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TOPICAL REVIEW

Molecular modeling of protein materials: case study of elastin

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Abstract

Molecular modeling of protein materials is a quickly growing area of research that has produced numerous contributions in fields ranging from structural engineering to medicine and biology. We review here the history and methods commonly employed in molecular modeling of protein materials, emphasizing the advantages for using modeling as a complement to experimental work. We then consider a case study of the protein elastin, a critically important 'mechanical protein' to exemplify the approach in an area where molecular modeling has made a significant impact. We outline the progression of computational modeling studies that have considerably enhanced our understanding of this important protein which endows elasticity and recoil to the tissues it is found in, including the skin, lungs, arteries and the heart. A vast collection of literature has been directed at studying the structure and function of this protein for over half a century, the first molecular dynamics study of elastin being reported in the 1980s. We review the pivotal computational works that have considerably enhanced our fundamental understanding of elastin's atomistic structure and its extraordinary qualities—focusing on two in particular: elastin's superb elasticity and the inverse temperature transition—the remarkable ability of elastin to take on a more structured conformation at higher temperatures, suggesting its effectiveness as a biomolecular switch. Our hope is to showcase these methods as both complementary and enriching to experimental approaches that have thus far dominated the study of most protein-based materials.

(Some figures may appear in colour only in the online journal)

1. Molecular modeling: an overview

The application of computational modeling to the study of protein molecules and protein-based materials has experienced an exponential boom in the last few decades, in parallel with the growth of ultrafast computers capable of capturing appropriate time and length scales, and in conjunction with the development of simulation techniques and theoretical specifications to describe, up to a suitable degree of accuracy, the physics within such complex materials. Even so, these factors persist as key limitations in the application of modeling techniques. Our goal here is to provide a brief history and general overview of molecular modeling methods, outline the advantages of applying such methods to protein materials and show, through the example of the elastin protein, how molecular modeling has enhanced the understanding of key physical properties of this important biomaterial.

Molecular modeling requires two main components: a system description and a simulation scheme that performs the calculation. The system description includes the specifications of the geometry and the intra- and intermolecular interactions, which are most commonly described by quantum mechanics or molecular mechanics. The second component involves the expensive calculation, using a scheme to minimize the potential or free energy, or methods such as molecular dynamics (MD) or Monte Carlo (MC). MD is a deterministic method that allows for prediction of atomic positions based on intra- and intermolecular interactions for a collection of atoms yielding a trajectory which can be treated as an ensemble to derive time-averaged properties. Successive configurations are calculated by numerically integrating Newton's second law of motion. By contrast, MC methods are not deterministic as the set of conformations defining the ensemble is generated randomly, based on the Boltzmann probability [1–3]. Although both MC and MD methods are widely used to perform molecular scale system calculations, there are several fundamental differences between the methods, which render them appropriate for different applications. Most significantly, MC methods provide no insights into the temporal relationships between configurations, unlike MD methods that capture the dynamics of non-equilibrium systems.

The MC method was developed first, at the end of the Second World War, to study diffusion of neutrons in fissionable materials [4, 5] and was first implemented on the MANIAC computer at Los Alamos National Laboratory [2]. Five years later the first MD simulations were performed by modeling a hard-sphere potential where colliding spheres interacted only upon perfectly elastic collisions [6]. The development of the Lennard-Jones (LJ) pair potential followed several years later [2, 7]. The LJ potential exhibits a continuous force variation between pairs of atoms, and is one of the simplest potentials used to describe molecular interactions in material models. Since, multi-body potentials have been advanced to more accurately describe the material energy landscapes. To capture differences between atoms in the bulk and on the surface of metals, for instance, the embedded atom method (EAM) and variations thereof were introduced [8, 9], to account for the effects of local electron energy density.

To accurately describe the physics of polymers, organic substances and proteins, more complicated multi-body potentials—or *force fields*—have been developed in the last three decades [3, 10]. These empirical potentials explicitly describe a full set of chemical bonds, including ionic, covalent and van der Waals (VdW) interactions, through a combination of energy terms, capturing the complexity at the atomic length scale, where the atoms are modeled as finite-mass particles. These potential descriptions are fit to reproduce the energy landscape for small systems derived from quantum-mechanics-based methods, such as first principle density functional theory [11]. Typically, contributions from terms including bond stretching, angle bending and torsion are used to define intermolecular interactions, while electrostatic

interactions and VdW terms account for intramolecular forces. The mathematical formulation for the empirical energy function, such as found in the CHARMM force field model [12], for example, includes terms capturing both intra- and intermolecular interactions:

$$U_{\text{system}} = U_{\text{bond}} + U_{\text{angle}} + U_{\text{torsion}} + U_{\text{coulomb}} + U_{\text{Van der Waals}} + \cdots. \quad (1)$$

Other force fields with similar interatomic force descriptions include the AMBER force field [13] and the DREIDING model [14].

In these potential models, the total energy of the system is described by the Hamiltonian, which includes the empirical potential formulation together with a kinetic energy term. The full system is described by a set of second-order nonlinear partial differential equations, corresponding to an N-body system. In classical Newtonian dynamics, the equations of motion are integrated numerically, using the Verlet integration scheme for example [15], to solve for the positions and velocities of the atoms. Traditional MD is performed in the microcanonical (*NVE*) ensemble. However, it is common to shift to other thermodynamic ensembles to better represent experimental controls. Because in experiment it is more common for the temperature of the system to be controlled instead of energy, various methods have been developed to modify equations of motion such that dynamics are simulated in a canonical (*NVT*) ensemble. A method proposed by Nose [16] and extended by Hoover [17], for instance, reduces the external heat reservoir into another internal degree of freedom, effectively simulating a temperature bath via an additional term in the Hamiltonian. Langevin dynamics is another approach to implement a canonical ensemble, where an additional solvent friction term and a random force term accounting for perturbations due to high velocity collisions are added to the equations of motions. In addition to approximating the canonical ensemble, Langevin dynamics can capture solvent viscosity effects. Other methods obtain a canonical ensemble by rescaling atomic velocities so that the temperature approaches a desired value [18, 19].

Once all system and simulation parameters are set, computational capacity is limited by the integration time-step, which must be small enough to accurately model vibrations of atomic bonds, on the order of one femtosecond. Algorithms such as SHAKE [20] can increase the time-step two- or three-fold by fixing the vibrations of the fastest atoms (the hydrogen atoms) into place. Beyond the time-step, system size, naturally, is directly related to computational efficiency. Proteins and other biological materials must generally be simulated in solution to capture solvent effects, and water molecules may compose over 90% of the total system size. Multiple models exist for describing water effects. Models where water molecules are explicitly represented range from simple rigid models where the potential is a combination of Coulombic and LJ terms to more computationally expensive models that can capture molecular flexibility and polarization effects [21]. With larger system sizes, modeling water explicitly can be very computationally expensive. Implicit solvent models rely on representing solvent as a continuous medium, a description that can provide insights into various solvation phenomena [22]. However, implicit solvation models have limited ability to capture certain entropic effects resulting from solute–solvent interactions, for example. Therefore, in choosing a solvation model, the scope and capacity of the model to capture specific effects must be carefully weighed.

In addition to model optimization, the development of high-performance computing, with faster computers and more efficient parallelization schemes has exponentially increased time scales accessible to MD simulation; however, because time cannot be easily parallelized, reaching long time scales still poses significant challenges [3]. Dynamics are governed by the free energy of the system, which can be trapped in local free energy minima that are difficult to overcome. Various accelerated sampling methods have been introduced to address this. Certain methods rely on thermal activation [23, 24] while others are based on the idea that

the free energy surface can be flattened to improve dynamics by including a bias potential [25, 26].

Alternatively, reduction in computational complexity can be carried out by coarse-graining (CG), or reduced representation methods. Implicit representation methods for water, discussed above, can be thought of as a way of CG the system. Additional methods exist to reduce the number of degrees of freedom, including both structural and interaction information, of both solute and solvent. These methods allow for simulations across biologically relevant time and length scales by lowering model resolution based on parameters rigorously derived from higher resolution models. CG is a very broad, quickly growing focus in the field of computational biomaterial modeling (an extensive overview can be found in [27]). Two successful methods are the 'bottom-up' multiscale coarse-graining (MS-CG) methodology and the 'top-down' Martini force field method [28–30]. In the MS-CG methodology, an explicit force-matching procedure is used to derive a coarse interaction potential directly from full-atomistic MD simulations where the coarse-grained sites are associated with the centers-of-mass of atomic groups. It was first demonstrated for a lipid bilayer system [30] and later extended to predicting protein folding dynamics [31]. In the Martini method [29, 32], an alternative, reverse approach is taken, such that the force field is parametrized from experimental thermodynamic data. A four-to-one mapping is used, on average, such that four heavy atoms are reduced to a single interaction site. Beyond CG methodologies listed above, lower resolution models which may bypass amino-acid resolution include elastic network models and other normal-mode based approaches [33]. Such approaches have been instrumental in identifying protein functions in ion gating and self-assembly (further references can be found in [33]).

Although first-principles methods are most accurate, they are limited to rather short length and time scales. Empirical potentials reduce the computational time and can handle much bigger system sizes. Figure 1 shows the most widely used modeling techniques for studying materials, with corresponding length and time scales. Classical continuum methods are included as they are commonly used for studying materials—although they lack appropriate discretization to capture atomic level phenomena. Coarse-grained models are used to bridge atomistic and continuum scales. Complementary experimental methods are included in figure 1, outlining both imaging and biomechanical testing techniques which probe varying material length scales, and can be used to validate simulation predictions.

Molecular modeling and simulation has gained wide popularity for its ability to link microscopic details to macroscopic experimentally observable properties and structural and mechanical parameters. The unique ability to capture events at very low length scales has elucidated the importance of hierarchical structure in biological materials, and has opened a new passageway for biomimetics and material design. In the following sections we provide a case study of the elastin protein to illustrate the power and benefits of using molecular modeling techniques for investigating biological systems.

2. Elastin: an introduction

Proteins are an intriguing class of biopolymers, responsible for a range of biological functions, including locomotion of cells, enzymatic biochemical reactions, extracellular matrix structure and material transport, among many others [34]. Proteins are fundamental building blocks of living things, dictating most processes within cells. These are macromolecules, composed of one or more polypeptide chains, which are in turn made of a series of amino acids (20 standard amino acids in total), bonded together by strong, covalent peptide bonds. The chemistry of the individual amino acids, which serve as the universal building blocks of proteins, dictates how the polypeptide chains will fold into secondary structures, and combine to form functional

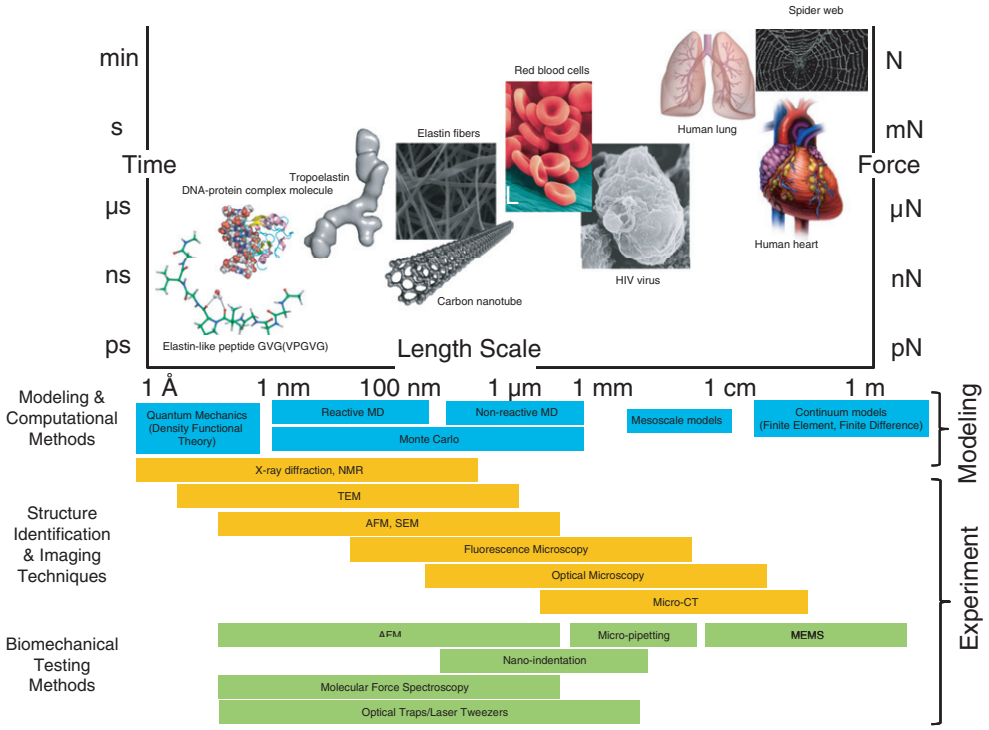

Figure 1. Material examples at different length scales. Time scales represent simulation times feasible for given material size, while force scales correspond to relevant forces applied in experiment and simulation to study biomechanics of materials at given length scales. Computational methods span scales from quantum mechanics accuracy to continuum methods. Experimental methods are divided into imaging and biomechanics methods. Imaging techniques include x-ray diffraction, nuclear magnetic resonance (NMR), transmission electron microscopy (TEM), atomic force microscopy (AFM), scanning electron microscopy (SEM), fluorescence microscopy, optical microscopy and micro-tomography (micro-CT). Biomechnical testing methods include AFM, molecular force spectroscopy, optical traps, laser tweezers, nano-indentation, micro-pipetting and microelectromechanical systems (MEMS) [37, 62, 73–76]. see footnote 3 for URLs.

protein molecules. The amino acids can be hydrophilic or hydrophobic (i.e. do or do not like to be exposed to water molecules), ranging in size and polarity. The hydrophilicity and hydrophobicity of amino acids is a key factor in defining the function of many proteins, such as elastin.

Elastin is a fascinating extracellular matrix protein that exhibits a highly conserved structure in mammals and is found in a very wide range of tissues in the human body [35, 36]. It confers reversible deformability, recoil and resilience to a variety of tissues, including the skin, arteries, heart and the lungs [36, 37]. The majority of elastin used by the body is produced in the fetal stages and early years of life, after which elastin production drops swiftly [38]. Consequently, any damage or injury incurred to elastic tissue is quite difficult to replace. Moreover, various diseases, including emphysema, cutis laxa and supravalvular aortic stenosis are associated with mutations within or improper function of elastic fibers [39]. As a result,

[3] www.topnews.in/health/malaria-parasite-caught-invading-red-blood-cells-210362, www.dana.org/news/publications/detail.aspx?id=4276, www.nih.gov/researchmatters/october2008/10272008lungs.htm, faculty.irsc.edu/faculty/sschwartz/AP%20II%20Ch18_JPS.htm, news.bbc.co.uk/2/hi/8496559.stm.

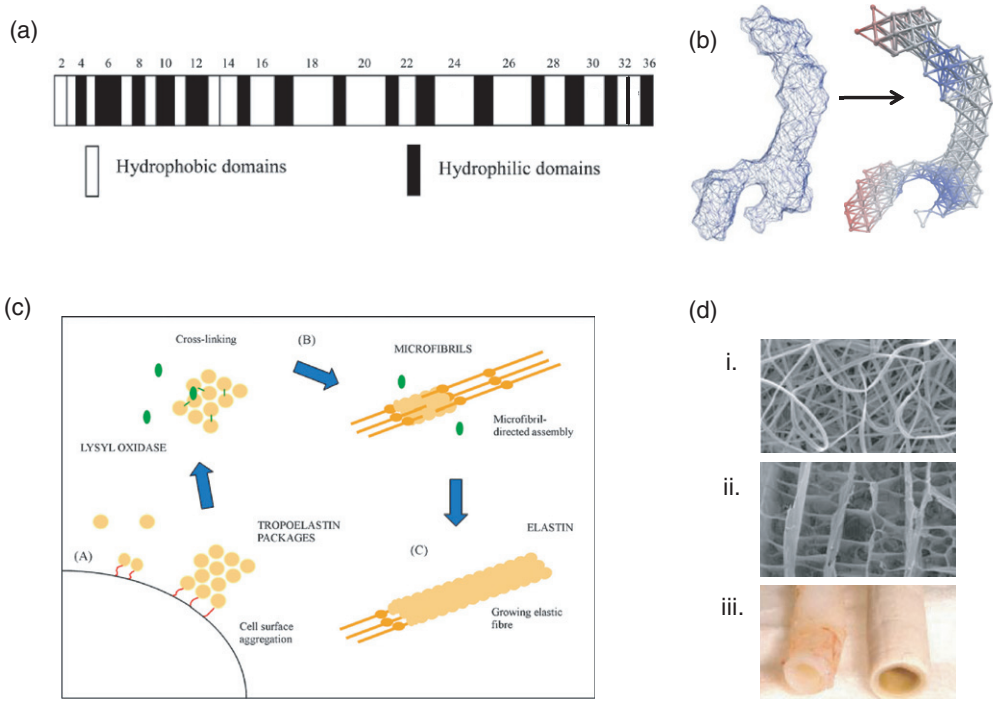

Figure 2. (*a*) Structure of human tropoelastin with alternating hydrophobic and hydrophilic domains. With permission from [77]. (*b*) Tropoelastin structure derived from small-angle x-ray scattering and small-angle neutron scattering (left). With permission from [75]. Elastic network model of tropoelastin, colored by least to most (blue to red) mobile regions for the largest amplitude, lowest frequency mode of motion (right). [For color scheme see online edition.] (*c*) Cross-linking and assembly mechanism of elastic fibers from tropoelastin globules. With permission from [78]. (*d*) (i) Synthetic elastin electrospun fibers, (ii) synthetic elastin hydrogel and (iii) electrospun conduit (left) next to human artery (right). With permission from [79].

elastin-based tissue replacements are in high demand as elastin's low thrombogenicity, capacity for favorable cell interactions, and blood compatibility make it an ideal candidate for dermal and vascular substitutes for tissue regeneration [40]. Beyond this, applications of elastin-based biomaterials are numerous: elastin can be used to create tunable electrospun elastin fiber scaffolds for large-scale tissue repair; elastin hydrogels are ideal for creating biodegradable matrices for drug delivery; elastin-based synthetic fibers can be used as prototypes for tissue engineering and artificial arteries [37].

The structure of the monomeric precursor to elastin, tropoelastin, a large, highly flexible molecule, is difficult to resolve with techniques such as nuclear magnetic resonance (NMR) and crystallography. At the same time native elastin is a very durable constitutive material, an insoluble and extensively cross-linked protein [36] that is difficult to isolate. As a result, elastin research has been restricted to elastin derivatives and recombinant elastin-like peptides. Tropoelastin, elastin's soluble precursor (figures 2(*a*) and (*b*)), is composed of alternating hydrophilic domains rich in lysine and alanine residues and hydrophobic domains, rich in valine, proline and glycine residues, often occurring in repeats of VPGVG. Native tropoelastin is secreted from smooth muscle cells and fibroblasts, packs into globules and is subsequently cross-linked and assembled into elastin fibers (figure 2(*c*)).

In addition to physiological compatibility, elastin-like peptides exhibit exceptional material properties that can be exploited to create smarter biomedical applications. In

particular, elastin-like peptides can be molded to create a diverse array of structures, including hydrogels, fibers and scaffolds (figure 2(*d*)). Most significant for such biomedical applications may be elastin's ability to extend beyond several times its resting length and reversibly return to its original state, at a capacity to undergo a human lifetime of extension and compression cycles, with minimal degradation. A molecular level understanding of this superb functionality holds great promise for tissue engineering applications and development of new, nature-inspired biomaterials even surpassing material properties of elastin.

The entropic origins behind the elasticity of elastin have been explored for the past several decades by a number of experimental research groups, and more recently, starting in the late 1980s, the first computational models of elastin-like polymers were created. Three primary mechanisms for the source of elasticity have been discussed in the literature. Hoeve and Flory first addressed the elasticity of elastin, proposing a perspective in line with the classical theory of rubber elasticity, where the protein is modeled as a collection of chains with a randomly distributed chain length, such that any displacement from this highest entropy state is responsible for the elastic restoring force [41, 42]. Later, Gosline suggested that the hydrophobic effect guiding protein–water interactions initiates the observed phenomenon [43]. Finally, Urry proposed alternatively a librational elasticity mechanism, suggesting that the elastic restoring force originates from a reduction in available configuration space upon extension as the peptide segments are stretched [44]. In our case study below, we present an overview of the computational studies that have addressed the question of elastin's elasticity, focusing on the development of models over time to capture a wider range of observable effects and mechanisms. By tracing the progression of MD implementations, we hope to highlight various aspects of model building and analysis, underscoring the considerations and limitations of different elements involved.

Related to the mechanisms of entropic elasticity is another unique property of elastin, the inverse temperature transition (ITT). Effectively, it describes the propensity of elastin to undergo a phase change from a less ordered to a more ordered state upon an increase in temperature, whereas generally the reverse effect is observed in elastic protein materials [45–47]. Early on, a number of studies observed filament formation in aqueous solution upon increasing temperature in elastin fragments and in elastin-like polymers [45, 48]. Elastin-like sequences have been even shown to crystallize upon rising temperature [49, 50]. Unlike most polymers, the soluble and insoluble phases of elastin are inverted such that solubility is increasingly observed at lower temperatures. As a result, various groups have described the possibility of making temperature modulated switches and controls based on other physical and chemical factors, such as pH, side chain identity and ions [51–57]. Other studies have revealed an important new direction in material design, specifically the combination of molecular mechanics of different natural proteins together with elastin. For example, the combination of elastin and silk has recently been achieved, resulting in exceptionally strong and elastic 'switchable' composites (figure 3). These properties open wide possibilities for material manipulation and material design with specific sensing capabilities. Because close parallels exist between elasticity and ITT driving mechanisms, below we note briefly relevant studies as references to the interested reader.

3. Case study: the source elastin's elasticity and ITT

The source of elastin's elasticity has been a disputed subject for the past half century. Three primary mechanisms have been proposed: the classical theory of rubber elasticity, librational entropic mechanisms and the hydrophobic effect. Before any dynamic simulation was attempted, the prevalent perspective was to attribute elastin's superb elasticity (figure 4)

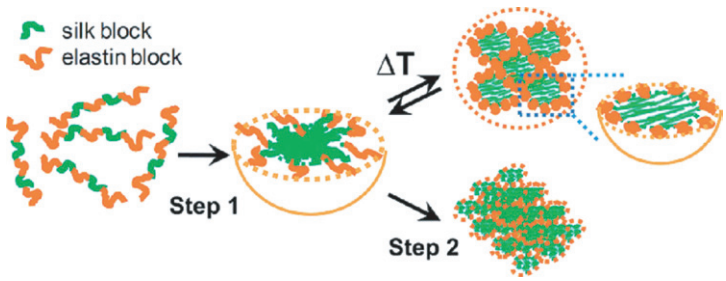

Figure 3. Silk-elastin block copolymers assemble into micellar-like particles, with the ability to either form reversible coacervates, controlled by temperature, or irreversible gel states. With permission from [80].

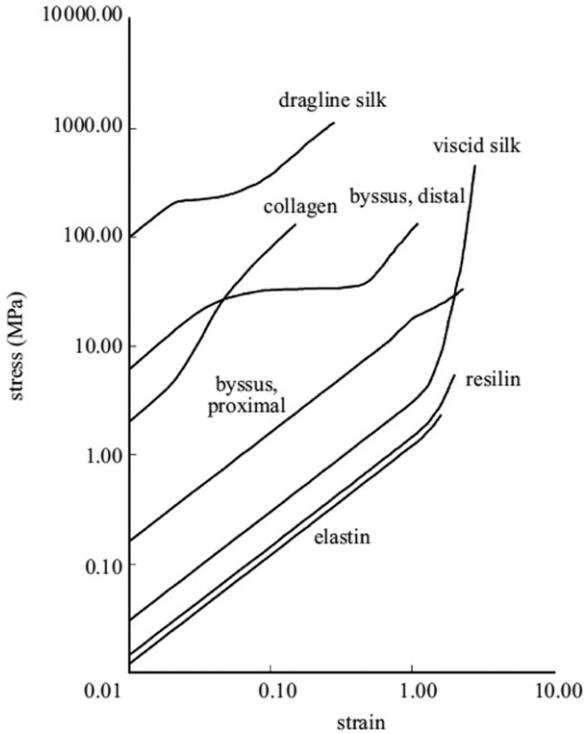

Figure 4. Stress–strain behavior for different biomaterials with exceptional mechanical properties. With permission from [81].

to the classical theory of rubber elasticity, first proposed for the macromolecule by Hoeve and Flory [41]. This model assumed that elastin was a single-phase system with randomly configured polymeric chains which assume the highest entropy at lowest end-to-end extension. Although this description was in line with certain experimental evidence, other observations surfaced, disputing this hypothesis. For instance, this model did not describe why, unlike for rubber, water was required for elastin's elasticity [58] and why a decrease in florescence was observed with the addition of an elastin-binding dye upon elongation, suggesting hydrophobic collapse [59]. The first MD simulations of elastin-like peptides addressed the mechanisms of elastin's elasticity, shifting away from the rubber elasticity viewpoint, as dynamics of

the molecules began to be 'observed' in real time. The first MD study to address elastin's elasticity was conducted by Chang and Urry in 1988 on the elastomeric polypentapeptide $(VPGVG)_7$ [60], starting from an initial spiral configuration of interconnected β-turns, as initially proposed by Urry and co-workers [61]. The simulations of relaxed and extended structures, with 50 ps production runs, were performed in vacuum, and were thus insufficient to capture water effects for full characterization. However, the particular strength of the study lay in the fact that full-atomistic resolution was used through a multiterm CHARMm potential implementation, which included contribution from energy terms of bond lengths, bond angles, torsional contributions, weak VdW and electrostatic interactions, to deduce molecular mechanisms contributing to elastin's entropic elasticity. The study observed that when VdW interactions are neglected, the change in internal energy between the relaxed and extended states is insignificant, as expected for a dominantly entropic elastomer [60]. The full-atomistic resolution of the model allowed a direct comparison of the backbone librational processes between relaxed and extended states. They found a damping of libration upon extension, suggesting an equally valid mechanism for elastin's elasticity. Nevertheless, the authors admit that longer production runs and the presence of explicit water would be needed to confirm these findings. (We note that in studies of the ITT, librational motion has been similarly implicated in stabilizing folded structures upon increasing temperatures. Further references can be found within [62, 63].)

An alternative proposal suggested a mechanism where the entropic mechanisms in elastin were attributed to a decreased solvent entropy associated with a changing size of the exposed surface area as the protein is stretched, forcing more order upon solvent molecules adjacent to the protein. The first MD studies, conducted in explicit solvent [64], rather than in vacuum as had been carried out by Chang and Urry two years prior [60], considered the elastin-like polypeptide $(VPGVG)_{18}$, starting from the same β-spiral starting configuration as used by Chang and Urry. The AMBER program with the united atom force field model that included only hydrogen atoms that can participate in hydrogen bonds was used with a TIP3P potential [21] for water molecules. In this work, Wasserman studied solvent-accessible surface area as the polymer is stretched, testing Gosline's proposal, based on experimental observations [43], which suggested that extended forms of elastin with greater hydrophobic surface area will have reduced solvent entropy, as water surrounding exposed hydrophobic side chains is rotationally and translationally ordered relative to bulk water. The addition of explicit water allowed the authors to accurately track the solvent-exposed surface area of the protein, concluding that protein–solvent interactions contribute to entropic elasticity mechanisms at low extensions. Tracking the time evolution of torsional angle pair correlations, the authors found a higher correlation in the collapsed form of the polymer compared with the extended state, suggesting that librational mechanisms are more significant at longer extensions [64], confirming Chang and Urry's results now in explicit water. (Analogous hydrophobic hydration effects in the ITT are addressed in [62, 63, 65, 66].

Li *et al* carried out full-atomistic MD simulations in explicit water for the same elastin-like polypeptide $(VPGVG)_{18}$ at two different temperatures, 10 and 42 °C but with nanosecond trajectory lengths comparable to experimentally determined relaxation times of elastin (figures 5(*a*) and (*b*)) [67]. By considering experimentally relevant time scales, the authors assert that solvent-based entropic effects are predominant factors for entropic elasticity of elastin, suggesting additional solvent-based entropic mechanisms, beyond those proposed by Wasserman. In addition to confirming the role of reduced orientational entropy of water molecules adjacent to protein at high extensions, they find that hydration waters form hydrogen bonds with main chain atoms, unlike in most globular proteins, which results in a fully dynamic system in both relaxed and extended states. Additionally they observe expulsion of water

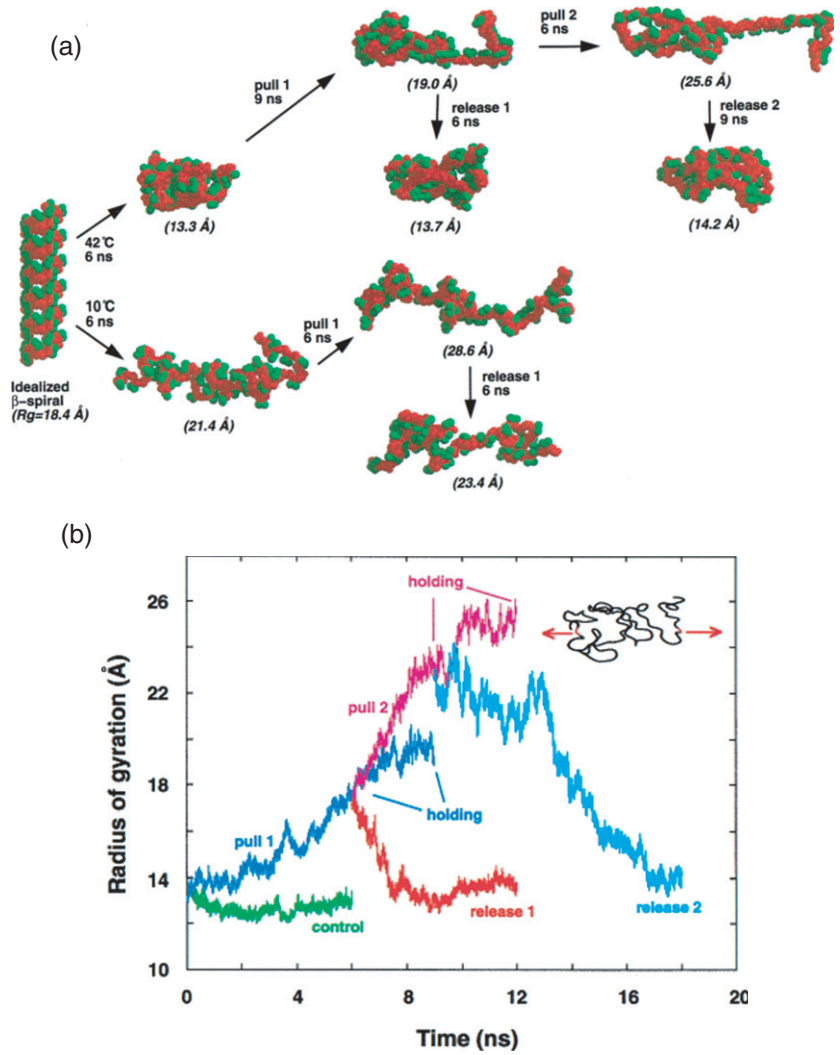

Figure 5. (*a*) Conformational structures during pull and release cycles, at 10 and 42 °C, starting from an initial β-spiral configuration. Radius of gyration is included in parentheses. With permission from [67]. (*b*) Radius of gyration for the system at 42 °C for two pull and release cycles. With permission from [67].

molecules from non-polar surfaces, as a result of hydrophobic collapse. These results are consistent with Gosline's observation that hydration is critical for elasticity, in particular that a 10% decrease in hydration has a substantial effect on the elastic modulus of elastin [68]. (Analogous studies for ITT in [62, 63, 65, 66] (figures 6(*a*) and (*b*)).)

Further evidence for the role of hydrophobic hydration in elastin's elasticity can be seen in a recent study focused on understanding diverging mechanisms in the function of elastin-like and amyloid-like materials [69]. In contrasting the two types of materials, proline and glycine, were found to be the two main sequence determinants for elastin-like materials. MD analysis of a series of sequences suggested that both amino acids are key for the hydrophobic hydration in elastin-like materials: prolines, because they are very stiff to form secondary structure,

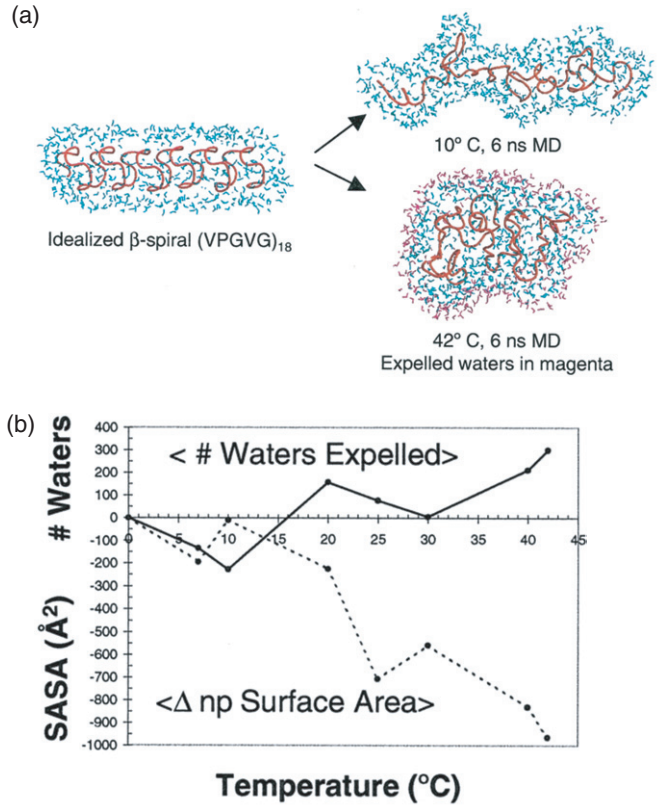

Figure 6. Silk-elastin block copolymers assemble into micellar-like particles, with the ability to either form reversible coacervates, controlled by temperature, or irreversible gel states. With permission from [80].

while glycines are very flexible, in the presence of water. The difference between the highly ordered amyloids and the relatively disordered, highly elastic elastin-like materials seems to be a result of the polypeptide's inability to form a fully compact, water-excluding core [69].

We have outlined a series of studies that employ various MD models of elastin-like segments to study entropic elasticity (or ITT) mechanisms that govern this fundamental property of elastin. The evolution of models addressing this topic presents a useful case study of the differences and flexibilities among different aspects in molecular modeling. In particular, we have considered topics such as the choice of force field, water model implications for the system considered and time-scale limitations. Together, these findings seem to suggest a dual entropic effect: a combination of the hydrophobic entropic effect together with a librational entropic component. Of significance, we note that throughout, these studies have been complementary to experiment, and in many cases serve as conclusive evidence for proposals derived based on experimental data [60, 64, 67, 69–72].

4. Conclusion

We have reviewed a large array of computational studies that provide a deeper fundamental understanding of the molecular mechanisms that guide and dictate the unique biological

(and potentially engineered) functions exhibited by elastin. The road to innovation and inquiry into the applications of elastin and elastin-like peptides is a newly emerging focus, with many future directions, including the development of new, enhanced biomaterials, functional composites and stimuli-responsive systems. Computational modeling has already supplemented and enhanced our understanding of elastin's extraordinary properties and suggested multiple avenues for implementing applications such as sensitive molecular switch systems. It seems clear that further work could vastly expand the applications of elastin, elastin-like peptides and elastin-based composites. Because time and length scale limitations persist in molecular modeling, it will be important to implement combined approaches, such as simulated annealing methods, for example. Finally, molecular modeling is a convenient and ultimately accessible method to probe the challenge of solving the structure and function of the full tropoelastin molecule and mechanisms of elastin assembly at the atomistic level. Such structural analyses are an important challenge that will likely involve a combination of experiment and computation. It is anticipated that significant impact of such work lies in several areas of medicine and bioengineering, where the function and failure of biomaterials such as elastin plays a critical role.

Acknowledgment

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