Attractive Casimir–Lifshitz Forces as a Universal Driver of Prebiotic Protocell Aggregation and Cluster Formation

Michael Massoth
Department of Computer Science, Hochschule Darmstadt (h_da)
University of Applied Sciences Darmstadt, member of European University of Technology (EUt+)
Darmstadt, Germany
e-mail: michael.massoth@h-da.de

***Abstract*—How fragile, RNA-free protocells could have formed stable clusters in a hot, saline and dynamically fluctuating prebiotic environment remains unresolved. Classical explanations—such as hydrophobic effects, Derjaguin–Landau–Verwey–Overbeek (DLVO) interactions and thermal noise—fail in the relevant 5–200 nm separation range. Here we propose that attractive Casimir–Lifshitz forces act as a universal and physically unavoidable coupling mechanism between protocells. Starting from the exact sphere–sphere solution in the classical (high-T) limit and a Derjaguin (PFA) approximation, we show that Casimir–Lifshitz attraction decays algebraically as $1/L^2$ under prebiotically plausible conditions (protocell radii 100–1,000 nm; separations 5–200 nm; 50–200 mMol salt; 20–90 °C) and can exceed exponentially suppressed DLVO contributions beyond a few nanometres. From this framework we derive testable predictions—including stronger clustering of PMBCs relative to fatty-acid vesicles, enhanced effective adhesivity of larger protocells and contact lifetimes on the order of minutes—and outline a three-stage experimental roadmap to evaluate Casimir–Lifshitz forces as a realistic driver of prebiotic protocell cluster formation.**

Keywords—Casimir–Lifshitz Forces; Prebiotic Protocell Aggregation; Mesoscale Fluctuation-Induced Interactions; Non-Chemical Cooperation Mechanisms; Proto-Cluster Formation and Stability; Experimentally Testable Origin-of-Life Framework.

I. INTRODUCTION

The emergence of life is commonly framed in terms of membranous protocells that provide confined reaction spaces, support concentration gradients, and enable molecular retention—features widely regarded as physical prerequisites for metabolism, information stabilization, and evolvable selection processes [4]. A broad range of experimental studies has demonstrated that simple amphiphilic systems can spontaneously assemble into membrane-bound vesicles under prebiotic conditions [5] and undergo primitive growth, fusion, and division dynamics.

What remains unresolved, however, is how mechanically fragile, RNA-free protocells could have formed stable dimers, trimers, and higher-order clusters in thermally active, saline, and dynamically fluctuating early environments. Classical interaction mechanisms offer no robust explanation in the mesoscale regime: hydrophobic forces act only at molecular contact, while electrostatic and van der Waals contributions described by Derjaguin–Landau–Verwey–Overbeek (DLVO) theory [3] are strongly screened under realistic ionic conditions and rapidly overwhelmed by thermal noise at the k_BT scale.

This gap motivates a central question: which physical mechanism could have supported reproducible, mesoscale, and non-chemical encoded protocell cooperation prior to genetic or metabolic specialization? Here we propose that attractive Casimir–Lifshitz (CL) interactions [1][2] —arising from quantum and thermal electromagnetic field fluctuations—constitute a physically unavoidable, material-dependent aggregation mechanism operating precisely in the regime where classical colloidal forces fail. Unlike DLVO-type interactions, CL forces do not rely on surface charge or molecular specificity and persist across nanometre-to-submicrometre separations in electrolyte environments.

In this work, we develop a quantitative theoretical framework for CL-mediated protocell interactions, establish their relevance relative to classical screened forces, and translate the resulting scaling laws into experimentally testable predictions for protocell clustering. By grounding early cooperative organization in fluctuation-induced physics rather than biochemical functionality, this study reframes protocell aggregation as a physically emergent precursor to later chemical and informational complexity.

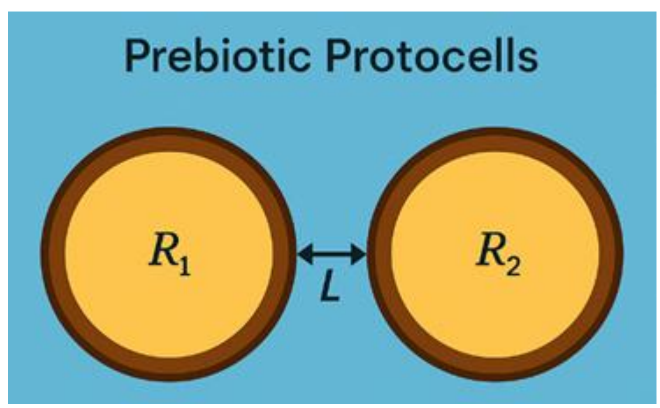

Figure 1. *Schematic of two prebiotic protocells with radii R_1 and R_2 and minimal surface-to-surface separation L in saline water*

In Figure 1 two prebiotic protocells with radii R_1 and R_2 are depicted at a minimal surface-to-surface separation L in saline water (primordial soup), defining the sphere–sphere geometry underlying the Casimir–Lifshitz interaction model.

Contribution Summary: In this study, we propose that attractive Casimir–Lifshitz (CL) forces provide a universal, physically unavoidable mechanism for mesoscale protocell aggregation under prebiotically plausible conditions where classical Derjaguin–Landau–Verwey–Overbeek (DLVO) interactions fail. Building on the exact sphere–sphere formulation in the classical (high-temperature) limit and a Derjaguin proximity-force approximation, we derive an algebraic interaction scaling that remains operative in regimes inaccessible to exponentially screened electrostatic forces. We identify the resulting dominance window relative to DLVO contributions and show that CL attraction can reach thermal relevance at the level of individual protocell contacts. Finally, we translate these scaling results into experimentally testable predictions—including material-dependent clustering, radius-dependent effective adhesivity, and finite contact lifetimes—and outline a staged experimental roadmap to evaluate fluctuation-induced forces as a candidate driver of early protocell cluster formation.

The structure of this paper is as follows:

In Section II, we contrast classical DLVO theory with Casimir–Lifshitz theory, highlighting their distinct physical origins, interaction ranges and relevance under ion-rich prebiotic conditions.

In Section III, we develop a quantitative Casimir–Lifshitz framework for spherical protocells, progressing from the fundamental Lifshitz formulation to exact sphere–sphere results and biologically tractable Derjaguin-type approximations, and directly compare these predictions with DLVO and van der Waals interactions.

In Section IV, we delineate a prebiotically realistic parameter window—geometry, dielectric properties, temperature and salinity—within which fluctuation-induced forces become physically and geochemically plausible.

In Section V, we derive experimentally testable predictions regarding material dependence, size scaling, temperature sensitivity and measurable deviations from DLVO behaviour.

Sections VI and VII integrate these physical results into a broader prebiotic evolutionary perspective, discussing implications for early protocell clustering, proto-cooperation and emergent organization.

Section VIII concludes with a summary and outlines directions for future experimental and theoretical work.

II. THEORETICAL BACKGROUND: CASIMIR–LIFSHITZ VERSUS DLVO

The physical interactions between protocells can be described largely by two frameworks: classical DLVO theory and the Casimir–Lifshitz theory [1][2] of quantum- and thermally induced fluctuation forces. Both include attractive and repulsive contributions at nanometre scales, but they differ fundamentally in physical origin, range and environmental robustness. For prebiotic scenarios this distinction is crucial, as early environments were ion-rich, thermally dynamic and chemically heterogeneous—conditions under which classical colloidal idealizations apply only in a limited sense.

A. DLVO Theory: Limitations in a Prebiotic Primordial Context

Classical DLVO theory models the force balance between colloidal objects as the sum of an electrostatic double-layer repulsion and a short-range van der Waals attraction [3]. The electrostatic component is governed by the Debye length, which shrinks exponentially with increasing ionic strength. In saline solutions—realistic for prebiotic environments—the Debye length is typically only ~1–2 nm, rendering electrostatic repulsion extremely short-ranged.

The van der Waals contribution is likewise confined to very small separations. Direct AFM force measurements in electrolyte solutions show that additional attractive components—depending on ion valency and surface chemistry—are typically significant only within ~0.3–1.0 nm, at most 1–3 nm, and fall below k_BT beyond these distances.

Under prebiotic ionic conditions, and for separations L of 2–200 nm relevant to protocell clustering, classical van der Waals and DLVO interactions therefore provide no robust mechanism for stable mesoscale association.

B. Casimir–Lifshitz Theory

The Casimir–Lifshitz theory [1][2] is a field-theoretic generalization of van der Waals interactions. It arises from quantum and thermally induced electromagnetic field fluctuations. Crucially, these forces do not depend on real charges, receptors or chemical bonds, but on how the fluctuating electromagnetic field couples to the material-dependent reflection properties of the interacting interfaces. The central quantity is therefore the dielectric response function $\varepsilon(i\xi_n)$, rather than surface charge.

Casimir–Lifshitz forces act irrespective of salt concentration or molecular specificity and operate over distances of 2–200 nm—the very regime in which prebiotic protocells would have interacted. This mechanism is present both at T=0 through quantum vacuum fluctuations and at finite temperature through additional thermal contributions.

C. Relevance for Prebiotic Protocell Clusters

Protocell membranes exhibit a strong dielectric contrast [12] relative to saline water: $\varepsilon_{Membran} \approx 2$ to $8 \ll \varepsilon_{Water}$ (at 50–200 mMol) $\approx$ 75 to 78. Such dielectric-contrast–driven fluctuation forces were first described by Casimir [1] and later generalized to real materials and media by Lifshitz [2]. This contrast satisfies the sign condition for attractive Casimir–Lifshitz interactions. Thermal activity further enhances the relevant fluctuation modes, yielding a robust, non-chemical aggregation mechanism capable of stabilizing mesoscale

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protocell assemblies without any genetic, metabolic or enzymatic specialization.

Empirical support for long-range, fluctuation-related forces in electrolyte environments includes AFM studies [13] on multivalent-ion-induced attraction (Moazzami-Gudarzi et al., 2016) [18], force measurements between silica particles in electrolytes (Valmacco et al., 2016) [19] and detailed AFM analyses of van der Waals [14] and DLVO contributions in saline media (Butt et al.; 1991) [20]. Together, these findings reinforce the plausibility of fluctuation-induced forces as contributors to mesoscale stability under prebiotic conditions.

III. Quantitative Casimir–Lifshitz theory and approximation methods

To assess the strength, range and biological relevance of Casimir–Lifshitz interactions in prebiotic protocell systems, we require a theoretical framework that links exact field-theoretic formulations with biologically tractable approximations. Protocells are mesoscale objects with radii of ~200 nm to 1000 nm; their interactions therefore cannot be captured by simple plate geometries but must be described using a sphere–sphere configuration that explicitly incorporates temperature, ionic strength and material properties.

In this section, we proceed from the universal Lifshitz formulation (*A.*) to an exact sphere–sphere description in the classical (high-T) limit (*B.*), derive an asymptotic Derjaguin (PFA) approximation (*C.*), and finally compare the resulting algebraic interaction range with the exponentially screened DLVO predictions (*D.*).

To ensure a clear distinction between physical results, model-dependent conclusions, and interpretative extensions, we explicitly differentiate three epistemic levels throughout this work.

Level I (Established Physics) refers to results derived directly from Casimir–Lifshitz theory and primary experimental literature.

Level II (Model-Based Deductions) comprises conclusions that follow from the specific geometries, parameters, and approximations introduced here.

Level III (Prebiotic Hypotheses) denotes interpretative extensions that apply these physical results to early protocell systems and evolutionary contexts. This epistemic distinction is independent of the formal subsection labeling used throughout the manuscript.

A. Casimir–Lifshitz Fundamental Formulation

The Casimir–Lifshitz interaction [1][2] between two bodies in a medium arises from modifications of the electromagnetic fluctuation spectrum between their interfaces. In the field-theoretic formulation, the free energy F(L) at a surface separation L is expressed as a Matsubara sum. The standard Lifshitz–Matsubara expression for F(L) follows the classical works of Lifshitz (1956) [2] and the formulation in Boström and Sernelius (2000) [17]. The frequency-dependent dielectric response enters through $\varepsilon(i\xi_n)$, with full specifications provided in these references. The summation runs over discrete Matsubara frequencies $\xi_n=2\pi n k_B T/\hbar$. The terms $r_1^{(n)}$ and $r_2^{(n)}$ represent reflection-coefficient-like material parameters determined by the dielectric response $\varepsilon(i\xi_n)$. Casimir–Lifshitz forces have been experimentally demonstrated [6].

(Level-I:) This formulation is universal and applies to arbitrary material combinations, geometries and intervening media. For biological systems, it implies that the resulting force does not rely on specific chemical bonds but emerges solely from the fundamental interfacial electromagnetic properties of membranes and their surrounding medium.

B. Exact Sphere–Sphere Geometry in the Classical Limit

Because prebiotic protocells are approximately spherical compartments suspended in electrolyte solutions, the sphere–sphere configuration [7][8] represents the physically most realistic interaction geometry. The exact description of the Casimir–Lifshitz interaction energy in the classical (high-T) limit was developed within the scattering-field formalism of Rahi et al. [9] and analytically evaluated by Bimonte and Emig [10] for two spheres of radii R_1 and R_2, separated by a surface-to-surface distance L, including Debye screening with $\kappa=1/\lambda_D$. Because the full expressions are not part of the methodological advance presented here, we refer to Eq. (3) in Bimonte and Emig [10] and use this formulation as the theoretical foundation for the practically relevant PFA scaling discussed in Section *III.C*.

(Level-I:) This formulation captures the exact curvature dependence of the interaction and does not rely on idealized parallel plates. In the classical limit, the n=0 Matsubara term dominates; in electrolyte media this contribution is partially screened by Debye damping, $\Lambda\rightarrow\Lambda e^{-\kappa L}$. Higher-order Matsubara modes ($n\geq1$) remain present and are fully included in the Lifshitz formalism [11].

(Level-II:) As a consequence, the interaction is only partially attenuated in saline environments rather than eliminated, because the higher modes persist. Thus, Casimir–Lifshitz forces remain operative over 5–200 nm even under realistic prebiotic conditions.

C. Derjaguin Approximation as a Practical Scaling

In the biologically relevant regime $L \ll R$ (here L=2–100 nm and R=200–1000 nm), the exact Casimir–Lifshitz description for a sphere–medium–sphere system can be reduced, via the Derjaguin proximity-force approximation (PFA), to a simple scaling form: $F_{CL}(L) \propto A_{eff}{*}R_{eff}/L^2$. Here, the effective curvature radius R_{eff} acts as the dominant amplification factor for biological cluster stability. A_{eff} is an effective, medium-dependent Hamaker constant derived from the full Lifshitz spectrum. Larger protocells therefore generate systematically stronger coupling at identical material parameters.

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The following applies:
$F_{CL}(L) \approx -(A_{eff}/6) * (R_{eff}/L^2)$ with $R_{eff} = (R_1 * R_2)/(R_1 + R_2)$.
(Level-I/II:) Here, A_{eff} denotes an effective Hamaker constant that integrates the spectral dielectric response of the membrane–water system. The force scales linearly with the effective curvature radius R_{eff} and decays algebraically as $1/L^2$. (Level-II:) For the parameter ranges considered below, the resulting potential wells reach several k_BT, making them relevant for mesoscale cluster stabilization.
The corresponding effective binding potential $U_{CL}(L)$ follows directly from integration: $U_{CL}(L) \propto -(A_{eff}/6) * (R_{eff}/L)$, with A_{eff} the membrane–water Hamaker constant, R_{eff} the reduced curvature of the two spheres, and L the minimal surface-to-surface distance. The approximation holds for $L \ll R_i$, L larger than the membrane thickness, and smooth, non-adhesively functionalized interfaces.
In Figure 2, the attractive Casimir–Lifshitz force $F_{CL}(L)$ between two PMBC-like protocells with $R_1 = R_2 = 500$ nm is shown as a function of separation L (logarithmic x-axis). The algebraic decay $F_{CL}(L) \propto 1/L^2$ yields a pronounced mesoscale attraction over distances of 5–200 nm. All numerical results are obtained using an effective Hamaker constant $A_{eff} = 5 \times 10^{-21}$ Joule. A_{eff} should be understood as an effective, medium-dependent Hamaker constant derived from the full Lifshitz spectrum, not a fitted free parameter.

Biophysical implication: Because $U_{CL}(L) \propto -R_{eff}/L$, large protocell radii and moderate separations favour mesoscale cluster stability.
Core statement: Fluctuation-induced attraction strengthens with protocell curvature R and decays only algebraically with distance L, enabling non-chemical mesoscale stabilization of protocell assemblies.

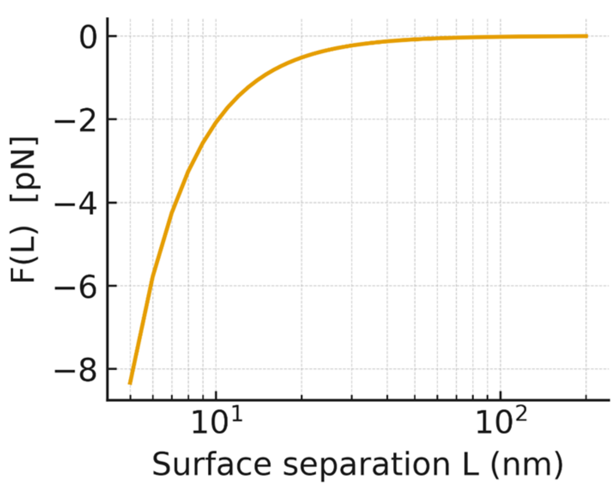

Figure 2. *Attractive Casimir–Lifshitz force $F_{CL}(L)$ between two PMBC-like protocells (R_1=R_2=500 nm) as a function of separation L.*

Quantum, crossover and classical regimes: For separations L ≤ 10 nm, the interaction is dominated by the quantum-fluctuation (T = 0) term, and a non-retarded PFA form $F_{CL}(L) \approx -(A_0/6) * (R_{eff}/L^2)$ is appropriate. Between 10–30 nm, a crossover regime appears in which the full Matsubara summation must be retained. Practically, this behaviour can be described by an effective Hamaker constant $A_{eff}(L,T) = A_0 + \Delta A_T(L)$, while the scaling $F_{CL} \propto R_{eff}/L^2$ remains unchanged. Above ~30–50 nm, the classical (high-T) contribution dominates, with thermal modes setting the leading term.
Across the relevant prebiotic range, the algebraic dependence $F_{CL} \propto R_{eff}/L^2$ is preserved, and the effective strength $A_{eff}(L,T)$ simply reflects the combined quantum and thermal contributions. No exponential screening occurs, in stark contrast to DLVO components.

D. Comparison: Brownian Motion vs. Casimir–Lifshitz vs. DLVO vs. Van-der-Waals

In a thermally active, ion-rich prebiotic environment at ~25 °C, stable protocell clusters require interaction wells deeper than ~3–5 k_BT per contact to persist on mesoscale timescales. Forces of order ≤ k_BT or with ranges shorter than ~3 nm are insufficient to stabilize assemblies against Brownian disruption over separations of 5–200 nm.
The key question, therefore, is which interaction dominates at prebiotically plausible distances. DLVO theory predicts an electrostatic contribution decaying as $V_{DLVO}(L) \propto \exp(-L/\lambda_D)$ with Debye lengths $\lambda_D \approx 0.7$–1.4nm for ionic strengths of 50–200 mM. Under these conditions the DLVO range is unavoidably exponential and extremely short.
(Level-I:) Classical van der Waals interactions are likewise restricted to sub-nanometre to few-nanometre separations. By contrast, the PFA scaling of the Casimir–Lifshitz force yields $F_{CL} \propto R_{eff}/L^2$, with no exponential collapse.
(Level-II:) For parameter ranges R ≈ 500–1000 nm and L ≈ 2–200 nm, a regime emerges in which the Casimir–Lifshitz contribution either dominates or is comparable to the residual DLVO terms. For realistic prebiotic distances (L > 2–100 nm) applies $|F_{CL}(L)| \geq |F_{DLVO}(L)|$.

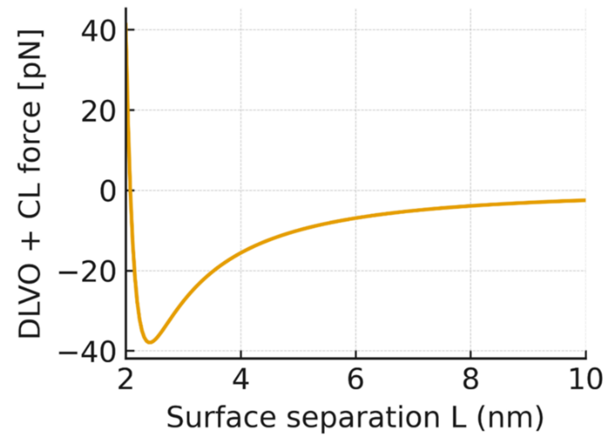

Figure 3. *Resulting total force from F_{DLVO} and F_{CL} contributions over L=2–10 nm.*

In Figure 3, the resulting total force from combined F_{DLVO} and F_{CL} contributions is shown over separations of 2–10 nm.

The algebraic Casimir–Lifshitz component generates a residual, non-DLVO-compatible attraction as potential well that remains experimentally detectable. The resulting attractive force (down to −38 pN) stabilizes the bound protocell cluster configuration.

(Level-III:) Under plausible prebiotic conditions, there therefore exist distance intervals where Casimir–Lifshitz interactions match or exceed the remaining DLVO contributions—without implying universal dominance. This supports the interpretation that Casimir–Lifshitz forces represent a general physical aggregation mechanism in saline, thermally dynamic early-Earth environments.

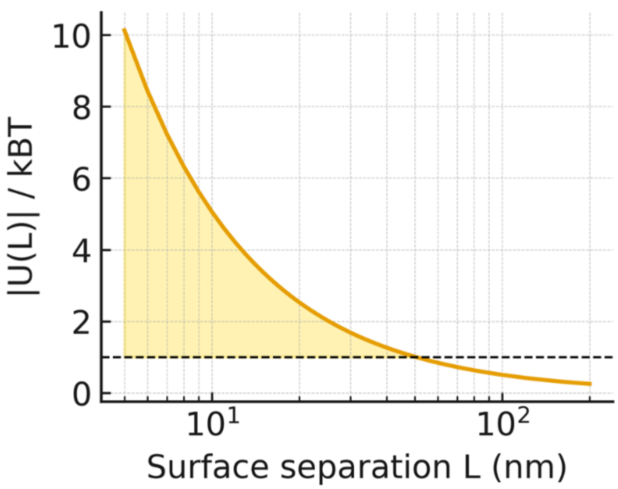

Figure 4. *Distance-dependent interaction potential |U(L)| / k_BT between two PMBC protocells (R=500 nm) as function of separation L.*

The quantity |U(L)| / k_BT is dimensionless and measures the strength of the interaction relative to thermal fluctuations at 25 °C (298.15 K). Values > 1 k_BT imply that the interaction can suppress Brownian separation and stabilize protocell contacts.
In Figure 4, the distance-dependent interaction potential |U(L)| / k_BT between two PMBC protocells with R = 500 nm is shown as a function of separation L. Values exceeding 1 k_BT define the *thermal relevance zone*, in which Casimir–Lifshitz interactions overcome Brownian motion and stabilize nanoscale protocell cluster building over separations L of 2–50 nm.

Sensitivity analysis:
The sensitivity analyses performed within this framework show that Casimir–Lifshitz–mediated protocell coupling is most strongly controlled by the inter-compartment separation L, reflecting the algebraic scaling $F_{CL} \propto L^{-2}$ and $U_{CL} \propto L^{-1}$. Variations in protocell size enter linearly via the effective curvature radius R_{eff}, such that larger compartments systematically exhibit stronger effective adhesion at fixed separation. Material-dependent parameters, captured through the effective Hamaker constant A_{eff}, scale the absolute interaction strength but do not alter the qualitative distance dependence. Temperature primarily modulates the relative contribution of quantum and thermal fluctuation modes, without changing the underlying algebraic scaling. In contrast, variations in ionic strength predominantly affect DLVO contributions through exponential screening, while Casimir–Lifshitz interactions remain only partially attenuated. Together, these sensitivities demonstrate that the dominance window of fluctuation-induced attraction is robust across realistic variations in geometry, material properties, temperature, and salinity.

IV. PREBIOTICALLY REALISTIC PARAMETER WINDOW

For the Casimir–Lifshitz interactions derived in Section 3 to function as realistic drivers of prebiotic self-organization, they must operate within a physically and geochemically plausible parameter space. We therefore consolidate ranges supported by geochemical considerations and experimental protocell research: geometry (*A.*), dielectric properties (*B.*), temperature (*C.*) and ionic environment (*D.*).

A. Geometry: Protocell Radii and Inter-Compartment Distances L

(Level-II:) Experimental and theoretical studies of prebiotic vesicles [5] suggest that early protocells commonly exhibited radii on the order of 200–1000 nm. At these sizes, effective compartmentalization is feasible and the Derjaguin-PFA interaction window of Casimir–Lifshitz forces becomes particularly relevant. Inter-protocell gaps within clusters of ~2–200 nm are plausible: smaller than the vesicle diameter but larger than hydration shells. These distances are experimentally accessible (e.g., cryo-TEM, confocal microscopy) and lie precisely in the regime where fluctuation-induced forces are not thermally overwhelmed, while classical Coulomb and DLVO contributions are already strongly attenuated.
(Level-III:) Geometrically, this yields a favourable region in which protocells are large enough to generate substantial Casimir–Lifshitz attraction through R_{eff}, yet small enough for thermal and chemical gradients within clusters to remain functionally effective.

B. Membrane Materials: Fatty-Acid Vesicles and PMBCs

(Level-II:) Prebiotic models commonly consider fatty-acid vesicles and protein-/polymer-based compartments (PMBCs). Simple fatty-acid membranes exhibit low effective permittivities $\varepsilon_{membrane} \approx 2–4$, far below that of saline water $\varepsilon_{water} \approx 75–78$ at 50–200 mMol ionic strength. This contrast satisfies the sign condition for attractive Casimir–Lifshitz interactions: two vesicles in water generally attract. PMBCs are thicker, mechanically more robust and have effective permittivities of $\varepsilon_{membrane} \approx 3–8$. Owing to their higher polarizability and stability, PMBCs represent particularly

suitable systems in which Casimir–Lifshitz forces should be pronounced and experimentally accessible.
(Level-III:) Both classes—fatty-acid vesicles and PMBCs—thus provide realistic membrane architectures yielding the dielectric contrast required for attractive fluctuation-induced coupling.

C. Temperature: 20–80 °C as an Activation Window

Many geochemical scenarios [5] place early compartments in hydrothermal or volcanic environments with temperatures between ~20 and 90 °C. (Level-I/II:) Temperature enters Casimir–Lifshitz theory explicitly through the classical contribution to the free energy, which scales ∝T in the high-T limit, thereby enhancing the thermal component of the attraction as long as membrane integrity is maintained. Temperature also modulates membrane fluidity, influencing the likelihood of fusion, hemifusion and transient pore formation.
(Level-II/III:) Fatty-acid vesicles typically remain stable between ~20 and 60 °C, whereas PMBCs can remain intact up to ~80 °C. This defines a temperature window in which Casimir–Lifshitz forces are sufficiently strong without thermal destruction dominating.

D. Salt and Ionic Strength: 50–200 mMol as the Screening Regime

(Level-II:) Prebiotic waters [5] likely exhibited ionic strengths of ~50–200 mMol [15][16], comparable to modern marine or brackish conditions. In this regime, the Debye length is only ~0.7–1.4 nm, limiting DLVO electrostatic double-layer repulsion to a few nanometres. Casimir–Lifshitz interactions behave differently: the zero-frequency term is partially screened by ions, but higher fluctuation modes largely persist. This leads to attenuation, but not elimination, of the total force over 2–100 nm.
(Level-III:) Even in saline prebiotic environments, an attractive, universal coupling remains active that can stabilize protocell clusters on mesoscale distances.

E. Consolidated Window Statement

(Level-III:) Protocell radii of 200–1000 nm, separations of 2–100 nm, temperatures of 20–80 °C and ionic strengths of 50–200 mMol [5] define a physically and geochemically plausible parameter window in which Casimir–Lifshitz interactions [1][2] arise and can contribute to non-chemical mesoscale aggregation of protocells.

V. PREDICTABLE EFFECTS AND EXPERIMENTALLY TESTABLE HYPOTHESES

The theoretical framework developed above leads to specific, quantitative and experimentally testable predictions. At its core, we propose that Casimir–Lifshitz (CL) interactions generate reproducible mesoscale stability and aggregation effects within prebiotically plausible parameter ranges. The following hypothesis groups constitute an empirically accessible test program for biophysical, prebiotic and synthetic-protolife experiments.

A. Material-dependent Clustering: PMBCs > Fatty-Acid Vesicles

Because of their higher polarizability and greater membrane thickness, PMBC compartments are expected to form deeper CL potential wells and more stable clusters than pure fatty-acid vesicles. PMBCs should therefore assemble into clusters more frequently, with larger diameters, longer-lived geometries and extended contact times. The underlying mechanism is the proportional enhancement of fluctuation coupling through the membrane's dielectric response: higher polarizability yields deeper potential wells and stronger *physical adhesion* without chemical bonding.

Experimental signature: increased co-residence probability (≤100 nm) of two labelled compartments in FRET, dual-fluorescence or confocal time-trace analyses.

B. Radius-dependent Adhesion: Larger Compartments Couple More Strongly

From the Derjaguin-PFA approximation (Section 3), the force contribution scales linearly with the effective radius R_{eff}: $F_{CL} \propto R_{eff}$. Larger protocells should therefore appear effectively more "adhesive'' at identical separations, exhibiting reduced relative drift, limited rotational freedom and enhanced contact persistence.
Biologically, this implies that volumetric growth or swelling processes may have conferred early selective advantages—not because of internal chemistry alone, but due to more stable physical coupling.

Experimental signature: systematic radius dependence in automated trajectory analysis (particle tracking, µPIV, confocal or epifluorescence time series).

C. Temperature Window for Maximal Coupling

Casimir–Lifshitz interactions contain a temperature-dependent component that scales ∝T in the classical regime. This yields the prediction of an optimal stability window around ~40–80 °C, where thermal amplification and membrane integrity are balanced. Below ~20 °C, viscoelastic membrane processes slow and may become too rigid; above ~80 °C, structural failures emerge more rapidly. This predicted window aligns remarkably well with hydrothermal and vulcanolimnic habitats [5] invoked in prebiotic models.

Experimental signature: maximal cluster persistence, contact time or dissociation half-life in thermostated microfluidic assays.

D. Minute-scale Contact Times from Shallow Potential Wells

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A characteristic feature of weak but sustained attraction is the formation of shallow potential wells with depths of several k_BT. Such wells permit semi-stable binding without irreversible fusion—an evolutionarily favourable regime that facilitates exchange, fusion events and lateral material transfer. We therefore predict that, under prebiotic conditions, two protocells should display contact times on the order of minutes before separation or remobilization occurs.

Experimental signature: dwell-time distributions (sub-100-nm regime) measured via Total Internal Reflection Fluorescence Microscopy (TIRF), Fluorescence Recovery After Photobleaching (FRAP) or single-particle dwell-time analysis.

E. Evidence for Algebraic Residual Attraction beyond DLVO Predictions

Because DLVO potentials decay exponentially with the Debye length, whereas CL forces decay algebraically, measurable discrepancies are expected between observed and DLVO-predicted force profiles—particularly within the 2–200 nm window. The critical finding would be the detection of residual attraction even when DLVO models predict neutrality or repulsion.

Experimental signature: non-zero adhesion or pull-off forces in optical or magnetic tweezers, AFM force spectroscopy or micro-traction assays.

VI. Prebiotic Evolutionary Implications

The results presented here demonstrate that Casimir–Lifshitz attraction, under prebiotically plausible conditions, provides a physically unavoidable and energetically relevant contribution to protocell stabilization and aggregation. Unlike DLVO-derived interactions, CL forces remain sensitive to material and geometric properties, act independently of metabolic or genetic mechanisms, and therefore precede classical biochemical modes of cooperation. The resulting cluster formation constitutes an early form of spatial coupling from which selectable chemical and informational organization could emerge.

A. Physical Emergence Preceding Chemical Specialization

Traditional origin-of-life models often assume that chemical functionality is a prerequisite for cooperation. Our findings indicate that attractive Casimir–Lifshitz coupling can already generate stability, cohesion and spatial coordination in the absence of biochemical instruction. Cooperation thus appears first as a physical order state, not as a product of pre-existing biofunction. This perspective aligns with dissipative self-organization frameworks in which mesoscale structuring arises deterministically from fluctuation-driven dynamics and forms an evolutionary precursor to chemical specialization.

B. Protocell Clusters as Precursors of Functional Micro-ecosystems

Metastable protocell clusters couple chemically relevant microenvironments, enhancing molecular retention, local concentration increases and stable microgradients—without requiring specialized transport machinery. The resulting exchange and recombination processes endow protocell ensembles with features of pre-ecological functional architectures, whose mesoscale connectivity may provide adaptive benefits independent of metabolic or genetic elaboration.

C. Preconditions for Proto-Informational Emergence

Physical coupling establishes a stable interaction space in which repeatable contact patterns, persistence and rudimentary memory effects arise. Such statistically non-random state differentiations constitute a minimal form of proto-informational structure, emerging long before sequence-based biopolymers existed. Information formation therefore appears as an emergent by-product of structurally stabilized interaction states rather than exclusively as an output of genetic systems.

D. Persistence and Resilience as Prebiotic Selection Factors

In prebiotic contexts, persistence rather than replication represents the primary mode of selection. CL-stabilized protocell clusters meet this requirement: they withstand environmental fluctuations, remain reversibly reconfigurable, passively harness external energy flows and form mesoscale networked structures. Casimir–Lifshitz attraction thus constitutes a coherent candidate for an early evolutionary selection filter, operating prior to genetic information systems and enabling structural durability in a noise-dominated environment.

E. Limitations and Scope Clarification

This work does not claim that attractive Casimir–Lifshitz forces alone account for protocell cooperation or aggregation. Rather, we propose that they represent a physically unavoidable under realistic material and environmental conditions, non-chemical baseline mechanism whose magnitude has been underestimated in prebiotic models. Additional chemical or environmental contributions may coexist, but CL forces provide a universal physical floor on which further stabilization processes may build.

VII. Discussion

In this work, we develop a theoretically coherent and experimentally actionable framework in which Casimir–Lifshitz (CL) forces act as a prebiotically relevant, physically determined aggregation mechanism between protocells. To clarify why physical coupling dominates under realistic early-Earth conditions (primordial soup), the interaction landscape is summarized schematically in Figure 5.

Physical vs. Chemical Interaction Landscape

Interaction	Range	Salt sensitivity	Chemistry required
Hydrophobic	< 1 nm	–	yes
DLVO	< 2 nm	high	yes
Casimir–Lifshitz	2–100 nm	low	no

Figure 5. Physical interaction regimes relevant to protocell clustering

Figure 5 compares interaction range, salt sensitivity, and chemical specificity of hydrophobic forces, DLVO interactions, and Casimir–Lifshitz forces. The schematic highlights that only Casimir–Lifshitz interactions combine mesoscale range (2–100 nm), low ionic sensitivity, and chemistry-independent operation, identifying them as a uniquely robust physical coupling mechanism under saline prebiotic conditions.

Based on field-theoretically consistent sphere–sphere models and biologically scalable parameter ranges, we show that these interactions operate with significant range and energetic relevance under plausible early-Earth conditions. They therefore constitute not merely a theoretical possibility but a functional mesoscale contribution to pre-cooperative organization.

The algebraic distance dependence of Casimir–Lifshitz forces provides a key plausibility advantage over exponentially screened DLVO components: above the DLVO damping regime, fluctuation-induced attraction remains dominant or energetically comparable, even in saline, thermally active, and dynamically perturbed early habitats. This addresses a long-standing gap in origin-of-life models that have traditionally explained mesoscale structural stability primarily through chemical, hydrophobic, or stochastic processes.

The resulting research logic reframes the emergence of cooperative protocell ensembles from a chemically metaphorical narrative into a metrically quantifiable mechanistic framework, as all relevant system parameters (permittivities, radii, ionic strengths, distances, temperatures) are experimentally tunable, measurable, and modelable. Cooperation thus appears not as a late by-product of biochemical innovation but as a physically grounded starting architecture upon which metabolic, genetic, and semantic complexity could later evolve.

VIII. CONCLUSION AND FUTURE WORK

This work establishes Casimir–Lifshitz forces as a physically unavoidable and prebiotically relevant baseline attraction between protocells operating at the mesoscale. Their algebraic distance dependence confers greater stability and range robustness than electrostatics-based models under realistic early-habitat conditions. As a result, the emergence of cooperative protocell assemblies becomes metrically modelable, experimentally accessible and decoupled from purely chemical or stochastic explanations. The model positions physical cooperation architecture as an evolutionary starting point rather than a late biochemical outcome, forming the foundation for a systematic research programme integrating physics, proto-ecology and proto-information. This framework directly motivates quantitative experimental tests of protocell clustering under controlled salinity, temperature, and material conditions.

Figure 6 translates the physical framework developed here into a concrete, staged experimental roadmap for future validation.

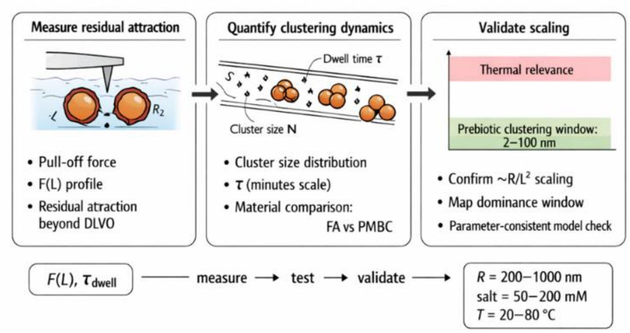

Figure 6. Experimental roadmap for physical protocell clustering validation

In Figure 6, a three-stage experimental roadmap is presented that operationalizes the physical framework introduced in this work. The schematic describes how residual fluctuation-induced forces, clustering dynamics, and scaling behavior can be systematically measured and validated, defining a practical experimental agenda for testing Casimir–Lifshitz–driven protocell cooperation under prebiotic conditions.

If prebiotic protocells did not drift alone in the chaos of the early oceans but were joined into semi-stable clusters by universal fluctuation forces, then the first evolutionary unit was not the isolated protocell, but the cluster (as dimers and tetrahedrons)—a naturally arising, collectively stabilized nanoscale assembly, shaped by physics into the earliest proto-ecosystem.

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