

LaMer's 1950 Model for Particle Formation of Instantaneous Nucleation and Diffusion-Controlled Growth: A Historical Look at the Model's Origins, Assumptions, Equations, and Underlying Sulfur Sol Formation Kinetics Data

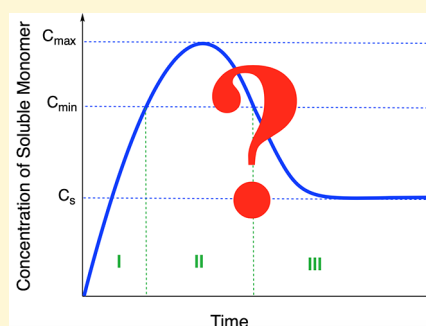
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S Supporting Information

ABSTRACT: A look back at LaMer's 1950 model of particle formation is undertaken (LaMer, V. K.; Dinegar, R. H. Theory, Production and Mechanism of Formation of Monodispersed Hydrosols. *J. Am. Chem. Soc.* **1950**, 72, 4847–4854), a highly cited paper that has more than 1953 citations as of March 2019. The nonmathematical, verbal version of LaMer's model, namely, the concepts of "instantaneous" (or "burst") nucleation and "diffusion-controlled" growth, continues to be heavily cited because, until recently, it was the only known way to try to explain how narrow particle-size distributions might form from self-assembly syntheses. The following specific topics are addressed in separate sections: (i) the chemical origins of the LaMer model, (ii) the original sulfur hydrosol formation system, (iii) the often-cited schematic and then associated words-only descriptions of the LaMer model, (iv) the nine assumptions underlying the LaMer equation and quantitative model, (v) the question of whether LaMer's model is actually primarily a "growth model" if one notes that "instantaneous nucleation" is an initial assumption made for mathematical purposes, and (vi) the actual LaMer equation (and the question of when it has been used to fit particle formation kinetics data). Additional topics discussed are (vii) the disconnect between LaMer's quantitative model and associated differential equation vs any testing against experimental kinetics data, (viii) a look at the kinetics data for, and the current understanding of, the mechanism of sulfur sol formation, (ix) the 1926, first kinetics data for sulfur sol formation, (x) light scattering data for sulfur sol formation, (xi) fitting of the 1926 kinetics data for sulfur sol formation by a minimalistic two-step mechanism, and (xii) the interesting effect of microfiltration and the removal of dust on the size distribution of sulfur sols. Also provided is (xiii) a summary and conclusions section.



1. INTRODUCTION

In the past approaching 70 years, the LaMer hypothesis (hereafter the LaMer model)¹ for particle formation has been one of the most cited qualitative, word-based explanations for describing the nucleation and growth of colloidal particles and nanoparticles. A Web of Science search reveals that Professor Victor LaMer's original 1950 *Journal of the American Chemical Society* paper¹ on his proposed "instantaneous nucleation" (also known as "burst nucleation") followed by "diffusion-controlled growth" model to account, at the time, for sulfur sol formation has garnered more than 1953 citations as of March 2019. As LaMer states in the final, sixth point of the summary in the 1950 paper,¹ "(6) A qualitative explanation is offered for the necessary conditions under which monodispersed colloids may be prepared for both the dilution and acid decomposition of sodium thiosulfate methods". The use of the words "necessary" will prove to be an unfortunate part of this 1950 statement (*vide infra*).

It is surprising, and an important void in the literature, that no look back at LaMer's model and its origins has previously appeared. Even in 1951, Turkevich believed that the LaMer

model was not applicable to his Au(0)_n formation system, commenting that it was, instead and already, "a theory of great tradition".² Forty-two years later in 1993, Matijević raised his own concerns about the LaMer model, noting that it was "limited".³ Then, in 1997 we noted⁴ that "perhaps much fairer to LaMer's pioneering work would be the term 'inappropriately cited', a phenomenon which really only points to the dearth of new, broadly applicable and kinetically verified alternative mechanisms (for particle formation) in the intervening nearly 50 years". Restated, at least prior to 1997,⁴ the LaMer model was being cited because there was literally no other model, and certainly no disproof-based^{5,6} chemical reaction mechanism for particle formation with an associated differential equation, which therefore allowed fitting of kinetics data! Moreover, the allure of LaMer's model has continued to be that it was, until recently,⁷ the only explanation of how one might form narrow dispersions of

Received: March 30, 2019

Revised: August 11, 2019

Published: September 4, 2019

particles from self-assembly syntheses. Finally, as we look back at the LaMer model with 70 years of hindsight, we wish to emphasize our description in 1997 of LaMer's work as "pioneering";⁴ it was, and still is.

This review examines the sulfur sol formation literature that gave rise to this popular model for particle formation. No review of that literature giving rise to the LaMer model has previously appeared; indeed, no review of any aspect of the model has appeared since LaMer's own 1952 review where he returned to the topic of nucleation in which he included a discussion of his 1950 paper.⁸

The goals of this review are (i) to understand the origins of the LaMer model, (ii) to take a look at the assumptions underlying the LaMer quantitative equation, (iii) to look at the LaMer equation and see how often that equation has been used to fit particle formation kinetics data, (iv) to try to understand how LaMer's model morphed from a differential equation to its highly cited, "words-only" version of instantaneous nucleation followed by diffusion-controlled growth, (v) to see if other functions or mechanisms might be able to account for the early sulfur sol (S_n) formation kinetics data for which the LaMer model was derived, and overall (vi) to try to understand the LaMer model more deeply so as to be able to advise the community about when and where one should (or should not) apply this model. Relevant to the latter is the documented but underappreciated problem of "the classic theories work(ing) poorly or not at all when applied beyond the validity of their assumptions".⁹

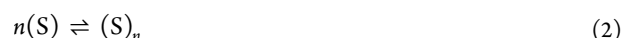
2. THE LAMER MODEL: A LOOK AT ITS CHEMICAL ORIGINS

2.1. The Original System: Sulfur Hydrosol Formation.

In 1950, LaMer and Dinegar¹ used classical nucleation theory (CNT) to describe the formation of sulfur sols from the decomposition of sodium hydrogen thiosulfate in dilute hydrochloric acid solution in an organic solvent (eq 1).



In the original 1950 paper, the reaction product was given as " S_2 ", suggesting that the sulfur had been converted to a soluble, dimeric form.^{10–12} Due to this, we retain the original notation of LaMer by referring to this soluble sulfur as " S ", although neither atomic, elemental " S " itself nor S_2 is an established solution form of sulfur. Instead, cyclic oligomers of sulfur exist such as S_6 – S_8 (LaMer specifically mentioned¹ "the diffusing species are almost certainly S_8 rings ..."). Each S–S bond of S_n falls in the "strong bonding" category of nucleating species;¹⁴ the S–S bond in gas-phase S_2 is ~ 99 kcal/mol¹⁵ [although this value drops significantly as $(-S)_n$ n -mers are formed,¹³ so that this high bond energy overestimates the S–S bond strength in a S_n n -mer]. The next steps in the formation of sulfur sols (S_n) were written at the time as an n -mer association from the monomer, S , eq 2, written retaining the original notation at this point to avoid confusion:



Sulfur sols have been shown to have a negative charge on the surface.^{16–18} The presence of negatively charged ions on the surface of sulfur sols implies that ionic sulfur species are likely adsorbed on the particle surface.

We will return to the kinetics data for, and any understanding of, the underlying mechanism for this classic colloidal

formation system of a sulfur sol, (S_n) in an upcoming section of this review.

2.2. Often-Cited Schematic and Associated Words-Only Descriptions of the LaMer Model.

The LaMer model considers the formation of colloidal particles ["sulfur sols" in the original work (*vide supra*)] from the soluble monomer in three stages, as schematically shown in Figure 1, where the concentration of the soluble monomer is qualitatively plotted

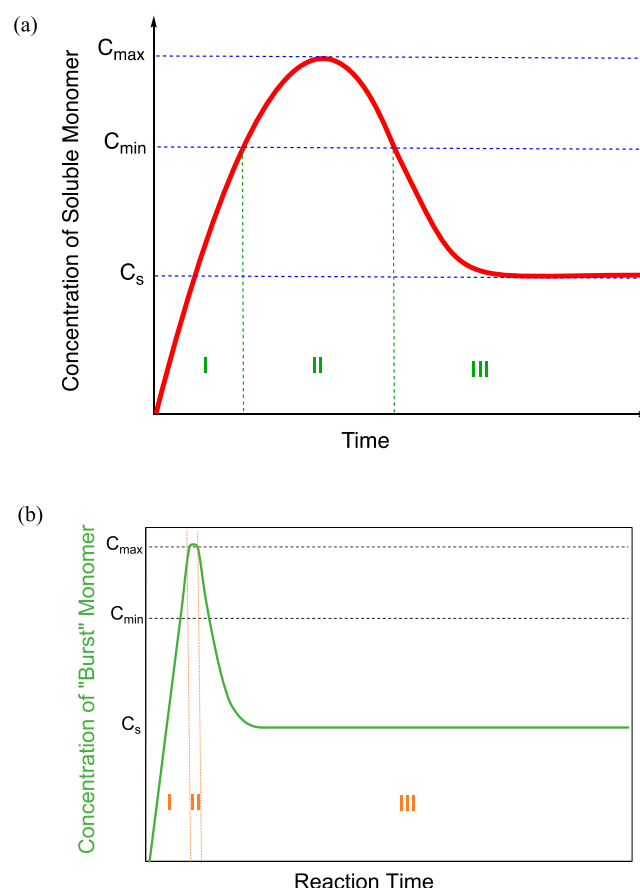


Figure 1. (a) Classic schematic illustration of the LaMer model/hypothesis for the formation of colloidal particles from the soluble monomer, S , in the case of sulfur sol formation, (S_n) as in the original 1950 paper.¹ Adapted in part with permission from ref 1. Copyright 1950 American Chemical Society. The hypothetical curve shows qualitatively the variation of soluble monomer concentration vs time during the whole formation process. C_s is the saturation concentration (solubility of the soluble monomer). C_{min} is the hypothetical minimum supersaturation for the nucleation; C_{max} is the hypothetical limiting supersaturation. Postulated stage I: formation of soluble monomer in solution. Postulated stage II: nucleation from the solution when the concentration of the soluble monomer is higher than the critical supersaturation level C_{min} , as typically presented, albeit not shown as the postulated "effectively infinite rate, burst nucleation".¹ Postulated stage III: growth by diffusion when the supersaturation concentration is lower than C_{min} but higher than C_s . It is critical to note that, in the intervening nearly 70 years and despite the widespread reproduction and quoting of this figure, no such experimental time dependence of soluble sulfur monomer has ever been published, at least that we have been able to find from an exhaustive literature search. (b) A more time-compressed schematic illustration of the LaMer model (green curve), constructed as part of the present work to more explicitly emphasize the model's "instantaneous" nucleation postulate (followed by diffusion-controlled growth).

versus time.¹ (I) In the pictorial and words-only version of the LaMer model, the concentration of soluble “monomers” in solution (LaMer specifically indicated S_2 and S_8) is postulated to build up to a critical supersaturation level, and (II) when the concentration of the soluble monomer reaches the critical supersaturation level (C_{\max}), “instantaneous self-nucleation” (i.e., instantaneous homogeneous, “burst” nucleation) is postulated to occur. A critical point to recognize is that, as a result of this assumption, LaMer’s quantitative model and equation (*vide infra*) will have no provision for accounting for or fitting experimental nucleation kinetics data. Instead, the LaMer model was the first to postulate “instantaneous”, very short time scale nucleation. LaMer made this assumption so that he then could develop mathematically what is primarily a growth model (a diffusion-controlled growth model). It follows that LaMer’s model should be applied only to cases in which experimental evidence exists for both burst nucleation and diffusion-controlled growth.

As a result of the postulated instantaneous nucleation, the soluble S monomer concentration is then postulated to fall below the threshold concentration level (C_{\min}). The rate of nucleation is postulated to be “effectively infinite”, consistent with the hypothesis of “instantaneous nucleation”,¹ even though it is never drawn that way in the classic figure shown (Figure 1), the figure representing LaMer’s words-only model that is commonly cited in the literature (i.e., but in which the time axis is unscaled so that one could be talking about microseconds, seconds, or even minutes or longer). The postulated burst nucleation is then believed to quickly decrease the concentration of the freely diffusing S monomer (i.e., S_2 or S_8 , etc.) in solution below the critical value, so that no new nuclei will form according to the model. Next, (III) the postulated growth stage in the LaMer model occurs where the system’s free energy drives the attachment of the S monomer to the preformed nuclei. Growth is postulated to be diffusion-controlled monomer addition.

At a sufficiently high monomer concentration, the model postulates that particle growth will be favored over dissolution back into monomers (i.e., eq 2 is postulated to be reversible, consistent with the thermodynamic and not kinetic control that is the basis of the model). Remaining monomers are assumed to preferentially adsorb onto smaller particles due to their higher surface energies relative to those of larger particles. Hence, the model predicts that the growth kinetics will result in a decrease in the particle-size distribution with time.¹ If the monomer concentration is too low during the growth stage, then particle dissolution back to monomers is postulated to be favored over monomer adsorption (Ostwald ripening¹⁹ per se was not mentioned by LaMer). The LaMer model is a CNT-based homogeneous nucleation model (i.e., no dust, although LaMer was fully aware of the importance of “foreign nuclei”⁸), a model in which nanoparticles evolve in size by interacting solely with monomers.^{20,21} Agglomeration is not taken into account, although we now know that agglomeration is likely a nearly universal phenomenon in nanoparticle formation^{22–28} under self-assembly conditions and unless experimental kinetics data for the system at hand demonstrate otherwise.

Upon closer examination of the LaMer model, it proposes a particulate spherical volume with radius h and a concentric spherical nucleus in it with radius x (Figure 2). Radial growth is then postulated to occur on the surface of nucleus in the center upon arrival of the diffusing sulfur monomer at the surface. A number of assumptions are necessary for

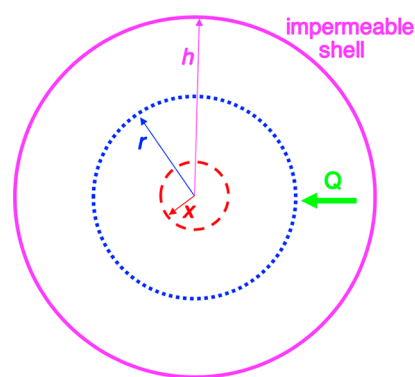


Figure 2. Schematic illustration of LaMer’s model consisting of a spherical volume with radius h (solid pink line), having a concentric spherical nucleus with radius x (red dashed line). In this model, radial growth occurs on the surface of the concentric spherical nucleus upon arrival of diffusing sulfur. Q is the flux of diffusing sulfur through any concentric spherical shell with radius r (blue dotted line) within the sphere of the impermeable shell (pink solid line).

implementation of the model,¹ several of which mirror assumptions in CNT.^{20,29–39} Below, each assumption behind the LaMer model is listed along with analysis and comments.

2.3. A Look Back at the Nine Assumptions Underlying the LaMer Quantitative Model and Equation with the Advantage of 70 Years of Hindsight. The nine explicit assumptions underlying the LaMer model are presented below, along with some analysis and commentary. To the best of our knowledge, no full list of, or commentary on, the assumptions behind the LaMer model has previously appeared, an important void filled by what follows, important so that workers citing the model can be fully aware of its assumptions and not use the model for cases or situations where its assumptions are invalid, applications LaMer surely would not have wanted.

Critical to note here—in an attempt to be fair and do our best to understand the scientific times in which LaMer developed his creative, pioneering model—is the fact that we have an additional 70 years of knowledge and technology over what LaMer had to work with in the 1950s. Hence, our analyses and comments are not meant to be critical of LaMer and his co-workers but, rather, to make apparent to users of the LaMer model the assumptions behind the model and, hence, the limits past which LaMer himself likely would have said the model is being misapplied.

2.3.1. Nucleation Is Postulated To Occur Instantaneously from a Supersaturated Solution Producing Nuclei of Equal Size. The Number of Nuclei per Unit Volume of the Reaction Solution Is n . Comments: Instantaneous nucleation is, of course, physically impossible, something that LaMer and co-workers likely fully understood judging from his 1952 review entitled “Nucleation in Phase Transitions”.⁸ But, in his 1950 paper LaMer and co-workers were trying to understand what must have been a fascinating question at the time—actually, a still fascinating question—of how near-monodisperse particles could possibly even conceivably be formed. Uniform nuclei—and hence the assumption of instantaneous nucleation—were a necessity at the time in setting up what is really a growth model (i.e., and past the assumption of instantaneous nucleation) so that the model could begin from a nucleus of radius x as shown in Figure 2. It follows that the many citations of LaMer’s model for its “instantaneous nucleation” feature are just (perhaps

unwitting) citations of its physically most unreasonable assumption, a practice that makes little sense and should be discontinued. Instead, researchers should actually study nucleation in their system and give any experimental evidence that nucleation is indeed anything like “instantaneous”.

A second hard problem is that quantification of supersaturation is required in the model and its associated differential equation, yet the true supersaturation value as a function of time is difficult to monitor directly. Even today, convincing measurements of supersaturation versus time are rare,^{40–43} at least that we have been able to find.

Additionally, dust would not be able to influence nucleation if it were already “instantaneous”, yet dust does change $(S)_n$ sol particle formation dramatically as will be discussed below. Indeed, heterogeneous nucleation (i.e., rather than “homogeneous” nucleation) is likely nearly universal^{30,39} and often mediated by omnipresent dust.^{40,44–48} In fairness to LaMer, he clearly understood that nucleation involved “foreign nuclei” and that a chemical mechanism for nucleation was what one wanted. Recommended reading in this regard is LaMer’s 1952 review,⁸ in which he is focused on nucleation and provides evidence that $(\text{BaSO}_4)_n$ formation likely has a nucleus achieved by an approximately sixth-order process, ostensibly $\alpha\text{-}[\text{Ba}^{2+}]^3[\text{SO}_4^{2-}]^3$ leading to $\text{Ba}_3(\text{SO}_4)_3$ as the nucleus in his writings, but he also mentions $\text{Ba}_4(\text{SO}_4)_3^{2+}$ and $\text{Ba}_3(\text{SO}_4)_4^{2-}$ as possible nuclei. Hence, he was aware of “low-molecularity nucleation”¹⁴ 64 years before it was subsequently published in a JACS article.¹⁴ He provided a chemical mechanism for nucleation in $(\text{BaSO}_4)_n$ formation on page 1277 of his 1952 review.⁸ One has to therefore believe that LaMer thought nucleation was never precisely “instantaneous”.

However, for his 1950 theoretical paper and model trying to understand how “monodisperse” particles could possibly be formed, he needed to postulate that all of the nuclei show up at once and to start (“instantaneous, or burst/spontaneous nucleation”). A critical point, then, is LaMer made the burst nucleation assumption to be able to provide the first mathematical model for growth that might, again, give any idea how near-monodisperse particles could possibly be formed from what we now call self-assembly syntheses. The formation of ostensibly “monodisperse” particles by the measurements available in the 1950s must have been a hugely puzzling and intriguing problem at that time, given that it is still puzzling even today: how can nearly monodisperse particles form from a self-assembly reaction that often has thousands if not tens of thousands of steps!^{7]}

2.3.2. The Growth of a Particle Is Postulated To Occur by Addition of a Diffusible Sulfur Monomer at the Surface of a Nucleus. The Diffusing S Monomer Is a Molarly Soluble Form of Elemental Sulfur. Comments: The exclusion of well-known aggregation/agglomeration processes during particle formation^{22–28} is likely an incorrect part of any and all models that fail to take it into account and unless compelling kinetic evidence against an aggregation component⁴ is available. Additionally, there is no direct evidence that the growth of the $(S)_n$ particles is an exclusive result of diffusible sulfur monomers or S_n species such as known S_6 , S_7 , and especially S_8 rings.¹³ Fortunately, mechanistic models are now available that do take aggregation specifically into account and do, therefore, have associated differential equations for fitting kinetics data and thereby testing those minimalistic mechanisms.^{22–28}

2.3.3. The Number of Nuclei Remains Unchanged throughout the Growth Stage. Comments: Unless one

knows the number of nuclei at the beginning, one cannot determine if the number of nuclei remains unchanged throughout the whole particle formation process; that is, one cannot tell if particles are lost due to agglomeration/aggregation. A couple of examples from the literature showing that the assumption of a constant number of nuclei is not true, for at least the systems cited, are the following. SAXS studies of the formation of poly(*N*-vinyl-2-pyrrolidone)-stabilized $\text{Ag}(0)_n$ nanoparticles formed by NaBH_4 reduction of AgNO_3 ⁴⁹ exhibit an increase in the number of particles over the nucleation period. Studies of trioctylphosphine-stabilized $\text{Pd}(0)_n$ nanoparticles from H_2 reduction of palladium(II) acetate⁵⁰ similarly show that the number of particles increases during the reaction. SAXS studies of another $\text{Pd}(0)_n$ nanoparticle formation^{51–55} system further show that (continuous⁴) nucleation and growth overlap throughout the particle formation reaction.

Even in $(\text{CdSe})_n$ semiconductor particle formation by the “heating-up” method, a recent study that gathered SAXS and WAXS evidence makes the excellent point that our understanding of nucleation and growth in otherwise well-studied semiconductor nanoparticles “... is still very limited mainly due to the lack of extensive, reliable, and quantitative *in situ* experimental data”.⁵⁶ Their SAXS data reveal that nucleation is continuous and growth is 10^{-8} slower than diffusion controlled in their $(\text{CdSe})_n$ nanoparticle formation system beginning with $\text{Cd}(\text{O}_2\text{CR})$ and Se^0 (RCO_2^- = myristate, in an octadecene solvent at 218 °C). What is remarkable in this otherwise state-of-the-art study is that despite noting the need for quantitative kinetics data (a) no fit is even attempted of the data to any mechanism- or model-based differential kinetics equation and (b) instead of noting that their data rule out a LaMer-like mechanism, the authors cite a “nucleation burst” and state that “Overall, a LaMer-type mechanism⁴² is observed” (where their ref 42 is to LaMer’s 1950 paper¹). As such, this is a telling example of the continuing, pervasive disconnect between any quantitative testing of the LaMer model versus claims that the model is followed, sometimes even despite experimental data to the contrary as in the example given above. This disconnect, and the lack of quantitative testing of the LaMer model, are important topics that are repeated throughout the literature citing the LaMer model, a disconnect that will be treated in more detail in an upcoming section.

The bulk of the literature of particle formation, where any kinetics of nucleation and growth have actually been monitored in real time and those processes deconvoluted by fitting to a chemical mechanism-derived differential equation, teaches that nucleation has much more often been shown to be continuous⁴ rather than anything like “instantaneous or burst”. But how, then, can narrow size distributions be formed if nucleation is actually, more often than not, continuous? Crucial here is the recent demonstration that continuous nucleation⁴ can and does lead to narrow particle-size distributions by the insight of smaller particles grow faster than larger ones, thereby catching up in size with the larger particles.⁷ That discovery is a critical paradigm shift in the thinking and understanding of how narrow distributions of particles can be formed,⁷ a discovery that provides an alternative to the previously seemingly compelling need to assume “instantaneous” nucleation by citing LaMer’s model as a way to get to narrow particle-size distributions.⁷ Hence, going forward, workers need to provide experimental evidence of whether their nucleation is “instantaneous” or, actually,

“continuous”,⁴ rather than just citing LaMer’s famous 1950 paper for its *assumption* of “instantaneous” nucleation, an assumption necessary mathematically at the time so that the first model of how “monodisperse” particles could possibly be formed could be developed.

2.3.4. The Particles Grow Independently of Each Other. Comments: This assumption is just what it says: that any interaction of particles that could influence particle growth, for example, agglomeration or any type of competing growth, is not allowed. Reiss, a student of LaMer’s, provides a critical discussion of the “growth by diffusion hypothesis”⁵⁷ and presents an improved model that takes competing diffusion-controlled growth into account, a discussion recommended to the interested reader. Of considerable interest in Reiss’ paper is (a) the list of seven state-of-the-art uses and importance of near monodisperse colloids to science at the time, ranging from standards for and experimental verification of light scattering theories, testing coagulation theories, measurements of Avogadro’s number, studies of particle size versus retention time in the human lung, meteorological applications, and studies of reaction kinetics of (S)_n sol formation. Also of significant historical interest is the fact that Reiss recognized (b) “What is needed is some demonstration of the existence of a natural growth-regulating mechanism founded on well-established physical chemical principles”.⁵⁷

2.3.5. The Total Amount of Sulfur To Be Deposited Is Distributed Homogeneously throughout the Solution; That Is, the Sulfur Is Distributed Proportionally 1/n Times of the Total Sulfur to Each Nucleus. Comments: This assumption ensures the hypothetical formation of perfectly monodisperse nanoparticles; again recall that by the physical methods of the time, the observed (S)_n sol particles looked truly of one size and hence “monodisperse” as determined by the physical methods available for particle-size determination in 1950.¹ However, we now know that, in the intervening 70 years since the model, truly monosized nanoparticles have never been seen in the history of nanoparticle formation by self-assembly for any material and by our now much better physical methods available for determining particle-size distributions. The narrowest of dispersions ever made by any self-assembly particle formation process (i.e., that do not involve some sort of lattice-crystallization process) are rarely lower^{58,59} than a ± 4 –8% particle-size dispersion, even for the best examples in the broader literature, as documented with appropriate referencing provided elsewhere.⁴⁴ This is an important, modern experimental fact, one that cannot be and hence is not intended as a criticism of the model because LaMer and co-workers did not have this fact. Instead, it calls awareness to the fact that “all” any modern model or mechanism of particle formation needs to explain is how particle-size distributions from self-assembly syntheses can achieve the still quite narrow, approximately $\pm 5\%$ range,⁷ sometimes even a bit lower.^{58,59}

2.3.6. Each Particle Will Grow Only by an Amount of Sulfur Contained in the Particulate Spherical Volume $4/3\pi h^3$, Where h Is the Radius of the Impermeable Shell. This Particulate Volume Is Associated with a Single Nucleus. Comments: This assumption is directly linked to assumption 2.3.5 above, whereby the sulfur is assumed to be distributed homogeneously throughout the solution, and only the sulfur present within the impermeable shell is assumed to be able to influence the growth of that particle. This assumption is, again, just a necessary assumption to ensure the formation of single-sized particles.

2.3.7. No Materials outside This Particulate Volume Are Allowed To Influence the Growth of a Given Particle. Comments: Studies available since the late 1800s and hence more than 50 years before LaMer’s model show that the presence of dust greatly affects the nucleation and growth processes.^{44–48} The common presence of, and the major effects from, dust and the resultant heterogeneous,^{30,39} not homogeneous, nucleation is an important point that upgraded, modern models and mechanisms of nucleation and growth must take into account. Again, LaMer was aware of “foreign objects”⁸ as a part of nucleation, but those objects such as dust were beyond anything one could treat in the first-pass, 1950s model of how monodisperse particles might possibly be formed.

2.3.8. The Growth Is Influenced by Three Variables: (a) The Number of Nuclei, Which Is Assumed To Be Constant throughout the Growth and Equal to the Number of Particles Present Initially; (b) the Total Diffusible Amount of Sulfur, Where C_0 Is the Difference in Concentration between the Supersaturated and Saturated Solutions ($C_0 = C_{ss} - C_s$); and (c) the Diffusion Coefficient D of Sulfur in the Medium. Comments: Others have attempted to incorporate particle stability into their modification of the model by reinterpreting the Fick’s law-based assumptions in the original model.⁶⁰ Moreover, during the past 70 years dust,^{44–48} aggregation/agglomeration,^{22–28} processes such as Ostwald ripening,¹⁹ and notably extensive evidence of surface capping ligands^{50,61} are now known to be additional variables that dramatically influence particle formation. Hence, and again with 70 years of hindsight, these additional variables are ones that particle formation models or mechanisms must take into account. The omnipresence of surface ligands that are key to the stabilization of particles^{61,62} is arguably the most important additional variable, one that is likely why growth can be 10^9 – 10^{12} -fold slower than diffusion control (*vide infra*). Noteworthy here is the fact that only today, 70 years later, are the effects of ligands beginning to be taken into account in quantitative kinetics and mechanistic models of nanoparticle formation.^{7,50,51,61,63–65}

2.3.9. The Product C_0D Is Assumed To Be Temperature-Independent; That Is, Growth Is Taken To Be Temperature-Independent. Comments: Viscosity and the diffusion coefficient, D , are temperature-dependent, and C_0 is slightly, too, due to changes in the solution volume with temperature. However, these should be generally minor effects, especially over small temperature ranges, so that this minor assumption is mentioned here only for the sake of completeness.

In summary, the original, creative, and pioneering model from LaMer and co-workers is based on nine assumptions required at the time to be able to start the model from preformed nuclei of radius x and then have them grow uniformly. It appears to be little recognized that the physical model (Figure 2) is actually a *growth model*, one that says nothing about the actual nucleation process. Instead and as a necessary part to be able to start the growth as Figure 2 shows, nucleation was simply postulated/assumed to be instantaneous so that the math for an assumed diffusion-controlled growth process would be developed. Hence, it makes no sense (as often done in the current 1953 papers citing the LaMer model) to cite the model only for its “instantaneous” nucleation (assumption!), often reproducing Figure 1a as “evidence”. That practice should stop, immediately. LaMer almost surely would not want us to be citing his model for only its burst nucleation assumption.

The seeming ability of the model, in its words-only form and according to Figure 1a, to rationalize the formation of narrow, approaching monodisperse size distributions of particles formed by self-assembly meant that the LaMer model was ensured a strong following, 1953 citations as of this writing, especially because no other model (and certainly no disproof-based mechanism) appeared until almost 50 years later.⁴

A problem that arose over those 50 years, indeed a problem that persists to this day, is that a qualitative, words-only “kinetics model” of postulated “instantaneous nucleation and diffusion-controlled growth” cannot actually be tested experimentally by attempted fitting of experimental kinetics data to the qualitative model. What one needs is the mathematical (differential) equation to try to fit one’s kinetics of particle formation. Hence, the quantitative equation corresponding to the LaMer model is the subject of the next section.

2.4. The Actual LaMer Equation, and the Question of When It Has Been Used To Fit Particle Formation Kinetics Data. Using the nine assumptions listed above, LaMer derived his differential equation (eq 3) for particle growth:

$$\frac{d}{dt}(x^2) = [C_{ss} - C_s(t)] \frac{2D}{\rho} - \frac{2D}{h^3} x^3 \quad (3)$$

where C_{ss} is the supersaturation concentration, $C_s(t)$ is the concentration of the soluble “monomer” above the saturation concentration as a function of time [the monomer nominally being “S” in the case of $(S)_n$ formation], D is the diffusion coefficient, ρ is the bulk density of elemental sulfur, h is the sphere radius, and x is the nucleus radius as shown in Figure 2. To derive this equation, LaMer started with Fick’s law⁶⁶ (eq 4) to describe the flux (Q) through a spherical shell [Figure 2 (*vide supra*)].

$$Q(t) = -4\pi r^2 D \frac{dC}{dr} \quad (4)$$

The concentration of sulfur is different at the individual boundaries, so LaMer established the following boundary conditions:¹

- (i) at the particle’s surface, $C(x, t) = C_s(t)$
- (ii) initially, anywhere in the system, $C(r, 0) = C_{ss}$
- (iii) at the “impermeable shell”, $\left(\frac{\partial C}{\partial t}\right)_{r=h} = \frac{3Q(t)}{4\pi h^3}$

Integrating the flux (eq 5) with respect to r and at $t = 0$ produces eq 6

$$C(r, 0) = \frac{Q(0)}{4\pi r D} + f(0) \quad (6)$$

and, because $\left(\frac{\partial C}{\partial r}\right)_{t=0} = 0$, $Q(0) = 0$, and $C(r, 0) = f(0) = C_{ss}$ (boundary condition ii), boundary condition (iii) can be applied so eq 6 is rearranged to produce eq 7.

$$\frac{df}{dt} = \frac{3Q(t)}{4\pi h^3} - \frac{1}{4\pi h D} \frac{dQ}{dt} \quad (7)$$

Next, eq 7 is integrated with respect to time, boundary condition (ii) is again applied, and because $h \gg r$ (and by extension $1/h \ll 1/r$), eq 8 is produced.

$$C(r, t) = C_{ss} + \frac{Q(t)}{4\pi r D} + \frac{3}{4\pi h^3} \int_0^t Q(t) dt \quad (8)$$

At this point in the derivation, LaMer remarks that “the particle is increasing with size as material is deposited on its surface, [therefore] $-Q(t)$ must be proportional to the rate of increase of volume.”¹ This can be mathematically expressed as eq 9

$$-Q(t) = 4\pi \rho x^2 \frac{dx}{dt} \quad (9)$$

which in turn is combined with eq 8 to yield eq 10.

$$C(r, t) = C_{ss} - \frac{\rho}{D} x^2 \frac{dx}{dt} \left(\frac{1}{r}\right) - \frac{3}{4\pi h^3} \int_0^t 4\pi \rho x^2 \frac{dx}{dt} dt \quad (10)$$

Finally, the integral from eq 10 can be evaluated with $x(0) = 0$ and $r = x$, and then from boundary condition (i), LaMer assumes $C(x, t) = C_s(t)$ to produce the previously given eq 3, reproduced below.

$$\frac{d}{dt}(x^2) = [C_{ss} - C_s(t)] \frac{2D}{\rho} - \frac{2D}{h^3} x^3$$

Interested readers are referred to the full, complete derivation on page 4852 of the original paper by LaMer and Dinegar.¹

Intriguingly, LaMer¹ integrated eq 3, using the method of Cauchy and Lipschitz,⁶⁷ as an analytical expression between x and t by assuming C_s is independent of t . This “special case” as LaMer¹ calls it yields eq 11.

$$t = \frac{h^2}{3D} \left(\frac{\rho}{C_0}\right)^{1/3} \left\{ \frac{1}{2} \ln \frac{\left(\frac{C_0}{\rho}\right)^{2/3} h^2 + \left(\frac{C_0}{\rho}\right)^{1/3} h x + x^2}{\left(x - \left|\frac{C_0}{\rho}\right|^{1/3} h\right)^2} + \sqrt{3} \left[\tan^{-1} \frac{-1\sqrt{3}}{3} - \tan^{-1} \left(\frac{2x + \left|\frac{C_0}{\rho}\right|^{1/3} h}{\left|\frac{C_0}{\rho}\right|^{1/3} h\sqrt{3}} \right) \right] \right\} \quad (11)$$

The assumption that C_s is constant with respect to time and, hence, equal to C_0 is of course a very special, nonphysical case that attempts to remove what is claimed¹ to be a small dependence of C_0 on t for the purpose of integration. Of note here is the fact that even LaMer himself never reported the use of eq 11 to analyze any data. LaMer was just doing the math he could at the time to see where it led him, just as he should have been doing. He instead used eq 3 in his fit of experimental data.

A remarkable insight from our scouring the literature citing the LaMer model (those 1953 citations as of this writing) is that the original differential equation,¹ eq 3, has been used only once in 70 years to fit particle size versus time data. It has, however, been referenced numerous times in the literature as a justification for the model’s applicability.^{68–71} The lack of use and testing over 70 years of eq 3 or 11 teaches that these equations have not proved to be useful to the particle formation community. They have effectively been completely abandoned. In other words, LaMer’s quantitative model has proved to be effectively “unfalsifiable” in the words of Platt.⁶

An important point here is that this is not the “fault” of LaMer and co-workers. Instead and indeed, the quantitative LaMer model was creative and pioneering and the first such model. It is on all of the rest of us to study and understand the model and then not apply or cite the model beyond the limits of applicability of its assumptions.⁹

2.5. The Resultant Disconnect between the LaMer Quantitative Model and Associated Differential Equation and, Hence, Any Quantitative Testing versus Experimental Kinetics Data. The fact that the LaMer model’s differential equations (eqs 3 and 11) have, together, been used successfully only once in 70 years despite 1953 papers citing the model is a previously unrecognized and telling insight. It explains rather unequivocally why the LaMer model morphed into what is the main citation of the model in ~90% of the 1953 references we have examined that cite the model, namely the oft-cited, words-only form of putative “instantaneous nucleation” followed by “diffusion-controlled growth”, all while citing or reproducing Figure 1a as “evidence” that the model is obeyed. Indeed, it was the lack of compelling evidence for the key assumptions of the model in comparison to the model’s huge and repeated citation, all while those citations often just reproduced Figure 1a, that has had us working on this review off and on starting in 1997⁴ and then in earnest by three of us over the past 3 years. The slow and tedious part of assembling this review was (i) combing through the 1953 papers citing LaMer’s model and (ii) reading carefully and critically examining the ~10% (192) references that we found to contain at least some evidence or deeper discussion regarding the LaMer model.

The disconnect between the LaMer words-only version of the model and experimental kinetics data is perhaps obvious. For testing kinetics models, one needs a differential equation that can and will be extensively experimentally tested by trying to fit that equation (i.e., and thereby its underlying, associated model) to measured kinetics data. Words alone will not suffice; one cannot fit kinetics data to words; one cannot disprove mechanisms without including attempting quantitative fitting to experimental kinetics data. The state-of-the-art (CdSe)_n formation system and elegantly obtained SAXS data cited earlier⁵⁶ are a classic example where despite obtaining superb, quantitative SAXS data and despite the fact that data providing evidence for continuous nucleation and growth 10⁸-fold slower than diffusion-controlled, the authors do not fit their data to any quantitative equation.⁵⁶ Instead, they opt for qualitative, confirmatory statements of “burst nucleation” and a “LaMer-type mechanism”.⁵⁶ Hence, proper, disproof-based^{5,6} and kinetics- and mechanism-based accounting of that superb data remains to be accomplished.

2.6. The Critical Difference between a Physical Chemical Model and a Physical Organic Chemistry-Type, Chemical Equation- and Disproof-Based, Reaction Mechanism. Getting at the true, underlying mechanism is where chemical reaction mechanism—as developed historically in and taught through classical physical organic chemistry^{72–74}—needs to be employed. Ideally elementary steps—or if not, sums of elementary steps known as pseudo-elementary steps^{4,75}—can be used to construct postulated chemical reaction mechanisms. Those steps must, first and foremost, add up to the observed (must be experimentally established) reaction stoichiometry, as otherwise one is postulating a mechanism for some reaction other than the one at hand. Hence, the first rule of reliable reaction mechanisms is “Know

Thy Stoichiometry”, a quote attributed to the late kinetics and mechanistic expert Ralph Pearson.⁷⁶

The second rule of reliable reaction mechanism—that there is no reliable experimentation-based mechanism without kinetics^{76–78}—must then be followed. Even with modern density functional theory (DFT), the evidence is strong that DFT used in a nondisproof-based, nonskeptical way can mislead one as to the true underlying mechanism, even for relatively simple, computationally more tractable organic chemistry systems.⁷⁹ In short, the second rule of reliable mechanistic studies is that there is no reliable mechanism without experimental kinetics data.

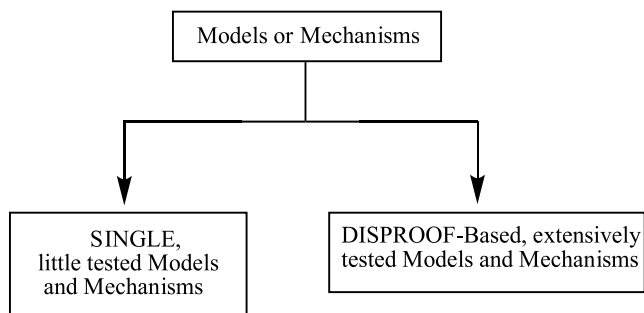
One also must then employ extensive disproof^{6,80} of multiple alternative hypotheses⁵—here multiple alternative mechanisms—en route to a reliable (albeit never precisely correct) reaction mechanism that has held up to the attempted disproof so far—that is the ideally one remaining mechanism that cannot so far be disproved. As Platt notes, any theory (i.e., or model or mechanism) that is inherently unfalsifiable is useless and must be discarded.⁶ One often hears that “you cannot prove a mechanism”. This is true. What this fails to say is the epistemological truth: you never prove anything in science. You can only disprove.^{5,6} S. Scott’s 2019 editorial “The Burden of Disproof” is an excellent short read to get one started emphasizing disproof in their science.⁸⁰

Fourth, Ockham’s razor⁸¹ must be adhered to as one culls through possible mechanisms, as there is always a more complicated mechanism, always a more complex possible “cause” for the observed “effects”. One excludes those more complex mechanisms and goes with the simplest explanation for all of the available data at the time, but one does so fully realizing that such exclusions via Ockham’s razor are conditional.⁸¹ This in turn means that mechanisms must always be revisited when new experimental, computational, or other methodology is developed; that is, disproof-based, deliberately minimal mechanisms must be what one strives for to start, but the fate of those typically oversimplified mechanisms will always be that they will get revised into more complex mechanisms over time and as additional experimental data, computational efforts, and other experimental insights become available. Researchers that are not trained in mechanistic chemistry seem not to understand these points in the senior author’s experience, namely, that (i) initial mechanisms must be the simplest possible but (ii) revising those original, oversimplified mechanisms (such as the two-step mechanism whose use follows⁴) by adding complexity as new experimental evidence demands is the normal route and expectation of rigorous, experimentally based mechanistic work.

Unfortunately, the 1950 paper does refer to that single model as a “mechanism”, even in the paper’s title,¹ and even though LaMer clearly understood and performed kinetics and mechanistic studies himself (“It is the purpose of this paper to present ... a mechanism ...”,¹ among other goals that were also listed in the 1950 paper¹). Reiss also used the specific word “mechanism” (“IV. The Regulating Mechanism”)⁵⁷ when discussing what is actually a single physical chemical model, the word “The” before mechanism being especially unfortunate in hindsight. The authors of this review realize that the use of the word “mechanism” has evolved to have a broader use and meaning across science. However, no single model can be a mechanism—a real mechanism requires disproof of other alternative mechanisms, ideally testing and disproof of all other

conceivable, reasonable mechanisms (Scheme 1). Hence, nanoparticle formation mechanistic science will progress only

Scheme 1. Fundamental Difference between Disproof-Based Models and Mechanisms versus Those That Are Effectively a Single, Little-Tested Hypothesis—The Extent of Attempted Disproof^{5,6,80} Is the Critical Difference



if there is a clear distinction, and the use of balanced reactions and associated differential equations, when presenting and discussing chemical reaction mechanisms versus other types of models that have little attempted disproof. We urge clear and careful distinction of disproof-based mechanisms (and disproof-based models of any type) from any other single theories or models, regardless of their origins (Scheme 1).

One other critical point here is that chemical mechanisms have one more all-important feature in addition to defining the rate constants and providing the differential equation that can then be tested against experimental kinetics data: The balanced reactions of chemical mechanisms also define the specific words and associated concepts with which one is then allowed to use to describe the physical processes at hand, because those processes are well-defined. Any reader that does not understand the significance of this statement is urged to read about the confusion that exists^{77,82–84} in, for just a few among many other examples, solid-state kinetics and mechanism,⁸⁴ large Ag_n nanoparticle formation,⁷⁷ or the use of semiempirical “dispersive kinetics” treatments.^{82,83} In those systems and associated confused literature (i.e., where nonbalanced equation, nonmechanistic approaches have been used), words have to be borrowed from other systems or, worse, simply “made up” to try to describe the physical processes that are occurring. This hugely insidious “borrowing” of (often incorrect) concepts and words not defined by the system at hand occurs because the kinetics are typically fit by (nonmechanistic) empirical functions^{82,83} that, therefore, lack the balanced equations^{77,82–84} that in turn define the proper words for the extant kinetic concepts and associated physical processes. Relevant here is the fact that IUPAC mechanism nomenclature is based on known elementary (chemical reaction) steps.⁸⁵ The bottom line point here is that keeping distinct single physical chemical theories and models from disproof-based, balanced reaction-formulated, physical organic-type chemical mechanisms, where multiple alternative mechanisms have been experimentally ruled out, is a critical conceptual step for making unconfused progress in not only nanoparticle formation science but also all other areas of chemical dynamics in the natural world.

3. A LOOK AT THE KINETICS DATA FOR, AND THE CURRENT UNDERSTANDING OF, THE MECHANISM OF SULFUR SOL FORMATION

In this section, we take a critical look at the kinetics data for the formation of sulfur sols from which the LaMer model originated. This literature starts in 1926 with kinetics data from Jablczynski,^{10,11} 24 years before LaMer’s 1950 paper,¹ and includes kinetics and mechanistic studies from LaMer’s laboratories (*vide infra*).

3.1. The 1926, First Kinetics Data for Sulfur Sol Formation.

The first kinetics data on sulfur sol formation were reported more than 93 years ago in 1926 by Jablczynski and Rytel,^{10,11} hence 24 years prior to LaMer’s 1950 paper.¹ Jablczynski and Rytel investigated the formation of sulfur sols in acidified solutions of sodium thiosulfate, the decomposition of thiosulfuric acid to sulfurous acid and sulfur written at the time as a unimolecular, reversible process (reversible in the sense that $\text{S}_2\text{O}_3^{2-} + \text{H}^+ \rightleftharpoons \text{HSO}_3^- + \text{S}$,^{10,11} which we now know is a largely irreversible process^{18,86}). The reaction solution becomes opalescent/turbid upon the formation of polyatomic aggregates, which are then postulated to adsorb atomic S from the solution. The opaqueness (turbidity) of the solution as the reaction progressed was monitored by a Koenig–Martens spectrophotometer.¹¹ The authors plotted their results (Figure S1) as the normalized sulfur concentration of sulfur sol versus time.¹¹ Surprisingly, the resultant data have never been fit by any kinetics scheme, at least until now and as we do as part of this work (Figure 3) (*vide infra*). The growth of the aggregates was thought to be autocatalytic,¹⁰ in agreement with the sigmoidal shape of the plots reproduced in Figure S1 and Figure 3.

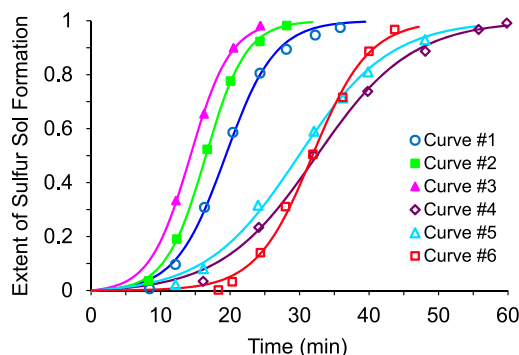


Figure 3. Extent of sulfur sol formation, determined by turbidity measurements and given as a fraction of reaction completion, vs time. The data were obtained by digitizing the scanned plots in the figure on page 412 of the 1926 paper.¹⁰ The experiments were performed starting with 5 mL of 0.1 M $\text{Na}_2\text{S}_2\text{O}_3$, 10 mL of water, and various amounts of HCl. As shown in this figure, all of the 1926 data are fit well by a minimalistic two-step mechanism,⁴ yielding rate constants k_1 for the postulated slow, continuous nucleation and k_2 for the postulated autocatalytic surface growth of sulfur sol formation, as listed in Table 1. Reprinted with permission from ref 10. Copyright 1926 Wiley-VCH Verlag GmbH & Co. KGaA.

3.2. Fitting of the 1926 Kinetics Data for Sulfur Sol Formation by a Minimalistic Two-Step Mechanism.

Figure 3 shows that the observed kinetics data, reproduced from Figure S1, can be fit with a 1997 two-step deliberately minimalistic mechanism⁴ consisting of slow continuous nucleation, $\text{A} \rightarrow \text{B}$ (rate constant of k_1), and then autocatalytic

Table 1. Rate Constants Obtained from the Fits of the 1926 Kinetics Data in Figure S1 to the Two-Step Mechanism As Shown in Figure 3^a

	parameter changed	k_1 (min ⁻¹)	k_2 (M ⁻¹ min ⁻¹)	R^2	χ^2
curve 1	5 mL of 0.5 M HCl	$(1.3 \pm 0.3) \times 10^{-3}$	0.278 ± 0.015	0.9975	4.39×10^{-4}
curve 2	5 mL of 1.0 M HCl	$(1.1 \pm 0.1) \times 10^{-3}$	0.345 ± 0.009	0.9995	8.35×10^{-5}
curve 3	5 mL of 5.0 M HCl	$(2.6 \pm 0.4) \times 10^{-3}$	0.340 ± 0.012	0.9994	9.52×10^{-5}
curve 4	5 mL of 0.25 M HCl	$(1.3 \pm 0.3) \times 10^{-3}$	0.144 ± 0.009	0.9971	4.91×10^{-4}
curve 5	2.5 mL of 0.5 M HCl and 2.5 mL of 0.5 M NaCl	$(1.7 \pm 0.3) \times 10^{-3}$	0.150 ± 0.008	0.9971	4.59×10^{-4}
curve 6	10 mL of water saturated with SO ₂ and 5 mL of 1.0 M HCl	$(1.0 \pm 0.4) \times 10^{-4}$	0.246 ± 0.013	0.9967	5.58×10^{-4}

^aThe 1926 experiments were performed starting with 5 mL of 0.1 M Na₂S₂O₃, 10 mL of water, and 5 mL of 0.5 M HCl. The parameter changed in each kinetics experiment and resultant curve shown in Figure 3 is given in the second column.

surface growth, $A + B \rightarrow 2B$ (rate constant of k_2), a disproof-based, Ockham's razor-obeying, and hence too simplistic mechanism to describe the likely thousands of chemical steps actually occurring. The fits provided in Figure 3 show for the first time that these classic $(S)_n$ sol formation kinetics data, which preceded and underlie the development of the LaMer model, can be accounted for quantitatively by a two-pseudoelementary step mechanism in which (i) nucleation is postulated in the phenomenological mechanistic model to be slow and continuous and (ii) autocatalytic growth is, now via Figure 3, an experimentally supported reaction descriptor for this $(S)_n$ formation reaction as was insightfully hypothesized back in 1926.¹⁰ [The underlying $(S)_n + S \rightarrow (S)_{n+1}$ steps are formally autocatalytic, and their sum will look and can be fit by the pseudoelementary step $A + B \rightarrow 2B$, as the simulations in the Supporting Information elsewhere document (there for an $Ir(O)_n$ formation system).⁸⁷]

In short, the interesting observation is that Jablczynski and co-workers (and then LaMer and then Turkevich) were perhaps the first researchers that might have discovered what was instead discovered 71 years later in 1997.⁴ LaMer wrote equations on page 1273 in eq 2 of his 1952 paper that are not far off of the two-step mechanism, but unfortunately all assuming reversible, equilibrium processes.⁸ If any of those workers had discovered the minimalistic two-step mechanism for particle formation back in 1926, then it is highly likely that the understanding of nanoparticle growth kinetics and mechanism would have taken quite a different, likely significantly accelerated route from its historical path. Specifically, the theory and model of “instantaneous nucleation” and “diffusion-controlled growth” would have then had an experimental phenomenological, kinetics, and mechanistic-based model as a competing hypothesis for subsequent experimental testing and refinement that, in nearly complete opposition and contrast, would have been the two pseudoelementary steps of “slow continuous nucleation” (i.e., as opposed to instantaneous, burst nucleation) and chemical reaction-based “autocatalytic surface growth” (as opposed to diffusion-controlled growth). Given that population balance modeling was started in 1964, the ability to use the massive amount of kinetics information in what was reported in only 2019 as (minimum, disproof-based) mechanism-enabled population balance modeling (ME-PBM)⁷ likely would have been available even in the 1960s and 1970s, not almost 50–60 years later in 2019. The two-step mechanism⁴ would, then, almost surely have been tested, refined, and likely abandoned in favor of a three-step⁷ or a more complex mechanism in perhaps the 1970s, not nearly 50 years later in 2019.⁷

Noteworthy regarding the growth stage is the fact that the k_2 growth rate constants obtained in Figure 3 and listed in Table

1 of $1\text{--}2 \times 10^{-1} \text{ M}^{-1} \text{ min}^{-1}$ (and hence $1\text{--}5 \times 10^{-3} \text{ M}^{-1} \text{ s}^{-1}$) are nearly 10^{10} smaller than the rate of diffusion control of a nanoparticle ($\sim 10^7 \text{ M}^{-1} \text{ s}^{-1}$) as postulated in the LaMer growth model. This fitting with even the too-simple two-step model shows the value of balanced equation-based chemical mechanisms and their associated differential equations. The fitting in Figure 3 goes far toward disproving the LaMer model for the sulfur sol formation system on which it is originally based. The greatly slowed growth hints at the importance of the previously cited surface anionic charge^{16–18} and probable associated ligands in the $(S)_n$ sols.

3.3. Light Scattering Data for Sulfur Sol Formation. In the late 1940s and then throughout the 1950s, LaMer and co-workers cleverly and expertly developed a method using light scattering to investigate the formation of sulfur sols,^{88–94} optical density measurements being the sole available kinetics data for sulfur sol formation at the time. LaMer and co-workers reported the following rate law for the decomposition reaction of sodium thiosulfate to sulfur in a 1948 paper:⁹⁵

$$\frac{d[S]}{dt} = k_{\text{obs}}[\text{Na}_2\text{S}_2\text{O}_3]^{1/2}[\text{HCl}]^{3/2} \quad (12)$$

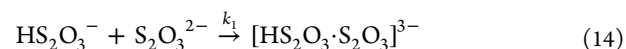
However, corrections to the fractional rate law for the decomposition of sodium thiosulfate in dilute solution were given in 1951 and 1954 papers by the LaMer group,^{96,97} so that the final reported rate law for the decomposition of sodium thiosulfate in dilute solution was corrected to that shown in eq 13:

$$\frac{d[S]}{dt} = k \left(\frac{[\text{H}^+]_0 [\text{S}_2\text{O}_3^{2-}]_0}{K_2 + [\text{H}^+]_0 [\text{S}_2\text{O}_3^{2-}]_0} \right)^2 \quad (13)$$

where K_2 is the equilibrium constant.

$$K_2 = \frac{([\text{H}^+]_0 - [\text{HS}_2\text{O}_3^-])([\text{S}_2\text{O}_3^{2-}]_0 - [\text{HS}_2\text{O}_3^-])}{[\text{HS}_2\text{O}_3^-]}$$

LaMer proposed a minimum mechanism as shown in eqs 14 and 15 as for the decomposition of thiosulfate, written as forming S_2 , and notably as an irreversible process:



From this mechanism, the rate law in eq 16 was derived by LaMer:⁹⁶

$$\frac{d[S]}{dt} = k_1[\text{HS}_2\text{O}_3^-][\text{S}_2\text{O}_3^{2-}](1 - e^{-k_2 t}) \quad (16)$$

An important point here is that LaMer obviously understood what a reaction mechanism is and its connection to chemical

kinetics, a noteworthy point given that he later offered only a physical chemistry model but neglected to provide the competing alternative hypothesis of a chemical mechanism for nucleation and growth. The failure to disprove adequately,^{5,6,80} the failure to provide a postulated, single chemical mechanism alongside his single physical chemical/mathematical model, is arguably the only but significant scientific error of LaMer and co-workers, even in light of our huge advantage of 70 years of hindsight.

The at the time state-of-the-art light scattering method of LaMer and co-workers produced valuable kinetics data for $(S)_n$ particle size as a function of time.^{1,88–94} Original plots of the size versus time data in LaMer's 1950 paper¹ are reproduced in Figure S2, while scanning and then digitizing those published plots yielded Figure 4. Two main problems with these data are

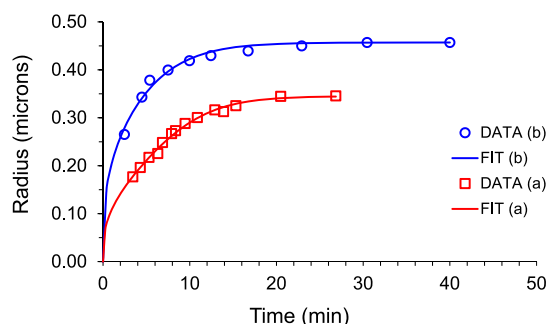


Figure 4. Radius vs time data obtained by digitizing the scanned plots in Figure S2 for the growth rates of sulfur particles, prepared by adding water to the solution of sulfur in (a) ethanol or (b) acetone at 25 °C.¹ The fit is to a two-step mechanism⁴ using eq 17 derived for that mechanism.⁹⁹ Adapted in part with permission from ref 1. Copyright 1950 American Chemical Society.

apparent. (i) The data do not provide the reactant or product concentration but instead particle size estimated by the light scattering method, and (ii) no information was obtained during the crucial first couple of minutes of the reaction where nucleation is more prevalent, most likely due to the detection limit of the light scattering (at the time, in 1950) to measure particles smaller than a rather large (by today's standards) 360 nm particle.¹ The authors¹ fit their data to their model using eq 3 (Figure S2).

Unfortunately, there is little attempt in the original 1950 paper to try to disprove the model. One's job as a scientist is not to try to "verify" one's model but instead to try to disprove especially that (your) model.⁶ One's job is to try to convert the model from being supported not only by necessary but also by sufficient experimental data, which means sufficient disproof of multiple alternative models and mechanisms, so that the model or mechanism left standing has an increasingly better chance of actually being the chemical truth. In fairness to those early workers, it merits mentioning that Platt's classic paper emphasizing the critical part of the scientific method involving

disproof of multiple alternative hypotheses⁶ did not appear until 1964,⁶ 14 years after LaMer's paper. Worth noting here is Platt's comment that "for exploring the unknown, there is no faster method".⁶ Chamberlin's 1897 paper extolling the importance of multiple alternative hypotheses⁵ was, however, available for more than half a century by the time of the 1950 paper.¹

The experimental data in Figures 7 and 8 of the original 1950 paper¹ appear to be fit well by eq 3, so that there was experimental evidence consistent with the LaMer model, an almost surely exciting and hugely pleasing result at the time given that virtually nothing was known about particle formation, much less how simply mixing a few reagents could lead to huge particles that appeared to be monodisperse by the physical methods available at the time! That said, we can now recognize that the data obtained by the light scattering technique available in 1950 are quite limited by today's standards in detecting nucleation, given that the smallest detectable particle is 0.36 μm —yes, micrometers—in diameter¹ [so that $2x = 0.36 \mu\text{m}$ in the model, where x is the radius (Figure 2) (*vide supra*)]. We now know that the nucleation was completely missed in those early studies. Indeed, nucleation from the available experimental perspective at the time was "instantaneous", spontaneous. We can speculate that what the authors were actually observing with the physical methods they had to work with, for example in the explosive growth of the optical density of "sulfur dissolved in ethanol-water mixtures as a function of the volume fraction of water", is what we could now label as the first observable clusters (FOC).¹⁴ In light of the fits in Figure 3 (and Figure 4), that "explosive growth" is probably due to continuous nucleation and autocatalytic growth.⁴ The explosive nature of autocatalytic growth likely confused any separation of and resultant understanding of the discrete stages of nucleation and growth—just as the ill-supported, words-only term of "autocatalytic nucleation" continues to confuse modern particle formation even today.⁹⁸

We wondered, in light of the results in Figure 4, if the hard-won, at the time state-of-the-art radius versus time data obtained by LaMer and co-workers might not also be fit by the two-step mechanism.⁴ Equation 17 is derived elsewhere⁹⁹ for the two-step mechanism⁴ [again, slow continuous nucleation, $A \rightarrow B$ (rate constant of k_1), and then autocatalytic surface growth, $A + B \rightarrow 2B$ (rate constant of k_2)], where A is nominally S and B nominally the growing $(S)_n$ in the present example.

$$D_t = D_f \left[1 - \frac{k_1 + k_2[A]_0}{k_2[A]_0 + k_1 e^{(k_1 + k_2[A]_0)t}} \right]^{1/3} \quad (17)$$

where D_t is the particle diameter at time t , D_f is the final diameter, and $[A]_0$ is the initial concentration of the precursor. Just as LaMer had to do in 1950, there are mathematically necessary assumptions used in deriving eq 17 that are detailed

Table 2. Average Phenomenological Rate Constants k_1 and k_2 , Obtained from the Curve Fit of Radius versus Time Data in Figure 4 to a Two-Step Mechanism⁴ Using eq 17,⁹⁹ for the Formation of Sulfur Sol Prepared by Adding Water to the Solution of Sulfur in Ethanol or Acetone at 25 °C¹

solvent	k_1 (min^{-1})	k_2 ($\text{M}^{-1} \text{min}^{-1}$)	R^2	χ^2
ethanol	$(2.8 \pm 0.2) \times 10^{-2}$	$(1.23 \pm 0.86) \times 10^2$	0.99701	2.33×10^{-5}
acetone	$(8.6 \pm 1.2) \times 10^{-2}$	$(0.81 \pm 0.25) \times 10^2$	0.99562	7.97×10^{-5}

in footnote 34 of the original publication in which eq 17 was first derived,⁹⁹ the most significant two of which are the assumptions that precisely one-size, truly monodisperse particles are formed (which we have already documented is never precisely true⁴⁴) and that nucleation and growth are separated completely in time by the end of the induction period (which is also never precisely true). Despite the assumptions—assumptions made to make the math workable, just as LaMer made the assumptions needed at the time to make the math doable—the fit of the 1950s kinetics data (Figure S2)¹ to the two-step mechanism (Figure 4) provides two well-defined, physically meaningful, albeit phenomenological and average⁴ rate constants (Table 2), k_1 and k_2 . Note the ability to describe the physical processes occurring as defined by the balanced, in this case pseudoelementary reactions: slow, continuous nucleation and autocatalytic surface growth leading to the sulfur sol product. Conversion of the k_2 , second-order ($\text{M}^{-1} \text{min}^{-1}$ units) rate constant in Table 2 once again shows that the observed growth rate constant is far below diffusion control, this time $\sim 10^9$ -fold slower than diffusion-controlled, disproving the LaMer model for this $(\text{S})_n$ sol formation.

Despite the initial success of the minimalistic treatment and fitting of the $(\text{S})_n$ formation kinetics data to the two $\text{A} \rightarrow \text{B}$ and $\text{A} + \text{B} \rightarrow 2\text{B}$ pseudoelementary steps, as is typical much remains to be better defined en route to the true, underlying and more complex elementary mechanism. The first issue is that higher, beyond first-order nucleation is known to be easily kinetically hidden in the $\text{A} \rightarrow \text{B}$ unimolecular formation of the two-step mechanism (because $[\text{A}]$ is constant often to $\geq 99\%$ during nucleation).¹⁴ However, testing the dependence of the kinetics on the concentration of $[\text{A}]$ (and any ligand dependence of the kinetics^{64,65}) can and has revealed the true nucleation mechanism, notably in the case of $\text{Ir}(\text{O})_n$ nanoparticle formation.^{14,64,65} Additionally, the steps that sum to and behave like autocatalytic growth remain to be identified, although we can now speculate with some confidence that those steps are likely really just “monomer” addition steps⁷ such as nominally $(\text{S})_n + \text{S} \rightarrow (\text{S})_{n+1}$.

The important point here is that anyone using the deliberately minimalistic two-step, three-step, and two four-step mechanisms provided elsewhere^{14,24–28} is urged to study carefully the repeatedly stated limitations^{28,61,65,77,84} of those mechanistic models, limitations that ultimately derive from the far too simple nature of the phenomenological, kinetic mechanisms that produce average k_1 and k_2 values (and, for the four-step mechanisms, two types of agglomeration, k_3 and k_4 values) while postulating a species “B” that represents the average growing particle (and in the four-step mechanisms, an average larger particle “C”).^{22–28} Other possible models (e.g., transition zone theory of crystallizations) for treating at least temperature-dependent solid growth dynamic data merit mention here, as well.¹⁰⁰

One more subtle point should be made here. Despite the good fit to the two-step mechanism and its associated equations, on the basis of our current understanding one might expect considerable agglomeration to be taking place in the last, observed $\sim 60\%$ of the $(\text{S})_n$ formation reaction. Hence, the precedented bimolecular nucleation of agglomeration, $\text{B} + \text{B} \rightarrow \text{C}$, and then autocatalytic agglomeration, $\text{B} + \text{C} \rightarrow 1.5 \text{C}$ [where B is the initial $(\text{S})_n$ and C is the larger $(\text{S})_m$], is one modern hypothesis for what was actually likely being observed^{24–27} in the $(\text{S})_n$ size versus time data. Details are

provided elsewhere as to why the A and B vs B and C formulations of this problem will provide identical fits to the kinetics data,^{24–27} the key being one has to know if you are starting with precursor “A” or preformed clusters “B” to properly formulate the kinetic and mechanistic problem.⁷⁷

Returning to the sulfur sol formation literature, specifically the 28 papers listed in Table S1, we found a careful reading of that literature reveals that the more intimate mechanism of sulfur sol formation remains poorly understood even today; that is, the fit to the two-step mechanism is nothing more than a start, and certainly not a panacea, to the true, underlying, stepwise, mechanism with likely thousands of chemical elementary steps. Lacking even after nearly 70 years are good, reliable kinetics data for the formation of sulfur sols, in which the concentration of at least one of the reactants or products (and, ideally, both) is precisely and accurately monitored versus time over the full course of the reaction, including the very early times where nucleation is the dominant process. Note how this statement reflects the $(\text{CdSe})_n$ system cited earlier where the authors insightfully noted “that our understanding of nucleation and growth ... is still very limited mainly due to the lack of extensive, reliable, and quantitative *in situ* experimental data”.⁵⁶ Hence, the underlying point here is a broader truism: More precise, accurate, better time-resolved experimental measurements of especially nucleation, down to the very earliest events in nucleation, are what are still needed even today to advance our understanding of especially nucleation, but also subsequent events such as growth and agglomeration, in particle formation science across nature. A key point here is that if you do not understand how particle formation begins—that is, the true nucleation mechanism—then how can one possibly get correct the resultant stages of particle formation such as growth and agglomeration? Recent mechanism-enabled population balance modeling drives home this point⁷ by revealing erroneous conclusions reached in the literature when starting with an assumed nucleation mechanism or using classical nucleation theory that cannot be applied to strong-bonding systems.¹⁴

Finally, others followed LaMer’s pioneering work by obtaining similar sulfur sol formation data (Figure S2).^{1,101–105} However, only one other report has appeared that attempts to fit experimental radius versus time data to the LaMer model using eq 3, an attempted fitting that failed. The main reason the data would not fit eq 3 is shown in Figure 2 of that 1977 paper;¹⁰⁴ an induction period of $7.8 \pm 0.6 \text{ h}$ is seen (as measured by extrapolating the growth curve to a particle size of zero). The underlying problem is the lack of data below $0.12 \mu\text{m}$, resulting from the insensitivity of the absorbance measurements possible at the time.¹⁰⁴ Levit and Rowel reported a similar observation of a long initial (induction) period in their $(\text{S})_n$ size versus time data.¹⁰³ They claim—almost surely incorrectly—that nucleation starts after this initial lag period and, therefore, simply delete the—critical!—induction time so that the size versus time curve can then be (erroneously) extrapolated to zero.¹⁰³ We now know of course that what this is doing is throwing away the crucial, very likely slow, and continuous nucleation⁴ period, now accounted for by the fit to the two-step mechanism shown in Figure 4. In other words, the independently observed induction period¹⁰² is additional evidence consistent with and supportive of the two-step mechanism used in the curve fitting in Figures 3 and 4 and, of course, the inapplicability of any model postulating “instantaneous/burst” nucleation.

3.4. The Interesting Effect of Microfiltration and the Removal of Dust on the Size Distribution of Sulfur Sols.

In a seminal 1963 paper,⁴⁶ Matijević and co-workers report the results of a study on the size distribution of sulfur sols obtained following a modified LaMer¹ procedure whereby careful attention to the purity of the starting reagents, the water solvent, efficient mixing, temperature control, and the removal of dust by use of a 0.22 μm filter are necessary to achieve a reproducible synthesis of $(\text{S})_n$ sols. Significantly, that careful experimental work narrowed the final size distribution (dispersity) 2-fold for 95% of the observed particles from a value of $0.51 \pm 0.08 \mu\text{m}$ (i.e., $\pm 16\%$) seen in an earlier,¹⁰⁶ ostensibly closely analogous synthesis to $0.48 \pm 0.04 \mu\text{m}$ (i.e., $\pm 8\%$).⁴⁶ More recently, work has appeared showing that removing the dust by filtration also significantly affects the nucleation kinetics of $\text{Ir}(0)_n$ nanoparticle formation.⁴⁴ There the decrease in the nucleation rate constant, k_1 , with a largely unchanged (by filtration) autocatalytic growth rate constant, k_2 , mechanistically readily accounts for the observed narrowing of the particle-size distribution.⁴⁴ The LaMer model is of course unable to explain the size distribution narrowing effect of filtration, nucleation being assumed to be homogeneous and “instantaneous” and, hence, of unchangeable rate. All that one could say with the LaMer model is that dust caused a different, must be smaller nuclei x to show up to start the growth process. The important point here is that a majority of particle formation studies even today, save the exceptions summarized elsewhere⁴⁴ that assume “homogeneous nucleation” suffer from this same limitation: a failure to account for the effects of dust in their particle formation kinetics/dynamics, and resultant size distributions.

4. CONCLUSIONS

The following conclusions can be reached on the basis of the information in this first review of the origins of the LaMer model and the equation that appeared ~ 70 years ago and which has been cited at least 1953 times to date. The conclusions that follow have the advantage of 70 years of additional data and the hindsight that data allow, information not available to LaMer and his co-workers when they published their creative 1950 paper.¹

(1) LaMer and his co-workers labored in a pioneering and creative way, both theoretically and experimentally (e.g., the latter via their state-of-the-art light scattering efforts), to try to begin to get any idea of how what looked at the time to be truly one-sized particles might possibly be formed. It is important to recognize that they labored in much different times, where physical methods were limited, modern computation power did not exist, and classical nucleation theory was a relatively new, exciting, and probably seductive theory that likely seemed compelling at the time. How to construct reliable mechanisms, and the importance of attempting disproof of one's models or mechanisms, was itself a developing topic,^{5,6} so that even a preferred scientific method of disproof of multiple alternative hypotheses^{5,6} was arguably not as keenly apparent and appreciated at the time as it perhaps should have been. This latter point is as true today as it was 70 years ago, in the writers' collective opinion, as judged by the applicability of this point—the lack of a proper, disproof-based scientific method—being apparent in far too high a fraction in selected areas of the current chemical literature. A 2019 editorial entitled “The Burden of Disproof”⁸⁰ provides independent evidence for the above assertion. Indeed,

many workers seem not to appreciate the fundamental difference between a single physical chemical model that has been postulated, but not received attempted disproof, and an extensively disproof-based physical chemical model or an extensively disproof-based chemical reaction mechanism (Scheme 1) (*vide supra*).

(2) The LaMer model is a growth model, one that says nothing about nucleation past making the assumption of “instantaneous/burst” nucleation as was necessary at the time for developing the growth model. Having all of the nuclei there instantaneously in uniform size x (Figure 2) (*vide supra*) then allowed a mathematical model for growth in this first, creative attempt to try to understand how “monodisperse” particles could possibly be formed.

(3) Approximately 90% of the 1953 citations of the 1950 model¹ appear to be citing it for its instantaneous/burst nucleation feature, that is citing the model for its assumption of “instantaneous nucleation”, often as a way to rationalize the formation of narrow, approaching monodisperse particle-size distributions.⁷

(4) Importantly, a way to get narrow particle-size distributions despite continuous nucleation has recently been discovered,⁷ thereby providing an alternative to the need to postulate that nucleation is somehow “instantaneous”. This does not in turn mean that the concept of what we would rephrase as “very fast, nearly instantaneous/burst” nucleation as compared to the rate of growth needs to be abandoned. It only, but significantly, means that one needs experimental measurements of one's nucleation kinetics rather than just assuming/claiming that they are either “burst” or “continuous”.

(5) The LaMer growth equation (eq 3) has been used only once, in 70 years and out of the 1953 papers as of March 2019 that cite the LaMer model, to actually fit particle formation kinetics data, namely by LaMer himself in his 1950 paper.¹ Additionally, 2008⁷⁰ and 2009⁷¹ attempts to improve the LaMer model fail to result in quantitative fits to those specific kinetics data.

(6) Hence, a critical disconnect exists in that LaMer's actual equations (eqs 3 and 11) have never been independently tested versus experimental kinetics data in the intervening nearly 70 years. This previously unappreciated insight goes a long way toward explaining how LaMer's model morphed into its present, highly cited, words-only model of “instantaneous nucleation” followed by “diffusion-controlled growth”, often along with a citation or reproduction of LaMer's famous qualitative figure, Figure 1a (*vide supra*). The model then and thereby, unfortunately, proved to be effectively “unfalsifiable”⁶ in at least the intervening 70 years due to this disconnect. An apparent qualitative agreement with Figure 1a (*vide supra*) then became the standard of “evidence” in an area that had no other model or mechanism to cite until 1997,¹ and no other model of mechanism to cite that could produce narrow distributions until⁷ 2019. With 70 years of hindsight, one has to believe that LaMer would have greatly preferred that we all carefully read and understand his paper and, then, not cite it for its assumption of “instantaneous” nucleation but, rather, cite, use, and build off of the early, creative, pioneering model of growth that it actually is.

(7) The LaMer model is not a chemical reaction mechanism, as it does not have the balanced chemical or even pseudoelementary reactions⁴ and, then, the differential equations defined by those reactions that can thereby be used

to experimentally test the model quantitatively against experimental kinetics data.

(8) The classic sulfur sol formation turbidity versus time data, and radius versus time data [Figures 3 and 4, respectively (*vide supra*)], were fit for the first time by a minimalistic two-step mechanistic model of slow continuous nucleation ($A \rightarrow B$, with a rate constant of k_1) and then autocatalytic surface growth ($A + B \rightarrow 2B$, with a rate constant of k_2).⁴ That fitting provides evidence for continuous nucleation, as well as for chemical reaction-controlled growth that is 10^9 – 10^{10} times slower than diffusion control. The two-step fits disprove any model for $(S)_n$ sol formation containing either burst nucleation or diffusion-controlled growth.

(9) The limitations of using such minimalistic, highly oversimplified kinetics schemes such as the two-step mechanistic model, which yields only average results for k_1 and k_2 and only an average particle size and that describes only average particles “B”, were emphasized and urged as required reading^{28,61,65,77,84}—please!—for anyone wishing to use the deliberately minimalistic particle formation two-step, three-step, and two four-step mechanistic models.

(10) Dust has been known since the late 1800s to be an intimate part of nucleation. It has been found to be a critical part of sulfur sol formation,⁴⁵ $Ir(0)_n$ nanoparticle formation⁴⁴ that follows the two-step mechanism,^{4,14,61,64} and an increasing number of other systems.^{30,40–48} Nucleation has long been known to typically be fastest when heterogeneous, not homogeneous,^{30,39–48} as even LaMer discusses in his 1952 review.⁸ Hence, any modern mechanism for particle formation not done in, for example, a Class 9 Clean Room needs to have a provision for dealing with omnipresent inorganic and organic dust.⁴⁴

(11) The only, but significant, error back in the 1950s in our opinion is the failure of anyone in the area to supply more than one type of model besides the 1950s physical chemical model¹⁰⁷—that is a failure of the field at that time—save, notably, Turkevich²—to use a sufficiently disproof-based, multiple-alternative hypothesis scientific method.^{5,6,80} In their defense, classical physical–organic chemistry and mechanism was just being developed. Chamberlin and Platt’s preferred scientific method of the disproof of multiple alternative hypotheses was still under-recognized,^{5,6} and almost surely not yet recognized that “for exploring the unknown, there is no faster method”.⁶ Indeed, pChem-based theoretical models were being emphasized at the time and likely expected to have broad generality. With 70 years of hindsight, we now know one must not “inappropriately cite”⁹ any pChem or other model as, “The classic theories work poorly or not at all when applied beyond the validity of their assumptions”.⁹ With 70 years of hindsight, the experimental- and disproof-based two-step chemical mechanism⁴ model would have been a good, second choice at the time of a competing, balanced equation-containing mechanistic model. The two-step mechanism would then have been thoroughly tested, maybe abandoned, or at least upgraded by a three-step model that can describe particle-size distributions,⁷ but all probably in the 1970s, not nearly 50 years later in 2019.⁷

In closing, we come back to Turkevich’s comment in 1951 that the LaMer model, even in 1951, was a “theory of great tradition”,² a tradition that we now see has grown to 1953 citations. Personally, we prefer our 1997 comment⁴ that “perhaps much fairer to LaMer’s pioneering work would be the term “inappropriately cited”, a phenomenon which really only

points to the dearth of new, broadly applicable and kinetically verified alternative mechanisms (for particle formation) in the intervening nearly 50 years”.⁴ The model of LaMer and co-workers was and still is a creative contribution on the still challenging problem of particle formation models and their underlying chemical reaction mechanisms. It is upon us to decide if the LaMer model or any other model is appropriate to our systems, or is simply being “inappropriately cited”,⁹ “beyond the validity of (the model’s) assumptions”.⁹ Indeed, the LaMer model has been placed through 1953 citations into a class by itself, being cited primarily for its (physically most invalid) assumption! That nonscientific practice should come to a complete stop, immediately. Instead, experimental evidence for the nucleation kinetics in the system at hand should be obtained and analyzed quantitatively by the differential equation of one’s choice, and the results should be provided with an emphasis on disproof-based science.

Finally, this review addresses only the basic LaMer model, the 28 papers specifically citing the model as part of sulfur sol formation, and any related literature deemed relevant. After viewing the 1953 available papers as of March 2019, we found 164 others of the 1953 (so $164 + 28 = 192$ papers, $\sim 10\%$ of the 1953) that, in our opinion and selection, do more than just cite the 1950 model, by for example providing evidence (or at least some more detailed discussion) for or against the model. Hence, remaining to be presented is an analysis of those 164 additional papers that can be divided into the following five categories, specifically studies of the formation of (i) transition metal particles (69 papers), (ii) metal oxide particles (39 papers), (iii) silver halide (13 papers), and (iv) semiconductor nanoparticles (26 papers) and (v) other papers that present alternative models or mechanisms relevant to the LaMer model not discussed herein (17 papers). It is just that additional task that constitutes a second, further review and analysis of the literature citing the LaMer growth model postulating instantaneous nucleation and then diffusion-controlled growth in a pioneering first attempt to begin to try to understand the still striking observation of the formation of near monodisperse particles of nearly micrometer size formed from self-assembly syntheses that often likely involve thousands of discrete chemical steps to $>10^6$ discrete chemical steps.⁷ No wonder LaMer, his co-workers, and the community at the time found the mechanistic problem of the formation of near-mono-disperse particles of extreme interest, just as our community still does today, 70 years later!

■ ASSOCIATED CONTENT

⑤ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: [10.1021/acs.chemmater.9b01273](https://doi.org/10.1021/acs.chemmater.9b01273).

Plots of the extent of the reaction versus time for the formation of sulfur sol from ref 10, radius versus time of sulfur sols from ref 1, and a summary of the literature on sulfur sols citing the LaMer model (Table S1) (PDF)

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Notes

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ACKNOWLEDGMENTS

The extensive comments of four referees were critical in constructing the final version of this review. The authors thank those referees for the generous donation of their time and their frank, thoughtful, and overall invaluable constructive criticism. This work was supported at Colorado State University by the U.S. Department of Energy (DOE), Office of Science, Office of Basic Energy Sciences, Division of Chemical Sciences, Geosciences and Biosciences, via DOE Grant SE-FG402-02ER15453.

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- (107) Rereading LaMer's 19501 and 1948⁹⁵ papers, with the best and most efficient scientific method of multiple-alternative hypotheses and disproof-based experimentation in mind,^{5,6} reveals that LaMer and co-workers were relying on CNT and their growth theory rather than trying to disprove their model by conceptualizing, and then testing and trying to disprove, all possible reasonable multiple-alternative hypotheses—either models or mechanisms—for particle formation. A few examples of the attempt at proof of the supersaturation hypothesis in his 1950 and 1948 papers are as follows. (i) On page 572, even before the experimental section or any experimental data, the "mechanism" is given in words only (i.e., and not the balanced chemical reactions underlying rigorous mechanisms) as three "steps" or really phases: "I. The homogeneous Reaction" (sulfur formation?), "II. The Condensation Stage" (i.e., burst nucleation from a supersaturated solution?), and "III. The Heterogeneous Stage" (diffusion-controlled growth?). Next, (ii) on page 577 we jump from the fractional kinetic data (page 575) to the mechanism "II. The Condensation Stage", without disproof of any

other mechanisms, or an explanation of the observed kinetics (at the time fractional kinetics that were later corrected^{96,97}). Instead, the first type of evidence offered under the heading “II. The condensation Stage” is “Theory”. This disconnect between the experimental evidence and proposed rate law, in the name of a superior theory, is a scientific method error that ultimately led LaMer not to propose a chemical mechanism with balanced equations and an associated differential equation that would account for his own experimentally observed kinetics. Proceeding to the summary section of the paper, LaMer (iii) again repeats his proposed stages of the reaction (“I. The homogeneous Reaction”, “II. The Condensation Stage”, and “III. The Heterogeneous Stage”) that can be recognized as really just his starting, rigorously untested, hypothesis. In the end, the failure to try to disprove their model/theory is where LaMer and co-workers made their one, but major, mistake in the opinion of the authors of this review. Rereading the 1950 paper as a check on this opinion reveals that this “theory” paper states what are really are the suppositions/hypotheses of the research as if they are facts and then produces deductive statements and conclusions from those starting points.¹ Disproof-based science requires, instead, inductive logic and associated strong inference en route to what could not be disproved^{5,6} as the proposed model or mechanism.