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Physicochemical Frameworks for Polymer Nanocomposite Dental Materials in Prosthodontics: A Cross-Disciplinary Review

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Abstract

Background: Optimization of polymer nanocomposite denture base materials has traditionally relied on empirical concentration screening, which involves testing various filler loadings and identifying the best-performing formulation after experimentation. Although this method has produced a substantial body data, it remains fundamentally limited in its ability to generate mechanistic insight, predict optimal formulations for untested conditions, or offer transferable design principles for novel material systems.

Objective: To systematically evaluate the applicability of seven established phytochemical and mathematical theoretical frameworks in predicting, designing, and optimizing the properties and performance of polymer nanocomposite denture base materials.

Methods: A structured narrative review was conducted, integrating foundational physics and chemistry literature with prosthodontic dental materials research. For each therotical framework, the original physical and chemical basis is presented, the mathematical formalism is described, prior applications in polymer composite and dental materials research are reviewed and a concrete illustration of applicability to PMMS-ZnO-nPLA-type ternary nanocomposite system is provided.

Conclusion: Despite the presence of these theoretical frameworks within the field of physics, chemistry, and engineering over many decades, they have not yet been integrated into the design of prosthodontic nanocomposites. Their combination provides a general theoretical framework that transforms the design of dental nanocomposites into a more scientific endeavor rather than an empirical one. This literature review highlights specific validation papers in the field of physics and chemistry that confirm the usefulness of these theoretical frameworks. It then shows how the gap in literature within prosthodontics is addressed by applying these theoretical frameworks.

Keywords: percolation threshold; DLVO theory; interfacial thermodynamics; Flory-Huggins theory; Halpin-Tsai model; Hill equation; Pareto optimisation; PMMA denture base; nanocomposite design; dental materials science; ZnO nanoparticles; polylactic acid

1. Introduction

The reinforcement of polymethyl methacrylate (PMMA) denture base resin with nanoscale fillers has generated an extensive and growing body of experimental literature over the past two decades. Inorganic metal oxide nanoparticles — principally zinc oxide (ZnO), titanium dioxide (TiO_2), zirconium dioxide (ZrO_2), and silica (SiO_2) — as well as organic polymeric nanoparticles including nano-polylactic acid (nPLA) and hydroxyapatite, have been incorporated at a range of concentrations and evaluated for their effects on mechanical properties, antimicrobial efficacy, surface characteristics, dimensional stability, and biocompatibility [1-6].

Despite the volume of this literature, a critical methodological limitation pervades the majority of these studies: concentration selection has been predominantly empirical. Authors typically select two to five filler concentrations based on the ranges used in prior literature, fabricate specimens at each concentration, test the properties of interest, and identify the best-performing concentration post-hoc as the 'optimum' [2-4]. This approach, while pragmatic, suffers from four fundamental limitations.

First, an empirically identified optimum cannot be distinguished from a best-from-those-tested result: no guarantee exists that the true optimum does not lie between the tested concentrations or outside the tested range. Second, the empirical optimum is not portable: it cannot be predicted a priori for a modified system (different particle size, different matrix material, different processing temperature) without a complete new round of experiments. Third, the approach generates no mechanistic insight into why a particular concentration is optimal. Fourth, it cannot resolve the competing objective

problem inherent in multifunctional nanocomposites: materials that must simultaneously optimize mechanical performance, antimicrobial activity, and biological safety face objectives that conflict with each other in ways that cannot be resolved by identifying the winner of a one-property-at-a-time comparison.

The disciplines of physics, physical chemistry, polymer thermodynamics, composite mechanics, pharmacology, and operations research have, over the preceding century, developed a suite of theoretical frameworks that collectively provide the tools to address all four of these limitations. These frameworks — percolation threshold theory [7], extended DLVO colloidal stability theory [8-11], interfacial thermodynamics [12,13], Flory-Huggins lattice theory [14-17], Halpin-Tsai micromechanical modelling [18-20], Hill equation dose-response modelling [21-23], and multi-objective Pareto optimization [24-26] — are individually well-established in their home disciplines, have been applied to polymer composite design in materials science and biomedical engineering, and have been partially and individually invoked in the dental. Prior to this review, a systematic and integrated presentation of these seven frameworks in the context of prosthodontic nanocomposite design has not been available. This synthesis maps each framework's foundational physics and chemistry, prior validation in composite science, and specific quantitative applicability to the design and optimization of PMMA-based nanocomposite denture base materials.

The scope deliberately bridges disciplines that do not routinely appear together in prosthodontic journals: the Scher-Zallen [7] percolation model from solid-state physics; the DLVO stability criterion from colloid chemistry; the Young-Dupré adhesion thermodynamics from surface science; the Flory-Huggins χ parameter from polymer statistical mechanics; the Halpin-Tsai effective medium theory from composite mechanics; the Hill sigmoid from pharmacological biophysics; and Pareto efficiency from operations research. Although these frameworks have been extensively validated through decades of theoretical and experimental research within their respective disciplines, they have not been systematically applied to prosthodontic nanocomposite research. This review provides the first comprehensive evaluation of their potential role in guiding the design and optimization of denture base nanocomposites.

2. Theoretical Frameworks: Foundational Principles, Prior Validation, And Prosthodontic Applicability

Table 1 represents an organized summary of all seven theories, discussing aspects like the discipline in which the theory emerged, the main principles involved in it, the application in polymer composite research, and specifically in prosthodontics nanocomposites. The following subsections elaborate on each framework in turn.

Table 1. Overview of seven physicochemical theoretical frameworks applicable to rational optimization of polymer nanocomposite denture base materials. Each framework is characterized by its originating discipline, physical/chemical principle, application in composite science, and prosthodontic relevance with key references.

Theoretical Framework	Discipline	Core principle	Application of Denture Base Nanocomposites	Key supporting Evidence
Percolation Threshold Theroy (Scher & Zallen, 1970)	Statistical physics; random graph theory	Critical filler volume fraction (φc) above which a continuous system-spanning networks forms. Applicable to electrical, thermal, mechanical, and steric properties.	Predicts minimum nanofiller loading required for continuous reinforcement and steric dispersant coverage; explains non-linear mechanical responses around φc.	Sharifzadeh et al. (2025); Barnasky et al. (2022) demonstrated agglomeration-dependent φc in polymer nanocomposites [27,28]. Zare (2016) integrated percolation theory with Halpin-Tsai modelling for polymer modulus prediction [18].
Extended DLVO Theory (Derjaguin, Landau, Verwey, Overbeek, 1940s; Napper 1977 extension)	Colloid chemistry; physical chemistry of interfaces	Total interaction energy (VT) is the sum of attractive and repulsive forces. Stable dispersions occur when the energy barrier exceeds 15-25Kt. Extended form (XDLVO) includes steric term in low-ε media	Predicts agglomeration tendency of inorganic NPs in polymer melts (low $\varepsilon_r \approx 3–4$, $V_R \approx 0$); steric coating by adsorbed polymer restores barrier; quantifies	Israelachvili (1991); Gregory (1981); Cierech et al. (2019) showed that ZnO agglomeration in PMMA above 2.5 wt% validated DLVO prediction [1,6,7]
Interfacial Thermodynamic (Young- Dupré; Owens-Wendt)	Surface chemistry; adhesion thermodynamics	Work of adhesion depends on surface energy interactions. Surface energy mismatch drives incompatibility, while coupling agents reduce interfacial tensions.	Predicts filler-matrix wettability; interfacial adhesion, and the need for compatibilisers to improve dispersion.	Janczuk et al. (2023); MacDowell et al. (2013). Silane coupling studies confirmed improved interfacial bonding and dispersion. [12,13]
Flory-Huggins Lattice Theory (Flory 1942; Huggins 1942)	Polymer thermodynamics; statistical mechanics	Gibbs free energy o9f mixing determines miscibility ($\Delta G_{mix} = RT[\varphi_1 \ln\varphi_1/n_1 + \varphi_2 \ln\varphi_2/n_2 + \chi \varphi_1 \varphi_2]$; $\chi > 0.5$ predicts phase separation in polymer pairs; $\chi_{PMMA-PLA} \approx 0.1–0.3$ at processing temperatures	Identifies miscibility limits and predicts phase separation at excessive co-dispersant concentrations.	Manias & Utracki (2011); Rubinstein & Colly (2003). PLA-based miscibility studies provide analogous evidence for polymer blend behavior [16,17].

Halpin-Tsai Micromechanical Model (Halpin & Tsai, 1969)	Composite mechanics; material science	Predicts composite modulus as a function of filler content, aspect ratio, and matrix properties.	Estimates reinforcement efficacy and identifies filler concentration where agglomeration causes diminishing mechanical returns.	Zare (2016) extended the model to nanocomposites incorporating interphase effects. Stochastic FEM studies further validated particulate-filled PMMA analogues [18].
Hill Equation Dose-Response Model (Hill 1910; toxicological adaptation ISO 10993-5)	Pharmacology; biophysics; toxicological chemistry	Describes sigmoidal relationship between concentration and biological response; Viability(C) = 100% × $CTC_{50}^n/(C^n + CTC_{50}^n)$; IC_{50}/CTC_{50} defines cytotoxic threshold; n = Hill coefficient (steepness)	Predicts cytotoxicity escalation at increasing nanofiller concentrations and establishes biological safety limits.	ISO 10993-5 (2009); AAMI/ISO guidelines (2021). Cierech et al. (2019) and Krishnamoorthi et al. (2022) demonstrated dose-dependent cytotoxicity in PMMA nanocomposites [21,22,29,10]
Multi-objective Pareto Optimization (Pareto, 1896; Marler &Arora, 2004)	Opertaions research; engineering optimization; material informatics	Identifies non-dominated solutions where improvement in one property requires compromise in another.	Simultaneously optimizes mechanical strength, antimicrobial activity, and biocompatibility without prioritizing a single outcome.	Low et al. (2023) demonstrated Pareto optimization in material discovery. Li et al. (2022) applied similar principles to multifunctional PMMA nanocomposites [24,26].

2.1 Percolation Threshold Theory: Geometric Connectivity as a Design Parameter

The concept of percolation — the sudden, threshold-like onset of a macroscopic property as a function of a local connectivity parameter — was formalized in the physics literature by Broadbent and Hammersley (1957) and given its continuum form, directly applicable to random particulate systems, by Scher and Zallen (1970) [7]. The key insight of Scher and Zallen was that for randomly distributed, overlapping spheres, geometric connectivity — the condition in which the dispersed phase forms a continuous, system-spanning network — is achieved at a universal critical volume fraction $\varphi_c \approx 0.16–0.29$, independent of the specific physical property being transmitted through the network.

The property-universality of this result is its most important characteristic for cross-disciplinary application. The Scher-Zallen threshold does not describe electrical percolation specifically; it describes geometric connectivity universally. The property that is conducted through the connected network — electrical charge, heat, mechanical stress, or, critically for our application, steric repulsion between nanoparticle surfaces — is a material-specific overlay on a geometry-universal mathematical framework [27,28].

In polymer nanocomposite science, percolation theory has been applied to electrical conductivity networks in CNT-PMMA composites [10], mechanical reinforcement percolation in clay nanocomposites [8], and thermal conduction networks in polymer-graphene systems. Sharifzadeh et al. (2025) demonstrated that the percolation threshold in real polymer nanocomposites is strongly dependent on nanoparticle aggregation/agglomeration: poor dispersion effectively reduces the percolating filler fraction, shifting φ_c to higher nominal concentrations [27]. This finding is directly applicable to the PMMA-ZnO-nPLA composite, in the absence of a steric dispersant, the tendency for agglomeration of ZnO particles decreases the effective volume fraction of ZnO distributed within the composite, as well as preventing the creation of an effective stress-transfer network; thus, increasing loading is necessary to obtain the same results.

With respect to prosthodontics, percolation theory offers an approach to calculating the minimum effective loading of the steric dispersant co-filler necessary to ensure complete steric coverage of the surface area of the inorganic nanoparticle filler through calculation based on principles of physics rather than experience alone. By using a random sequential adsorption approach to the problem of polydispersed spheres, the minimum nPLA volume fraction that ensures that mean inter-nPLA particle distance is kept below the ZnO van der Waals approach distance (approximately 5-10 nm) can be obtained as a function of the loading of ZnO and its particle size ratio. This transforms a parameter that had been chosen through precedent in literature to a theoretically derived value with a calculable confidence interval.

2.2 Extended DLVO Theory: Predicting Stability of Nanoparticles in Polymer Melts

Derjaguin-Landau-Verwey-Overbeek (DLVO) theory for colloidal stability, independently derived by Derjaguin & Landau (1941) and Verwey & Overbeek (1948), is based on the principle that the total interaction energy of the approach of two colloidal particles is equal to the sum of attractive van der Waals interactions (V_A) and repulsive double layer interactions (V_R): V_T = V_A + V_R [6]. Colloidal stability exists where there is a minimum in the potential interaction energy (V_T > ~15–25 kT).

Van der Waals attractive energy can be expressed by the equation, which does not include retardation effects: V_A = -A_eff·R/(12·h). Here, A_eff is the effective Hamaker constant for the particle couple, R is the particle radius, h is the separation distance between their surfaces. The Hamaker constant A_eff can be estimated from the Lifshitz theory using published dielectric spectra, or approximated from the combining rule A_eff ≈ (√A_11 − √A_22)² where A_11 and A_22 are the Hamaker constants of the particle and medium, respectively [8,9].

In aqueous systems, V_R arises from the overlap of electric double layers and is controlled by ionic strength and surface potential. In low-dielectric polymer melts (ε_r ≈ 3–4), V_R ≈ 0 because double-layer formation is negligible in the absence of free ions and the high-dielectric conditions needed for charge screening. This means that inorganic nanoparticles in polymer matrices are thermodynamically unstable against agglomeration unless an alternative repulsive mechanism is introduced. Napper (1977) and de Gennes (1987) provided the theoretical basis for steric stabilization as this alternative mechanism: adsorbed or grafted polymer chains generate a conformational entropy-driven repulsion (V_steric > 0) when two coated surfaces approach within the range of the polymer chain layer, restoring the energy barrier against contact [10,11]. This extended formulation, known as XDLVO theory, has been confirmed experimentally in multiple polymer-coated nanoparticle systems [31].

In dental materials science, DLVO theory has not been explicitly applied, but its consequences are evident throughout the prosthodontic literature. The well-documented finding that ZnO NPs agglomerate in PMMA above 2–3 wt% [1,2,32], that the agglomeration is concentration-dependent, and that mechanical properties deteriorate above this threshold, is precisely the behavior predicted by XDLVO for an inorganic particle (A_ZnO ≈ 9.21×10^{-20} J) interacting across a low-dielectric polymer matrix (A_PMMA ≈ 6.8×10^{-20} J) without steric stabilization. The effective Hamaker constant A_eff ≈ (√A_ZnO − √A_PMMA)² generates a van der Waals attraction of approximately 5–10 kT at 5 nm separation — below the DLVO stability threshold — predicting spontaneous agglomeration. The application of XDLVO analysis to this system converts a post-hoc observation into an a priori, quantitative prediction.

2.3 Interfacial Thermodynamics: Work of Adhesion and Compatibilisation

The thermodynamics of adhesion at solid-polymer interfaces is described by the Young-Dupré equation for work of adhesion: $W_{AB} = \gamma_A + \gamma_B - \gamma_{AB}$, where γ_A and γ_B are the surface free energies of the two contacting phases and γ_{AB} is their interfacial energy. High surface energy mismatch between phases produces a high γ_{AB} and therefore a low W_{AB}, indicating thermodynamically unfavourable interfacial wetting [12,13].

MacDowell et al. (2013), working in a direct analogue of the PMMA nanocomposite system (PMMA matrix with surface-energy-modified colloidal silica nanoparticles), demonstrated that the ratio W_{PF}/W_{FF} — the work of adhesion between polymer and filler relative to the work of adhesion of filler to filler — predicts the final dispersion state of nanoparticles in PMMA with quantitative accuracy [12]. When $W_{PF}/W_{FF} > 1$, nanoparticles disperse homogeneously; when $W_{PF}/W_{FF} < 1$, agglomeration is thermodynamically favored. The aforementioned ratio may be obtained based on publicly available data on surface energies using the Owens-Wendt method; thus, dispersibility assessment would become quantifiable.

The closest example of the use of the aforementioned theory in prosthodontics is provided by Janczuk et al. (2023) [13] who used the Young-Dupré equation and wettability measurements for the analysis of the interfacial thermodynamics of commercial mouth rinses on PMMA denture base surfaces. The value of the PMMA surface free energy ($\gamma_{SV} = 36.6$ mJ/m²; $\gamma_{SV} = 31.8$ mJ/m² under salivary conditioning) allows to consider an interfacial thermodynamic parameter specific to prosthodontics. The same framework, applied to ZnO ($\gamma \approx 54–62$ mN/m) versus PMMA ($\gamma \approx 38–41$ mN/m), quantitatively predicts the magnitude of surface energy modification required — through silane coupling agent treatment and/or co-dispersant polymer coating — to achieve $W_{PF}/W_{FF} > 1$ and thermodynamically stable dispersion.

γ-Methacryloxypropyltrimethoxysilane (γ-MPTS), the most widely used coupling agent for metal oxide nanoparticles in dental composites, achieves surface energy modification through a well-characterised four-step mechanism: hydrolysis of methoxy groups, adsorption of silanols onto ZnO surface hydroxyl groups (Zn-OH), condensation to form covalent Zn-O-Si bonds, and polymerization of the silane layer — confirmed by FTIR (Zn-O-Si stretching at ≈1050–1100 cm^{-1}) and solid-state NMR [33-35]. The methacrylate functional group exposed after silanisation is available for co-polymerization with MMA monomer during heat curing, converting the ZnO-PMMA interface from a weak van der Waals contact to a covalent chemical bond and dramatically increasing W_{PF} [33,35].

2.4 Flory-Huggins Lattice Theory: Predicting the Upper Loading Limit of Co-Dispersant Polymers

The Flory-Huggins lattice theory of polymer solution and blend thermodynamics, developed independently by Flory (1942) and Huggins (1942), provides the thermodynamic basis for predicting miscibility and phase separation in polymer mixtures [14-16]. The Gibbs free energy of mixing is given by: $\Delta G_{mix} = RT[\varphi_1 \ln \varphi_1/n_1 + \varphi_2 \ln \varphi_2/n_2 + \chi \varphi_1 \varphi_2]$, where φ_1 and φ_2 are the volume fractions of the two components, n_1 and n_2 are the degrees of polymerization, and χ is the dimensionless Flory-Huggins interaction parameter characterizing enthalpic incompatibility [14,16]. Miscibility requires $\Delta G_{mix} < 0$; phase separation occurs when χ exceeds a critical value $\chi_c \approx \frac{1}{2}(1/\sqrt{n_1} + 1/\sqrt{n_2})^2$.

For polymer blend nanocomposites in which an organic co-filler (such as nPLA) is dispersed within a polymer matrix (PMMA), Flory-Huggins theory predicts the maximum loading of the co-filler below which thermodynamically homogeneous dispersion is maintained during processing. Above the critical concentration, the thermodynamic driving force for phase separation — characterised by $\chi_{PMMA-PLA}$ — overcomes the kinetic trapping of the dispersed phase during rapid polymerization, generating macroscopic co-filler-rich domains that compromise nanocomposite homogeneity [17,36].

The positive value of $\chi_{PMMA-PLA}$ (≈0.1–0.3 at typical heat-curing temperatures of 70–100°C) indicates limited thermodynamic compatibility between PMMA and PLA [17]. This predicts that at sufficiently high nPLA loadings, phase separation will produce PLA-rich inclusions that act as stress concentration sites rather than as reinforcing nanodispersants. Flory-Huggins analysis thus provides an independent, thermodynamically-derived upper boundary for nPLA loading — complementing and corroborating the upper boundary derived from biological dose-response modelling (Section 2.6). No published prosthodontic study has applied Flory-Huggins

analysis to determine the upper concentration limit of an organic co-filler in PMMA; this represents a direct, high-impact transfer of established polymer thermodynamics to dental materials design.

2.5 Halpin-Tsai Micromechanical Model: Predicting Composite Modulus and Identifying the Concentration Inversion Point

The Halpin-Tsai model, developed by Halpin and Tsai (1969) as a semi-empirical interpolation between the Voigt and Reuss bounds for composite modulus, expresses the effective Young's modulus of a composite as: $E_c = E_m(1 + \zeta\eta\varphi)/(1 - \eta\varphi)$, where $\eta = (E_f/E_m - 1)/(E_f/E_m + \zeta)$, E_m and E_f are the matrix and filler moduli, φ is the filler volume fraction, and ζ is a shape parameter ($\zeta = 2$ for spherical particles) [18,20]. Zare (2016) extended this model to account for interphase properties (thickness, modulus) and nanofiller size effects that are critical in particulate nanocomposites where the interphase volume fraction is comparable to the filler volume fraction [18].

According to the Halpin-Tsai model, the modulus of the composite increases monotonically with filler loading if ideal conditions are assumed (ideal interface adhesion, uniform dispersion of the filler). The key understanding for designing nanocomposites comes from knowing that the model fails when assumptions are not met; low interface adhesion (low W_PF/W_FF) would make η non-ideal, thereby resulting in either a plateau or reduction of composite modulus as the filler loading increases — something seen experimentally in the ZnO-PMMA system when filler loading exceeded 2-3 wt% [2,37]. Through the Halpin-Tsai model, one can quantify the point where mechanical deterioration occurs as a consequence of weak interface adhesion and stress concentration arising from agglomeration.

Stochastic finite element modelling of particulate-modified polymer composites has further demonstrated that the Halpin-Tsai analytical framework accurately predicts the modulus of PMMA-analogue matrices reinforced with spherical nanoparticles, providing computational validation of its applicability to dental polymer systems [38]. Application of the extended Halpin-Tsai model to the PMMA-nPLA-ZnO system would allow quantitative prediction of the concentration range in which nPLA addition transitions from reinforcing (above percolation threshold, high W_PF) to detrimental (above Flory-Huggins miscibility limit, phase separation-induced heterogeneity).

2.6 Hill Equation Biological Dose-Response Modelling: Pre-Experimental Safety Boundary Definition

The Hill equation, originally proposed by A.V. Hill (1910) to describe haemoglobin oxygen binding and subsequently adopted as the universal dose-response model in pharmacology and toxicology, describes the relationship between extract/dose concentration C and biological response (e.g., cell viability) as: $\text{Viability}(C) = 100\% \times CTC_{50}^n / (C^n + CTC_{50}^n)$, where CTC_{50} is the half-maximal cytotoxic concentration and n is the Hill coefficient determining the steepness of the sigmoidal response curve [21,13]. This is the same mathematical form as the IC_{50} formalism adopted by ISO 10993-5 for in vitro cytotoxicity evaluation of medical device materials [21].

The application of Hill equation modelling to nanoparticle cytotoxicity in dental materials has been validated by multiple studies. Cierech et al. (2019) demonstrated concentration-dependent Zn^{2+} cytotoxicity in PMMA-ZnO composites [1,29]; the dose-response relationships they reported are consistent with Hill equation kinetics, with CTC_{50} values that decrease as ZnO loading (and therefore Zn^{2+} release surface area) increases. The cytotoxicity of selected nanoparticles on dental pulp stem cells (PMC5421267) demonstrated dose- and time-dependent responses for ZnO, TiO_2, SiO_2, and Al_2O_3 at 25–100 µg/mL — confirming Hill-type kinetics for metal oxide nanoparticles in the dental cell context [39]. The systematic review of resin-based composite cytotoxicity confirmed that dose- and time-dependent cytotoxic effects are universal across dental polymer composite formulations [40].

The key innovation in applying Hill equation modelling pre-experimentally — rather than post-hoc, as in all prior cited studies — is that it converts biological safety assessment from a descriptive exercise into a predictive design constraint. If the CTC_{50} can be estimated for a given filler system from the published cytotoxicity literature, the maximum safe filler concentration can be calculated before any experiments are performed. This enables biological safety to be included in the process of material selection as a constraint rather than an attribute that is

evaluated post hoc. In prosthodontics, when the material is constantly in contact with the mucosal tissue of medically compromised and elderly patients, such a safety concept before experimentation is not only scientifically preferable but also ethically mandatory [41-44].

2.7 Multi-Objective Pareto Optimisation: Formalising the Trade-Off Between Competing Clinical Objectives

Multiple objective optimization problems occur when there are multiple objectives that need to be met at the same time, and improving the quality of one objective means deteriorating the other. In material science, such a phenomenon – represented by strength and ductility dilemma in metallic alloys [25], or efficiency-stability tradeoff in photovoltaic devices [26] – is modelled using Pareto efficiency principle, where a solution is defined as Pareto-efficient if any improvement in one objective requires worsening another objective [24]. The set of all Pareto-optimal solutions constitute the Pareto front.

Pareto front mapping was shown by Low et al. (2023) as an effective method of multi-objective materials discovery through machine learning, whereby the direct calculation of the Pareto front leads to a tremendous reduction in the number of experimental studies needed to find optimal materials compositions relative to the case where only a single objective is considered at a time [24]. Concerning the prosthodontic nanocomposite area, the best parallel to the method is seen in the empirical work carried out by Li et al. (2022), whereby it was found that the optimal loading amount to improve flexural strength properties in a BN/Ag-PMMA composition (1 wt%) differed from that required for antibacterial purposes (1.4 wt%), showing the presence of a Pareto trade-off without a formal framework to resolve it [5].

When Pareto optimization is applied formally to the design of PMMA nanocomposites, the question “Which concentration gives the highest level of all-around effectiveness?” changes from an imprecise empirical query (depending entirely upon which objective the researcher places greatest emphasis upon) into a precise mathematical one – which concentration falls within the set of points that define the Pareto front of the three-objective space of mechanical performance, antimicrobial activity, and biocompatibility? The answer to this question depends not on any subjective weighting scheme employed by the researcher, but is replicable and theoretically derived.

3. Cross-Disciplinary Literature Mapping

Table 2 maps the key foundational references from physics and chemistry to their prosthodontic applications, identifying both the supporting evidence for each framework's applicability and the specific mechanistic contribution each reference makes to dental nanocomposite design. Table 3 maps the prosthodontics literature to identify where each framework's predictions were implicitly confirmed by empirical findings — but not explicitly derived.

Table 2. Foundational physics and chemistry references for each theoretical framework, mapped to the specific systems studied, key findings applicable to PMMA nanocomposites, and the direct prosthodontic relevance of each finding.

Theoretical Framework	**Reference**	**System Studied**	Key Findings	**Relevance to Denture Base Composite**
Continuum percolation and Geometric connectivity	[7]	Random resistor networks; Continuum disordered systems	Critical percolation threshold ($\varphi c \approx 0.16$-0.29) forrandomly dispersed spheres; threshold is geometry-dependent but property-independent, governing ant	Predicts the minimum nPLA loading required to establish steric connectivity around ZnO nanoparticles and the onset of stress-trasnfer

			transport process through connected networks.	reinforcement networks within PMMA.
Aggregation-dependent percolation in polymer nanocomposite	[27]	Electrically conductive spherical nanoparticles dispersed in polymer matrices	Percolation threshold (φ_c) strongly dependent on NP dispersion quality, size, interphase properties; agglomeration reduces effective percolating filler fraction	Supports DLVO/XDLVO predictions that poor ZnO dispersion increases the effective percolation threshold, requiring greater nPLA loading than predicted by ideal monodisperse models.
XDLVO steric stabilization theory	[10,11]	Polymer-grafted colloidal surfaces	Steric barrier from adsorbed chains scales with chain extension (≈R_g); effective in low-dielectric media where electrostatic repulsion is negligible	PLA chains adsorbed onto ZnO surfaces create a steric barrier within low-dielectric PMMA matrix. Positive steric free energy ((ΔGsteric > 0) prevents ZnO-ZnO contact and aggregation above the percolation threshold.
Surface energy & dispersion in PMMA nanocomposites	[12]	PMMA filled with silane-modified silica NPs; P2VP, PEMA, PS matrices	The ratio of polymer to filler-filler interaction energy (W_PF/W_FF) predicts final dispersion state; ΔW_a determines whether filler aggregates or disperses; higher W_PF → better dispersion	For ZnO PMMA systems, WZnO-PMMA/ WZnO-ZnO < 1 predicts agglomeration. Γ-MPTS silanization and nPLA coating increase polymer-filler interactions, promoting uniform nanoparticle dispersion.
Flory-Huggins thermodynamics interaction parameters (χ)	[16,17]	PLA-PMMA polymer blends	χ_PLA-PMMA ≈ 0.1–0.3 at 70–100°C; positive χ indicates limited miscibility; spinodal decomposition above critical nPLA loading	Predicts phase separation beyond approximately 15wt% nPLA in heat-cured PMMA and established the upper concentration limit for maintain

				homogeneous nanocomposite morphology.
Halpin-Tsai + interphase for modulus prediction in particulate nanocomposites	[18,19]	Spherical NP-reinforced polymer matrices; interphase thickness/modulus effects	Ignoring the interphase region underestimates composite modulus. Inclusion of interphase properties improves prediction accuracy. Mechanical reinforcement plateaus or decreases when interfacial adhesion becomes inadequate.	Explains the experimentally observed modulus plateau and reversal above ~3wt% ZnO in binary PMMA composites. nPLA enhances interfacial adhesion, delaying the onset of modulus deterioration at higher filler loadings.
γ-MPTS Silanization mechanism of ZnO nanoparticle	[33-35]	Silane-treated ZnO nanoparticles and methacrylate-based polymer systems	Hydrolyzed silane forms Si-OH groups, which condense with Zn-OH surface groups to create covalent Zn-O-Si bonds. Methacrylate functionality remains available for polymerization. FTIR and NMR confirm successful surface modification.	Provides the chemical basis for improved ZnO-PMMA interfacial adhesion. Appearance of Zn-O-Si stretching bands near 1050-1100 cm^{-1} serves as a definitive FTIR indicator of successful silanization.
Hill model for nanoparticle dose-response; IC_{50}/CTC_{50} interpretation	[21-23]	Metal oxide NPs on fibroblast/keratinocyte cell lines; MTT and NRU assays	Cytotoxic concentration (CTC50) id dependent on exposure duration and dose. Nanoparticle surface area is often a better toxicity predictor than mass concentration, Zn^{2+} ion release correlates strongly with cytotoxic effects.	Predicts potential reduction in CTC50 at elevated nPLA loadings due to increased ZnO dispension surface area and lactic acid accumulation, helping define safe nanoparticle concentrations for denture base applications.

Table 3. Prosthodontic dental materials studies contextualised against the theoretical frameworks. For each study, the empirical finding is identified alongside the methodological limitation that theory-driven application would have addressed, and the nearest theoretical framework able to predict that finding a priori.

Reference	System Studied	Approach/Framework Used	Key Findings	Limitations
[2]	PMMA + ZnO nanoparticles (1–3 wt%;20–30 nm)	Empirical range screening	Flexural strength peak at 2 wt% (~85 MPa); decline at 3 wt% due to agglomeration	No mechanistic basis for 2 wt% selection beyond empirical observation; cannot predict whether optimum shifts with particle size or processing change; agglomeration confirmed but not predicted a priori
[1]	PMMA + ZnO NPs 2.5–7.5 wt% (≤100 nm)	Empirical cytotoxicity + agglomeration characterisation	Agglomeration increases with concentration; Zn^{2+} release measurable; cytotoxicity concentration-dependent	Cytotoxic threshold identified post-hoc from data; no pre-experimental Hill model prediction; no steric dispersant strategy to extend safe ZnO loading range
[3]	PMMA + ZrO_2, TiO_2, SiO_2 at 3 and 7 wt%	Empirical comparison across NP types and two concentrations	All NP types improve mechanical properties; 3 wt% generally optimal for strength	Two-concentration design cannot distinguish optimal from arbitrary; no theoretical basis for 3 vs 7 wt% selection; interfacial thermodynamics not considered
[4]	PMMA + ZnO, TiO_2, SiO_2 NPs at 3 and 7 wt%; colour stability evaluation	Empirical; concentrations selected from prior literature	Both concentrations affect colour; concentration >7 wt% causes obvious colour change	Concentration selected by citing precedent: 'up to 7 wt% recommended'; no percolation or thermodynamic analysis to determine why 7 wt% is an empirical limit
[5]	PMMA + h-BNN / AgNPs binary nanocomposite;	Dual-objective design: mechanical + antibacterial; concentration varied to find best balance	1 wt% optimal for flexural strength (↑56.7%); 1.4 wt% optimal for antibacterial	Demonstrates Pareto tension between mechanical and antibacterial objectives empirically; no

	variable concentration		(92.1% reduction); different optima for different objectives	formal multi-objective framework applied; optimal combination not pre-predicted
[12]	PMMA filled with silane-modified colloidal silica; systematic surface energy variation	Theory-driven: W_PF/W_FF ratio used to predict and control dispersion	When W_PF/W_FF > 1, homogeneous dispersion achieved; when < 1, agglomeration; Tg shifts correlate with dispersion	Physics study directly applicable to prosthodontics: same framework predicts PMMA-ZnO incompatibility and quantifies improvement expected from γ-MPTS + nPLA compatibilisation
[13]	PMMA surface + commercial mouthrinse solutions; Young-Dupré analysis	Theory-driven: wettability/adhesion parameters calculated from contact angles and surface free energy	SFE of PMMA decreases from 36.6 to 31.8 mJ/m² after salivary coating; work of adhesion decreases with surfactant exposure	Provides prosthodontic-specific interfacial thermodynamic baseline for PMMA; confirms Young-Dupré framework applicability to dental polymer surfaces
[39]	TiO_2, SiO_2, ZnO, Al_2O_3 NPs at 25–100 µg/mL; dental pulp stem cells	Dose-response; MTT assay at 24, 48, 72 h	All NPs dose- and time-dependent cytotoxicity; ZnO most cytotoxic at equivalent concentrations; minimum viability at 100 µg/mL	Validates Hill-model dose-response framework for metal oxide NPs in dental context; confirms ZnO occupies highest cytotoxic risk position — rationale for nPLA-mediated controlled release strategy

4. Integration Of Frameworks: From Independent Theories To A Unified Optimisation Strategy

The seven frameworks described above are individually established and individually applicable to polymer nanocomposite design. Their power is maximized, however, when they are applied as an integrated system rather than in isolation. Specifically, the frameworks provide constraints from independent directions that, when combined, define a feasible optimization space substantially narrower — and more rigorously justified — than any single framework could produce.

Consider their collective application to a ternary PMMA + ZnO NPs + nPLA system. Extended DLVO analysis establishes the maximum ZnO loading without steric stabilization (≤3 wt%), above which thermodynamically

driven agglomeration becomes spontaneous. Percolation threshold analysis establishes the minimum nPLA loading required for effective steric dispersancy ($\varphi_c \approx 4–6$ wt%), converting this minimum into a calculable quantity rather than an empirical estimate. Interfacial thermodynamics (Young-Dupré, W_PF/W_FF ratio) quantifies the surface energy modification required from γ-MPTS silanisation and nPLA coating to achieve W_PF/W_FF > 1 and thermodynamically stable dispersion. Flory-Huggins analysis determines the maximum nPLA content above which PMMA-PLA demixing occurs ($\chi_{PMMA-PLA} > 0$), resulting in heterogeneity on a macroscopic scale that is not consistent with a homogeneous nanocomposite morphology. Halpin-Tsai analysis determines the region within which mechanical strength is expected to first improve, plateau, and ultimately decrease. This approach independently determines the optimal mechanical strength of the system without taking into account biological factors. The Hill equation modelling provides the hard biological threshold below which the material is safe for biological testing, ensuring that the highest concentration in question is not cytotoxic but still safely within experimental limits. Lastly, Pareto analysis captures the trade-off between mechanical strength and antimicrobial effects using all five of these constraints, identifying the formulation that maximizes both simultaneously [45-47].

This intersection of the seven constraint boundaries gives rise to a feasible domain for optimization which is both theoretically sound and experimentally verifiable. Importantly, there are no contradictions between the constraints; in other words, it means that the DLVO theory, percolation approach, thermodynamic theory, Flory-Huggins theory, Halpin-Tsai theory, and Hill's theory do not contradict each other in any way, making such an agreement a strong indicator of the validity of the approach since a contradiction would indicate model failure and require further work prior to experimentation – a feature unavailable in empirical approaches. Table 4 maps the physics/chemistry references to the prosthodontics literature, identifying for each framework the specific gap in the dental literature that theory-driven application would close.

Table 4. Cross-disciplinary reference mapping: foundational physics/chemistry references paired with the prosthodontics literature, where the framework's predictions were implicitly evidenced, and the specific contribution theory-driven application makes to close the identified methodological gap.

Theoretical Framework & Reference	**Existing Prosthodontic/Dental Evidence**	**Contribution to the present PMMA nanocomposite model**
continuum percolation φc for disordered systems [7]	No prosthodontics study has formally applied percolation theory to PMMA nanocomposite concentration selection; agglomeration threshold recognised empirically (Cierech 2019, Vikram 2020) but not theoretically derived [1,2]	Percolation analysis bridges the gap between physics of geometric connectivity and prosthodontic materials design: provides the first principled derivation of minimum dispersant loading
Intermolecular & Surface Forces [8]; Hamaker constant methods [9]	Cierech et al. (2019): agglomeration confirmed experimentally above 2.5 wt% ZnO in PMMA — but DLVO analysis not applied [1]	Extended DLVO applied to PMMA melt predicts agglomeration onset quantitatively; provides thermodynamic basis for empirically-observed concentration limits in prosthodontic literature
Macromolecules: W_PF/W_FF ratio governs dispersion in PMMA nanocomposites [12]	Janczuk et al. (2023), Materials: Young-Dupré interfacial thermodynamics applied to PMMA/mouthrinse — nearest	Work of adhesion framework generalises from mouthrinse-PMMA interaction to ZnO-PMMA incompatibility; predicts

	dental parallel, but not applied to NP dispersion [13]	magnitude of improvement needed from silane treatment
Flory-Huggins χ for polymer miscibility [17]; Polymer Physics [16]	No published PMMA denture base study has used Flory-Huggins analysis to predict the upper loading limit of a co-dispersant polymer	χ_PMMA-PLA predicts phase separation onset above critical nPLA concentration — provides thermodynamic upper boundary complementing the biological Hill-model boundary
Composites Sci & Tech: Halpin-Tsai for particulate nanocomposites with interphase [18]	Empirical observation of modulus plateau/decline in PMMA-ZnO by Vikram & Chander (2020), Al-Douri & Sadoon (2023) — attributed to agglomeration without micromechanical modelling	Halpin-Tsai analysis predicts concentration at which mechanical reinforcement inverts; converts post-hoc empirical observation into an a priori, testable prediction
IC_{50} review [21,22]; Hill equation formalism [23]	Cytotoxicity of metal oxide NPs on dental pulp cells (PMC5421267); Cierech et al. (2019): Zn^{2+} cytotoxicity; Krishnamoorthi et al. (2022): PMMA nanocomposite biocompatibility [1,30]	Hill model converts dose-response data into a quantitative pre-experimental prediction of cytotoxic concentration boundary; enables ethical pre-selection of safe concentration domain
Pareto fronts for materials discovery [24]; strength-ductility Pareto conflict in alloys [25].	Li et al. (2022) Biomimetics: empirically identified dual-objective tension in BN/Ag-PMMA — nearest dental Pareto analogue — without formal framework [5]	Pareto optimisation formalises the trade-off between antimicrobial performance and mechanical integrity observed empirically; replaces post-hoc 'best performer' identification with a priori optimal formulation prediction

5. Implications For Study Design, Reporting, And Peer Review

The adoption of theory-driven optimization frameworks in prosthodontic dental materials research has direct implications for study design, reporting standards, and peer review criteria that extend beyond any individual material system.

In study design, the frameworks described here enable a priori power analysis to be conducted at the level of individual concentration points rather than at the level of experimental groups in aggregate. If the predicted functional form of the concentration-property relationship is known (non-monotonic, with a predicted optimum at a specific loading), the statistical power calculation can be tailored to the specific hypothesis being tested — detection of a peak at the predicted optimum — rather than to an undifferentiated comparison of means. This is both statistically more efficient and scientifically more rigorous than the generic ANOVA power calculations that dominate the current prosthodontic literature.

In terms of reporting, the frameworks offer a useful guideline for the justification part of dental material research articles: Instead of referring to multiple studies, which by coincidence may have used similar concentrations, the authors can refer to a mechanistically based calculation supporting each of those concentration points. Reporting

like this, similar to hypothesis pre-registration in clinical trials, greatly enhances reproducibility and interpretation of the results, since the reader or scientist in the future will be able to understand how the conclusions were reached.

For peer review of the literature, these models provide an objective standard by which the choice of concentrations may be judged. Instead of posing the subjective question "Were these concentrations appropriate?" and relying on equally subjective answers, it is possible to pose the questions "Do these concentrations match the theoretically expected values for the percolation transition concentration, DLVO limit for stability, Flory-Huggins limit for phase separation, and Hill limit for cytotoxicity?" In this way, the scientific proof for concentration choices becomes higher in prosthodontic dental material publications.

6. Limitations Of Theory-Driven Approaches And Directions For Future Research

The models described above are highly effective in terms of aiding experimental design, although their use is associated with certain restrictions, which must be kept in mind during implementation in the material systems.

Models used to calculate percolation thresholds make assumptions regarding ideal shapes of particles (monodisperse or log-normal distribution of spheres), as well as random distribution of particles in space. Actual nanocomposite systems can involve nonspherical particles, as well as specific orientation caused by the manufacturing process, leading to correlated, as opposed to random, spatial distribution of particles. The presence of polydispersity reduces the calculated percolation threshold; therefore, monodisperse-based estimates are conservative [27,28,48].

XDLVO theory in polymer melts is necessarily an approximation since the classic Hamaker model for calculating van der Waals forces makes use of additive pair potentials, which is an approximation that breaks down at shorter distances between particles, and the assumption of ideal entropic springs for polymer chains is true only under certain conditions of concentration and molecular weight. The quantitative applicability of XDLVO theory in polymer solutions is limited as compared to aqueous solutions [8,31,49].

The Flory-Huggins approach assumes that polymers have flexibility and can be approximated to have the ideal properties of a Gaussian chain in a lattice system. This assumption tends to overestimate entropy of mixing for stiff chain segments (for example, crystalline PLA) and underestimate the concentration dependence of χ for highly specific interaction systems. There are better approaches such as equations of state models (SAFT, PC-SAFT) or molecular simulations that need advanced computing capabilities [17,36].

Halpin-Tsai theory assumes perfect adhesion at the interfaces before the mechanical percolation threshold and fails to account for the ductile-to-brittle transition observed in filled polymers above high filler concentration levels. The theory is accurate only for the linear range and becomes inaccurate when predicting toughness and impact strength because of the non-linear fracture mechanics involved [18,19,50].

Even though there are certain limitations in the frameworks, the theories are still sufficient for what the main task of designing nanocomposites for prosthodontics is; determining the limits for the feasible concentration range that requires experimental testing. It is very helpful even to determine the limits approximately because that will lessen the workload in searching for the best formulation.

Future research directions include: (1) computational validation of framework predictions using molecular dynamics or Monte Carlo simulation for specific PMMA-nPLA-ZnO systems; (2) systematic experimental measurement of surface free energies (γ, W_{AB}) for dental nanocomposite components using contact angle goniometry and Owens-Wendt analysis; (3) direct measurement of $\chi_{PMMA-PLA}$ by small-angle X-ray or neutron scattering for the specific molecular weights and nanoscale formulations used in dental composites; and (4) development of multi-objective Bayesian optimisation workflows for dental nanocomposite design that formally integrate all seven framework constraints as prior knowledge.

7. Conclusions

This review has presented, for the first time in the prosthodontic literature, a systematic and integrated analysis of seven physicochemical and mathematical theoretical frameworks applicable to the rational optimisation of

PMMA-based nanocomposite denture base materials. These frameworks — percolation threshold theory, extended DLVO colloidal stability theory, interfacial thermodynamics, Flory-Huggins lattice theory, Halpin-Tsai micromechanical modelling, Hill equation dose-response modelling, and multi-objective Pareto optimisation — are individually established in physics, physical chemistry, polymer thermodynamics, composite mechanics, pharmacology, and operations research respectively.

Their collective application to prosthodontic nanocomposite design provides what empirical screening cannot: a mechanistically transparent, theoretically grounded, and internally consistent basis for concentration selection; a set of falsifiable, pre-registered predictions against which experimental results can be objectively evaluated; a portable framework whose predictions remain valid when particle size, processing modality, or matrix material is modified; and a formal resolution of the multi-objective trade-off between mechanical performance, antimicrobial efficacy, and biological safety that characterizes all multifunctional dental nanocomposites.

However, the results of the literature mapping in Tables 2-4 show that the findings of the current literature on prosthetics are quite consistent with the expectations of the theories; nonetheless, none of the theories has been used in a way to generate these findings. This is clearly the greatest opportunity in the methodology for development in the field of materials in dentistry. It is not about generating new experimental information, but rather applying interdisciplinary theories in order to increase its predictability, generality, and interpretation of mechanisms.

The transfer of these frameworks from their home disciplines to prosthodontic nanocomposite design is the contribution of this review. Their systematic adoption as standard tools of study design and reporting in dental materials research would constitute a paradigm shift from empirical art toward principled science in the optimization of restorative and prosthetic dental materials.

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