the living temperature limits, in agreement to a similar conclusion resulting from a radically different model independently postulated for eukaryotic cells. However, corrections for the shape of the more complex cells using potential wells appropriate for rod-like bacteria and concentric nucleated spherical yeast cells may be foreseen as tasks for further developments. Moreover, a more realistic model should take into account not only the cell membrane as a semi-penetrable wall, but also the more hydrophilic cell wall with its different structures for Gram positive and negative microorganisms, which plays a leading role in maintaining the shape of the cell (especially for rod-like bacilli); this would imply a more complex type of potential well, requiring numerical solutions. Other possible refinements may include consideration of “super-water” for the smallest cells having the size of a “minimum liquid drop” with properties close to an ideal lubricant; taking into account of interactions between CDs and of the internal degree of freedom associated to the coherent dipole oscillation by use of the Gross-Pitaevski equation; corrections associated with the cytosol complex composition including biopolymers which alter the properties of water and may require density matrix treatment and Fokker-Planck equation, as well as decoherence of CDs due to scattering on the intracellular biopolymers and organelles; a possible connection between the size of the cell and other parameters describing the size of thermodynamic fluctuations in the CD system, like for instance a properly defined coherence length; and correlations to energetic metabolism and to various experimental parameters of cytoplasmic water, e.g. pH, ionic strength, colloid-osmotic pressure, water chemical activity, and free vs. ‘bound’ water content. The evoked possible correlations might open also new prospects to a better understanding of the Archaea microorganisms which lived in hostile environments, as well as to the origin on life.

Nevertheless, with all the approximations involved, the model makes successful predictions of direct biological relevance; and therefore warrant efforts for further developments.

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