In silico design of self-assembly nanostructured polymer systems by multiscale molecular modeling

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Abstract

The fast development of digitalization and computational science is opening new possibilities for a rapid design of new materials. Computational tools coupled with focused experiments can be successfully used for the design of new nanostructured materials in different sectors, particularly in the area of biomedical applications. This paper starts with a general introduction on the future of computational tools for the design of new materials and introduces the paradigm of multiscale molecular modeling. It then continues with the description of the multiscale (i.e., atomistic, mesoscale and finite element calculations) computational recipe for the prediction of novel materials and structures for biomedical applications. Finally, the comparison of in silico and experimental results on selected systems of interest in the area of life sciences is reported and discussed. The quality of the agreement obtained between virtual and real data for such complex systems indeed confirms the validity of computational tools for the design of nanostructured polymer systems for biomedical applications.

Introduction

One of the major goals of computational material science is the rapid and accurate prediction of properties of new materials and complex systems. Despite the tremendous advances made in the modeling of structural, thermal, mechanical and transport properties of materials at the macroscopic level (finite element (FE) analysis of complicated structures), they leave a tremendous uncertainty about how to predict many critical properties related to performance, which strongly depends on nanostructure.

It is then essential to analyze the structure at molecular level, with all the chemical and physical implications. Currently, simulations at atomistic level such as molecular dynamics (MD) or Monte Carlo (MC) techniques allows to predict the structure and properties for systems of considerably large number of atoms and time scales of the order of microseconds. Although this can lead to many relevant results in material design, many critical issues in materials design still require time and length scales far too large for practical MD/MC simulations. This requires developing techniques useful to design engineers, by incorporating the methods and results of the lower scales (e.g., MD) to mesoscale simulations.

Advanced materials are essential to economic security and human well-being, with applications in industries aiming at addressing challenges in clean energy, national security, and human welfare. Despite this paramount importance, the development of a new advanced material can take 20+ years from initial discovery to put it on the market [1]. Accelerating the pace of discovery and deployment of advanced materials will therefore be crucial to achieving global competitiveness in the 21st century. In 2011 the Federal government of United States launched the Materials Genome Initiative (MGI) with an investment of over $250 million in new R&D and innovation infrastructure [2]. The basic idea of MGI is the integration of three different tools, namely simulations, experiments and big data (Figure 1). In the MGI strategy, simulations and experiments are coupled and optimized in order to provide reliable data in different conditions and for different properties: they are tightly integrated with slight overlapping for defining the relative ranges of uncertainties. In particular, simulation is used for complementing experiments in ranges of conditions where experiments are difficult to be carried out as well as for speeding up the procedure of characterization of new materials with different formulations. All relevant results obtained by both tools are stored in databases (big data), which in turn are queried by specific analytical tools capable of obtaining the necessary information from the data, and provide them to the industrial sectors.

The MGI philosophy for the design of new materials is also central to the concept of Industry 4.0, in which digitalization is going to deeply convert the way new products and new processes will be developed [3]. Industry 4.0 is related to the use of big data, cloud computing, internet-of-things and simulation tools, coupled with robotics and sensors able to acquire data. Big data are then analyzed using business intelligence and advanced

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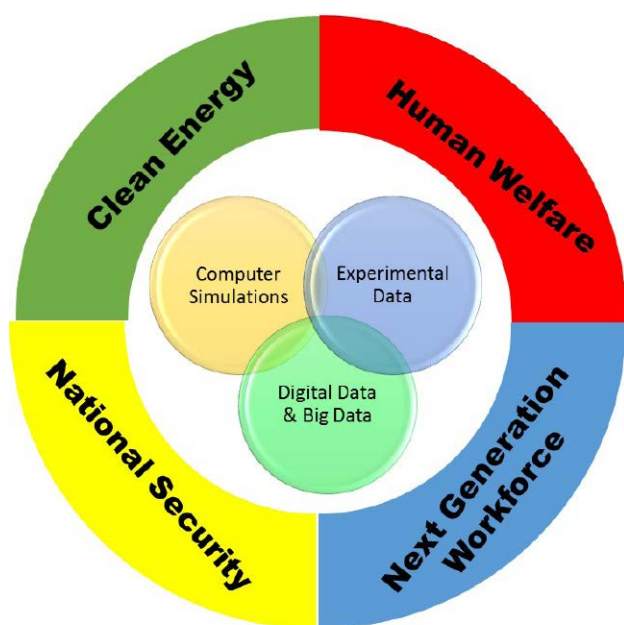**www.stijournal.pl**

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Figure 1. Materials Genome Initiative: a materials innovation infrastructure combining simulation with experiments and digital data [2]

analytical tools in order to give feedback to initiators aiming at enhancing the efficiency of the production processes.

In the last years, another important issue strongly related to the multiscale modeling was investigated and developed: the convergence of technologies in the area on nano-bio sciences. The phrase "convergent technologies" refers to the synergistic combination of four major "NBIC" (nano-bio-info-cogni) fields of science and technology, each of which is currently progressing at a rapid rate: (a) nanoscience and nanotechnology; (b) biotechnology and biomedicine, including genetic engineering; (c) information technology, including advanced computing and communications; (d) cognitive science, including cognitive neuroscience [4, 5].

Convergence of diverse technologies is based on material unity at the nanoscale and on technology integration from that scale: the building blocks of matter originate at the nanoscale (atoms). NBIC aims at using not only atoms to build processes and products of the future, but aims at combining atoms with bits, genes and synapses.

This paper focuses on multiscale molecular modeling of complex nanostructured polymeric materials consisting of polymeric matrices in which nano-objects are dispersed and/or are interacting via chemical or physical bonds.

These materials display structure features that span several length scales, from the Å level of the individual backbone of a single chain to the mesoscopic system morphology, reaching far into hundreds of nanometers. In addition, the time scales of the characteristic dynamic processes relevant to such different nanostructured material properties span a wider range, from femtoseconds to milliseconds or even seconds or hours in glassy materials or for large-scale ordering processes (e.g. phase sepa-

ration in blends). Unfortunately, no single model or simulation algorithm can cover such an interval of length and time scales; therefore, the seamless integration of many different models, each suitable for describing the chemistry and the physics at a given time and/or length scale, is required.

This concept indeed constitutes the pillar of multiscale molecular modeling and simulation, which is the bridging of length and time scales by linking computational methods for predicting macroscopic properties and behavior of complex systems from fundamental molecular processes [6–9]. Thus, the idea of performing simulations of materials across several characteristic length and time scales, starting from fundamental physical principles and experimental data, is highly appealing as a tool of potentially great effect on technological innovation and material design [10].

Multiscale molecular modeling can be applied to almost all materials whose properties depend on their nano-structure or microstructure. Accordingly, this contribution is not conceived as a thorough presentation of all state-of-the-art current multiscale molecular modeling [8, 11–15]. Rather, the selected examples presented in this overview reflect authors' own research interests, and are by no means exhaustive. Nevertheless, it is our hope that they can serve as inspiration for further developments in this exciting branch of science. The concept of multiscale molecular modeling has been successfully applied in other fields as it is reported in several review papers [8–10, 13, 16–20].

Multiscale molecular modeling

The recent years have observed a rapid expansion in the use of computer modeling techniques in both materials and life sciences. Many important driving forces increased the use of computer molecular modeling and simulations in materials science, but probably the most important one is the availability of (relatively) inexpensive commodity processing power, driven in part by Moore's law, which, in its original form, related to the doubling of the transistor density in integrated circuits every 18 months [21]. In practice, this has led to a rapid decrease in the unit price of CPUs (Central Processing Units) – and today – GPUs (Graphical Processing Units), physical memory and hard disk space, as machines suitable for scientific calculations have found their way onto the mass market. Parallel to hardware improvement, a plethora of free and commercially available integrated modeling software packages now exists, a selection of notable examples includes Gaussian® (mainly for quantum mechanics calculations), AMBER and NAMD (for atomistic simulations), Materials Studio®, Culgi, GROMACS, and LAMMPS (for both atomistic and mesoscale simulations), and Digimat and ABAQUS® (for continuum (i.e., finite element) calculations).

By definition, multiscale molecular modeling entails the application of computational techniques at two or more different length and time scales, which are often, but not always, dissim-

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ilar in their theoretical character due to the change in scale. A distinction is made between the *hierarchical approach*, which involves running separate models with some sort of parametric coupling, and the *hybrid approach*, in which models are run concurrently over different spatial regions of a simulation. The relationships between different categories of methods commonly used in the multiscale modeling hierarchy are shown in Figure 2 [8-20]. Although some techniques have been known for a long time and are currently widely used (e.g., molecular dynamics (MD) and Monte Carlo (MC) methods), other such as mesoscale simulation (MS) and some more advanced methods for accelerating atomistic simulations are not as common yet,

ferent classes of interactions (collectively known as force fields), typically consisting in: (i) bonded interactions, including bond-length (stretch) potentials, bond-angle (bend) potentials, torsion (twist) potentials and cross-terms, and (ii) non-bonded interactions, mostly comprising in Coulomb interactions and dispersion forces.

3. the *mesoscopic scale* (10^{-9}–10^{-1} m and 10^{-6}–10^{1} s). In these methods, a molecule is usually treated with a field description (field-based model) or microscopic particles (particle-based model) that incorporate molecular details implicitly. Therefore, they are able to simulate phenomena on length and time scales currently inaccessible by classical
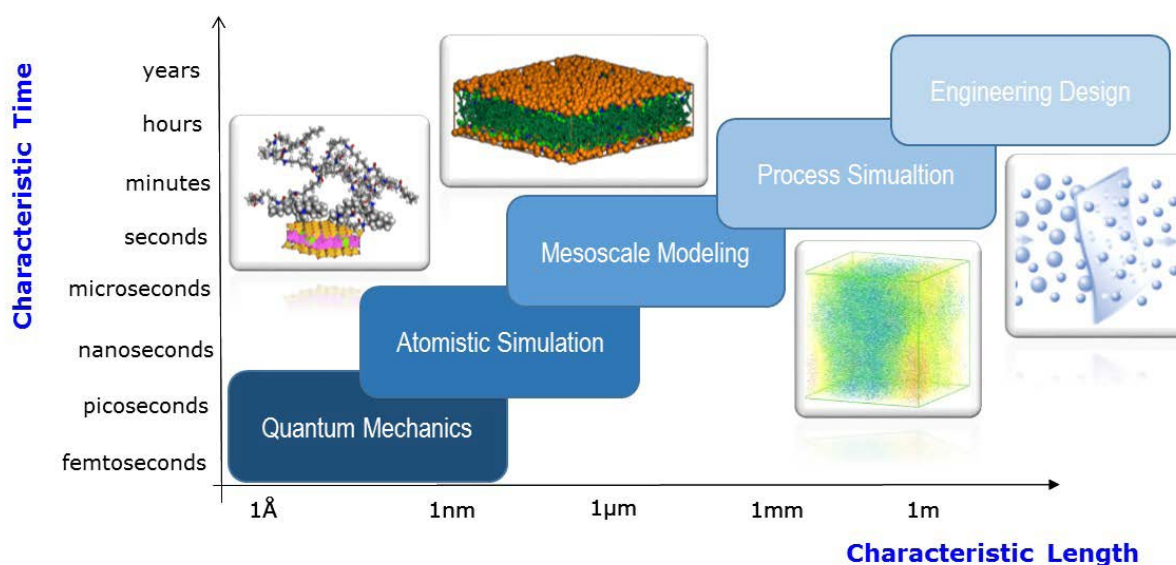

Figure 2. The hierarchy of multiscale molecular modeling techniques, showing approximate range of temporal and spatial scales covered by different categories of methods. Areas of overlap permit "mapping" or "zooming" from one scale to the next, which is often required for parameterization of higher scale methods or for obtaining a finer scale resolution of selected parts of the larger system [8-20]

and require more advanced experience and specialized background in the field.

In the context of materials simulations shown in Figure 2, four characteristic time and length levels can be envisaged before reaching the last step, i.e. engineering design [22].

1. *the quantum scale* (10^{-10}–10^{-9} m and 10^{-12} s), in which nuclei and electrons are the main players, and their quantum-mechanical state dictates the interactions among atoms. The possibility of obtaining data describing structural and electronic features of the system under consideration and of taking into account effects associated with rupture and formation of chemical bonds in molecules, changes in electron configurations, and other similar phenomena are the main advantages of methods working at the quantum scale.

2. *the atomistic scale* (10^{-10}–10^{-7} m and 10^{-12}–10^{-6} s). In atomistic simulations, all atoms are explicitly represented or in some cases, small groups of atoms are treated by single sites referred to as pseudo or united atoms. The potential energy in the system is estimated using a number of dif-

atomistic approach. At the simplest mesoscopic level, a polymer system may be modeled by a phenomenological expression for the free energy (field-based approach). For example, the Flory-Huggins or Landau free energies of mixing may be used to model aspects of polymer mixtures. In such models, the details of the system are incorporated into, e.g., the Flory parameter and the monomer segment mobility. Such phenomenological expressions are equivalent to truncated expansions of a more complicated free energy expression. Instead, in particle-based models the fluid is portrayed as a collection of point particles that represent lumps of fluid containing many molecules or segments of chains, termed beads. The interaction between beads is considered mesoscopic because the internal degrees of freedom of the fluid elements are ignored and only their center-of-mass motion is resolved.

4. the *macroscopic scale* (10^{-3}–10^{1} m and 10^{1}–10^{3} s). At this level, constitutive laws govern the behavior of the physical system, which is considered as a continuous medium, ig-

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noring discrete atomic and molecular structures and their influence on the overall system behavior. The basic assumption then consists in representing a heterogeneous material as an equivalent of homogeneous one. A medium is called a continuum, if its volume contains an apparent continuity of material mass over the physical scale of the problem of interest. In general, this requires the domain of interest to be several orders of magnitude larger than the length scale of the elemental components. All mathematical functions (e.g., velocity or displacement fields) used to describe the state of the system are continuous, except possibly at a finite number of interior surfaces separating regions of continuity. Stress and strain tensors may be split into isotropic and deviatory parts, allowing to predict the behavior of the medium under both static and dynamic loading with separate descriptions of constitutive behavior of material under hydrostatic and non-hydrostatic circumstances.

At each length and timescale, well-established and efficient computational approaches have been developed over the years to handle the relevant, underlying phenomena. To treat electrons

insight into atomic processes involving considerably large systems [26].

At the mesoscopic scale, the atomic degrees of freedom are not explicitly treated, and only large-scale entities are modeled (that is, agglomeration of atoms called *beads*, obtained through a coarse-graining procedure, *vide infra*). Mesoscale models are particularly useful for studying the behavior of polymers and soft materials. They can model even larger molecular systems, but with the commensurate trade-off in accuracy. Typical results of mesoscale simulations are morphologies of matter in the nanometer - millimeter range at specific conditions of temperature, composition, and shear. Various simulation methods have been proposed to study the mesoscale structures in polymer-based materials, the most common being Brownian Dynamics (BD), Dissipative Particle Dynamics (DPD), Lattice Boltzmann (LB), time-dependent Ginzburg–Landau theory, and Dynamic Density Functional Theory (DDFT) [27–32]. Eventually, it is possible to transfer the simulated mesoscopic structure to finite elements modeling (FEM) tools to calculate macroscopic properties for the systems of interest [33, 34].
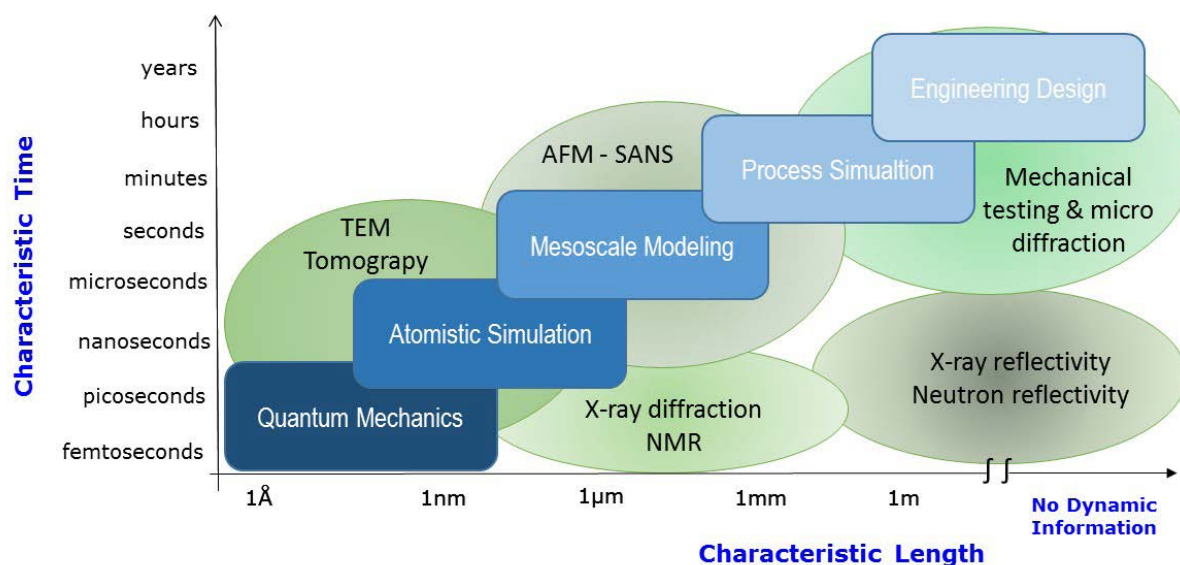

Figure 3. Experimental and theoretical tools for characterization and modeling of polymer-based nanocomposites, plotted over their respective time and length scale domain of applicability. Experimental methods include X-ray diffraction, nuclear magnetic resonance (NMR), transmission electron microscopy (TEM), tomography, atomic force microscopy (AFM), small-angle neutron scattering (SANS), small-angle X-ray scattering (SAXS), mechanical testing, X-ray reflectivity and neutron reflectivity [13]

explicitly and accurately at the lower scale, electronic models based on quantum mechanical (QM) methods can be employed. QM methods have undergone enormous advances in the last decades, enabling simulation of systems containing several hundred atoms with good accuracy [23].

For material properties at the atomic level, molecular dynamics and Monte Carlo simulations are usually performed employing classical interatomic potential, which can often be derived from QM calculations [24, 25]. Although not as accurate as QM methods, classical MD and MC simulations are able to provide

Whatever the multiscale protocol has been developed, it is important to be able to compare the calculated results with experimental evidences at each scale a computation is performed. Fortunately, the experimental methods available now allow this comparison along the entire multiscale procedure, as shown in Figure 3. Experimental tools and methodologies available at different time and length scales allow not only to check the validity of the simulations but also to feed data to the big data repository in the framework of the MGI mentioned above.

In summary, the ultimate goal of the multiscale modeling is

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the prediction of the macroscopic behavior of an engineering process from first principles, by adopting a sequential simulation pathway where we compute information at a smaller (finer) scale and pass it to a model at a larger (coarser) scale. This procedure leaves out (i.e. coarse grains) all the degrees of freedom pertaining to the smaller scale, which is considered to be in equilibrium [22, 35–39].

This *message-passing* approach can be performed in sequence for multiple-length scales. The vital attribute of the sequential approach is that the simulation at a higher level critically depends on the completeness and the correctness of the information gathered at the lower level, as well as on the efficiency and reliability of the model at the coarser level.

To obtain first principles-based results for macroscale systems, a sufficient degree of overlap between each simulation scale and the finer description must be ensured, so that all input parameters and constitutive laws at each level of theory can be determined from a more fundamental theory. Equally important, these relations must be invertible so that the results of coarse level simulations can be used to suggest the best choices for finer level parameters, which, in turn, can be employed to formulate new choices of material composition and structure.

The problem for polymers is that the method of coarsening the description from atomistic to mesoscale or mesoscale to continuum is not as obvious as it is in going from electrons to atoms [8].

In other words, the coarsening from QM to MD relies on basic principles and can be easily generalized in a method and in a procedure, while the coarsening at higher scales is system specific. Multiscale simulation poses, in some sense, greater challenges for polymer materials than for seemingly more complex systems such as metals and ceramics due to the larger range of length and time scales that characterize macromolecules.

Scale integration in specific contexts in the field of polymer modeling can be done in different ways. All approaches are initially based on the application of a force field (FF) that transfers information from quantum chemistry to atomistic simulation. From atomistic simulation to mesoscale model, essential features of the system have to be maintained while reducing the degree of freedom [40–43].

So far, the features chosen for the reproduction by coarse-grained models have been mainly structural, thermodynamic or both, with structure prevailing [44]. This linking through the mesoscale in which we can describe microstructure is probably the most challenging step toward the developing reliable first principles methods for practical material design applications.

Among the possibilities to achieve seamless zooming multiscale simulations in the field of polymer-based nanocomposites, we present and discuss here one strategy that proved to yield accurate and reliable results for many different systems of industrial interest [45]. According to this multiscale computational recipe, four sequential steps need to be performed, as follows:

i. QM calculations are employed (when required) to derive specific (and, hence, highly accurate) force fields, that is, material energy functions (aka interatomic potentials) comprising in the functional form and parameter sets used to calculate the potential energy of a system of atoms or coarse-grained particles in molecular mechanics/molecular dynamics simulations.

ii. Having chosen the appropriate FF for the system under consideration (either already available in the literature or derived ad hoc at point i)), fully atomistic molecular dynamics (MD) simulations are performed to retrieve fundamental structural and energetical information at the molecular level.

iii. The data gathered at point ii) are mapped into the corresponding structural and energetical input parameters required to run simulations at a mesoscopic level.

iv. The main output of point iii), i.e., the mesoscopic morphologies and density distributions of the system are finally used as the input for finite element calculations and macroscopic property predictions.

In the next paragraph, we will present and discuss the application of such hierarchical multiscale molecular modeling approach to the prediction of self-assembly nanostructured polymer systems for biomedical applications.

Multiscale molecular simulation for nanostructured polymer systems for biomedical applications

In this paragraph, the multiscale molecular modeling procedure described in the previous paragraph has been applied to two selected systems relevant in biomedical applications: (i) nanovectors for drug delivery system and (ii) self-assembly of polymer chains on gold nanoparticles.

Systems for biomedical applications ranges from few nanometers up to several thousand nanometers. Figure 4 shows examples of systems of interest in biomedical applications grouped by type and dimensions of representative agglomeration of atoms.

The first system considered is a block polymer system used as a drug carrier. The idea is that diblock or triblock copolymers may form reverse micelles under certain conditions and that the micelles could be used for incorporating drugs, aiming at delivery of drugs to the target without dissolution in the environment, thus maximizing the therapeutic effect [46].

Several questions could be answered by molecular simulations in the preliminary process of selecting the most promising system, namely, is it better to have a diblock or a triblock copolymer? Under which thermodynamic conditions the micelle is formed? If the micelle is formed, what is its size? In addition, what is the maximum drug concentration inside the micelle that maintain the micelle intact? The diblock copolymer considered in this application is the Poly(ethylene oxide) PEG (Mw = 3670 Da) / Poly-DL(lactic acid) PLA (Mw = 3300 Da) and the triblock
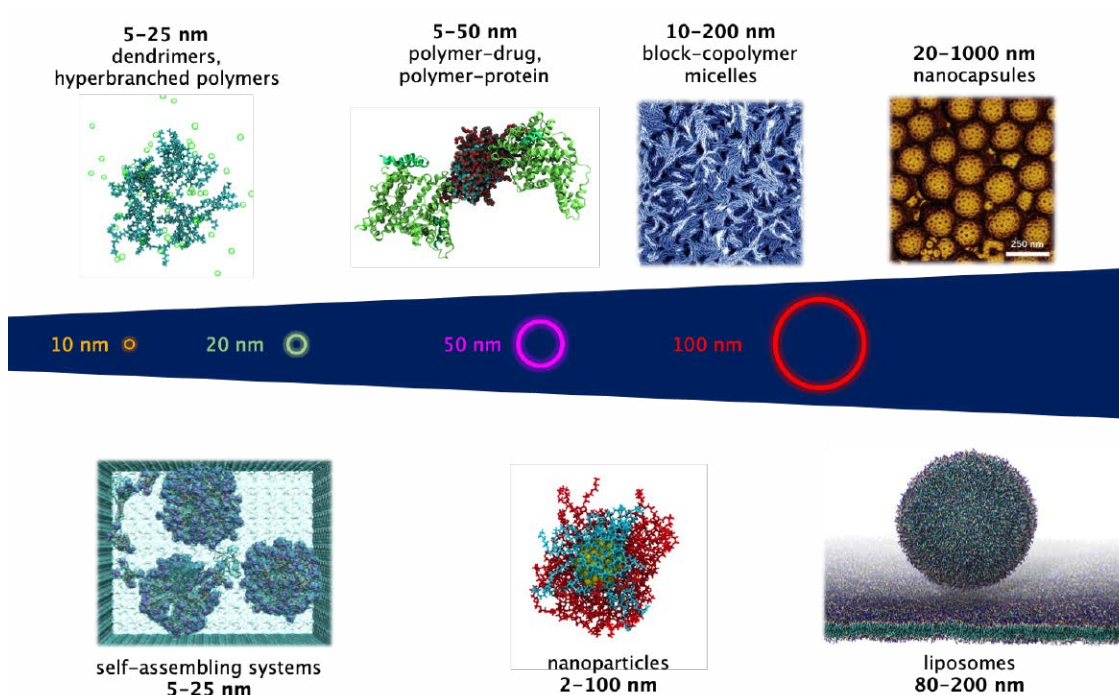
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Figure 4. Nanostructure of potential interest for biomedical applications. Dimensions span from few nanometers to hundreds of nanometers with increasing structural complexity

copolymer is the PLA5875-PEO7761-PLA5875. Both copolymers are FDA approved and therefore suitable to be used as drug carrier in the human body.

The effect of copolymer composition and concentration on system morphology is investigated by using multiscale molecular modeling described in the previous paragraph. The model drug under consideration is NIFEDIPINE (Adalat®, Nifedical®, Procardia®) which is a Calcium channel blocker intended for use in several applications (ischemic cardiopathy, chronic arterial hypertension, Raynaud syndrome, premature delivery). This drug is highly hydrophobic and has side effects, therefore it needs a well-designed delivery system to be used in therapy.

The first objective of the simulation was the description of the phase diagram of the block copolymers. Figure 5 shows the phase diagram for the diblock copolymer system obtained by the mesoscale simulation: all the experimental available structures are reliably simulated including the formation of micelles in the upper part of the diagram. The results of the simulations are successfully used for answering the questions about the conditions of formation and the size of the micelles.

The next step was the simulation of the complete system made up by the block copolymer with the drug. For the diblock copolymer the maximum drug load, before the collapse of the micelle, was determined to be around 15% v/v (volume of drug/
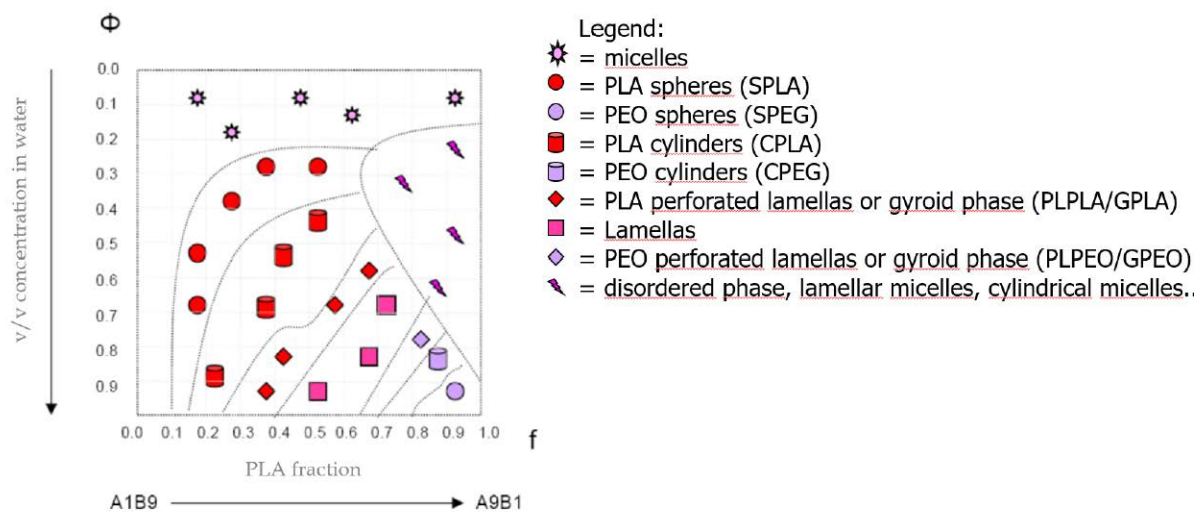

Figure 5. Phase diagram of the diblock copolymer Poly(ethylene oxide) PEG as a function of concentration in water and PLKA fraction [46]

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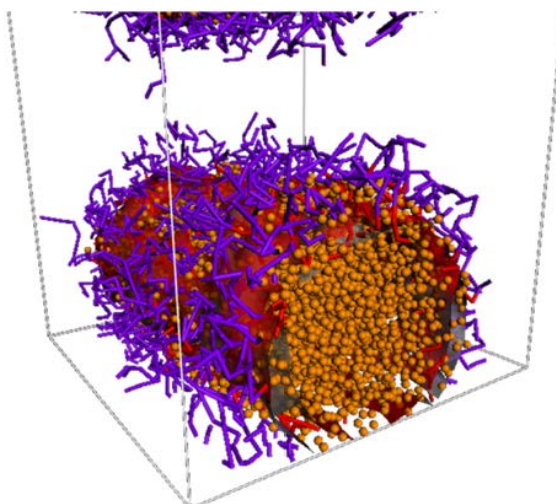
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Figure 6. Simulation of the diblock copolymer with model drug for a Nifedipine loading greater than 15% v/v; it is observed that drug (brown) is escaping out of the micelle (red and violet) [46]

total volume), while for the triblock copolymer system the same limit was between 2–3% v/v, thus showing the superiority of the diblock copolymer system with respect to the other.

Figure 6 shows the results of the simulation of the diblock copolymer system with a drug concentration of 22% v/v: it is evident from the figure that the drug is not kept inside the micelle.

The second system investigated shows how nanostructures may self-assembly on gold nanoparticles for creating well defined structures (i.e., self-assembled monolayers – SAMs) suitable for biomedical applications. The grafted chains are made by Fluorine (F) and carbon (CH) and, depending upon the thermodynamic conditions, they may create stripe/patch, Janus or random nano-structures (Figure 7) after successful grafting [47, 48].

It is important to simulate the different structures for determining which condition will give raise to a specific one. The quality of the simulations have been tested versus NMR and STM experiments, showing a very good agreement, as it is shown in Figure 8 where comparison between predicted and experimental NMR chemical shift decay as a function of the SAM composition for random, janus and striped morphology are reported. Figure 8 (middle panel) presents also the comparison of simulated and experimental STM images for the different morphologies considered.
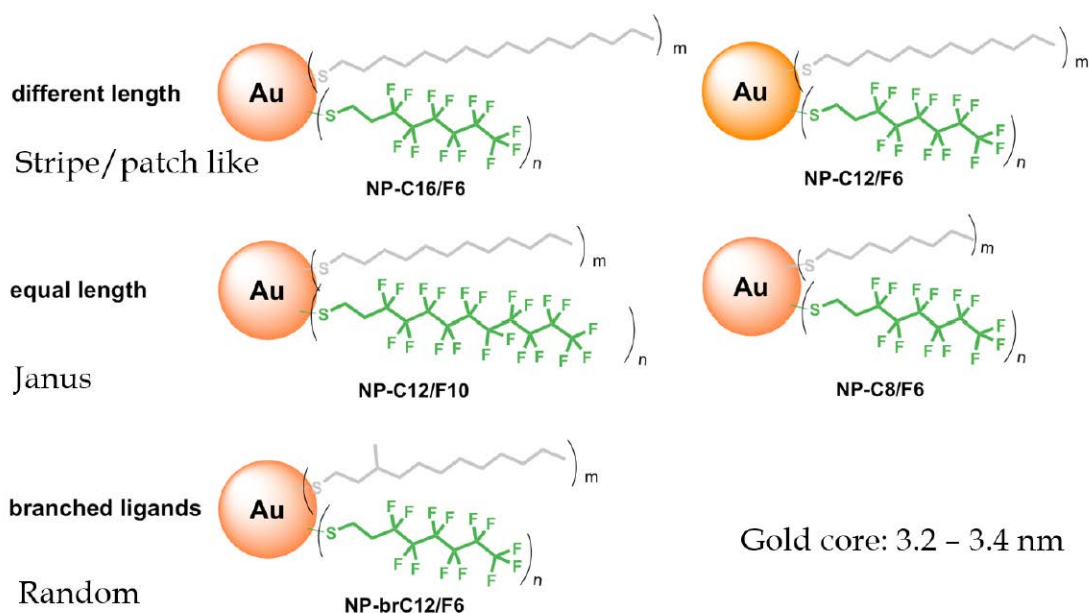

Figure 7. Different grafting chains topologies give different nanostructure of chains around the gold nanoparticle [47, 48]

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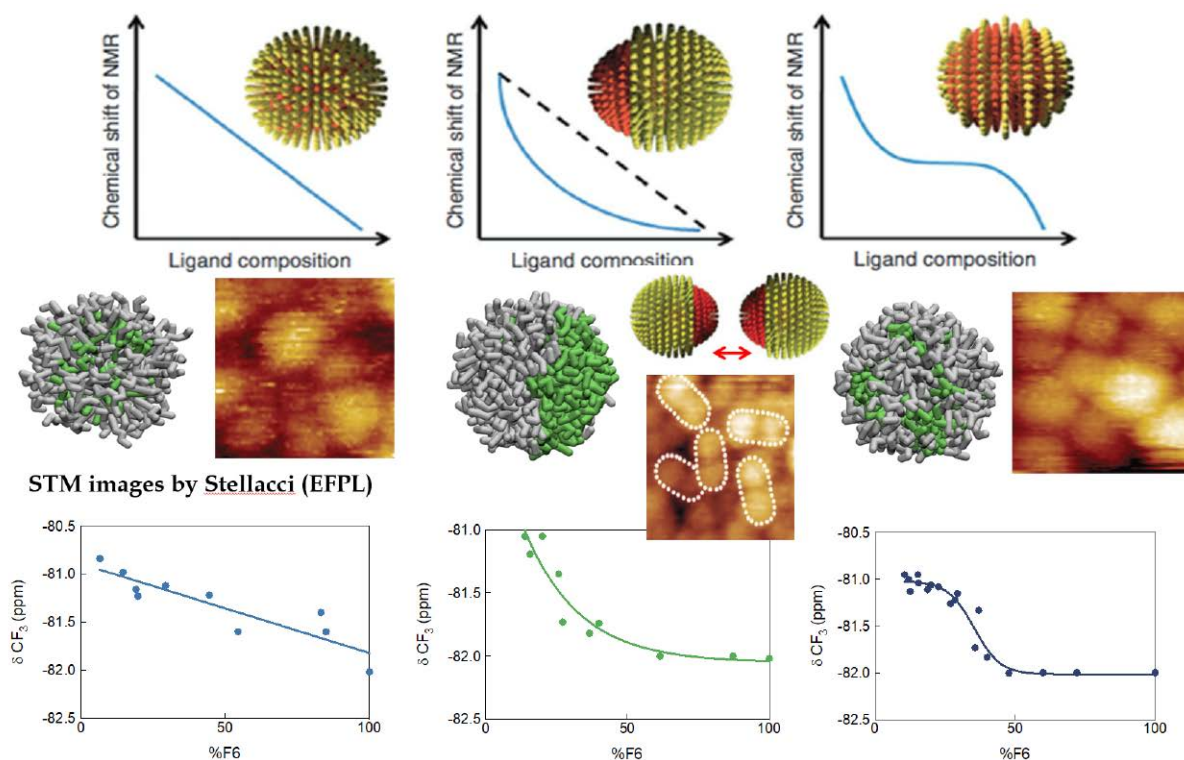
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Figure 8. Top panel: predicted NMR chemical shift decay as a function of the SAM composition for random (left), janus (center) and striped (right) morphology of the SAM. Middle panel: comparison of simulated (left) and experimental STM images (right) for random (left), janus (center) and striped SAMs. Bottom panel: experimental 19F NMR chemical shift as a function of the SAM composition for random (left), janus (center) and striped (right) morphology of the SAM [47, 48].

Conclusions

Nanostructured polymer systems are an area of substantial scientific interest and of emerging industrial practice, as it is clearly indicated by the convergence of technologies (NBIC). Since the systems are complex, the only possible way to support the design is through the combination of experiments and modeling (MGI). Once more, due to the peculiarities of the systems of interest, no single technique can be applied for their simulation: it is therefore necessary to rely on a multiscale molecular modeling approach that has been introduced and explained in this paper.

The methodology presented in this paper can be considered a general design approach for complex nanostructured systems to be successfully used for the interpretation of experiments and for the design of active nano materials and nano systems. The approach is not at all limited to applications in biomedicine, but can be used from classical nanotechnology and beyond. Successful applications of the multiscale molecular modeling method described above have been implemented in classical industries (automotive, opto-electronic, polymer…) and in industry 4.0, in pharmaceutical industry, in nano medicine & personalized medicine and in the internet of nano things and NBIC.

It is expected that NBIC will have the same importance in 21st century as the oil, polymers and semi-conductors had in the 20th century.

References

1. Plunket JW, *Plunkett's Nanotechnology & Mems Industry Almanac 2017: Nanotechnology & Mems Industry Market Research, Statistics, Trends & Leading Companies*, 30 May 2017, Editor Plunkett's Nanotechnology & Mems Industry Almanac.

2. White A, The Materials Genome Initiative: One year on, MRS Bull., 2012; 37:715–716.

3. Hermann M, Pentek T, Otto B, Proceedings of the 49th Hawaii International Conference on System Sciences (HICSS), Koloa, HI, 2016, 3928 (doi: 10.1109/HICSS.2016.488).

4. Roco MC, Bainbridge WS, Tonn B, Whitesides G, (Eds.), Convergence of Knowledge, Technology and Society. Beyond Convergence of Nano-Bio-Info-Cognitive Technologies. Springer Verlag, 2013.

5. Scot T, Walsh A, Anderson B, O'Connor A, Economic Analysis of National Needs for Technology Infrastructure to Support the Materials Genome Initiative, 2018, Final Report, RTI International Project Number 0215231,

6. Charpentier JC, The triplet "molecular processes–product–process" engineering: the future of chemical engineering ?, Chem. Eng. Sci., 2002; 57:4667–4690.

7. Glotzer SC, Paul W, Molecular and Mesoscale Simulation Methods for Polymer Materials, Annu. Rev. Mater. Res., 2002; 32:401–436.

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8. Zeng QH, Yu AB, Lu GQ, Multiscale modeling and simulation of polymer nanocomposites, Progr. Polym. Sci., 2008, 33, 191–269.

9. Jancar J, Douglas JF, Starr FW, Kumar SK, Cassgnau P, Lesser AJ, Sternstein SS, Buehler MJ, Current issues in research on structure-property relationships in polymer nanocomposites, Polymer, 2010; 51:3321–3343.

10. Yip S, Synergistic science, Nat. Mater., 2003; 2:3–5.

11. Mohanty S, Ross R, Multiscale Simulation Methods for Nanomaterials, ed. Mohanty S and Ross R, John Wiley & Sons, Hoboken, 2008, p.1.

12. Scocchi G, Posocco P, Handgraaf JW, Fraaije JGEM, Fermeglia M, Pricl S, A Complete Multiscale Modelling Approach for Polymer–Clay Nanocomposites, Chem. Eur. J., 2009; 15:7586–7592.

13. Pricl S, Posocco P, Scocchi G, Fermeglia M, Handbook of Nanophysics: Functional Nanomaterials, ed. K.D. Sattler, CRC Press, Boca Raton, 2010, pp. 3-1- 3-15.

14. Pereira SP, Scocchi G, Toth R, Posocco P, Romero-Nieto D, Pricl S, Fermeglia M, Multiscale modeling of polymer/clay nanocomposites, J. Multiscale Model., 2011; 3:151–176.

15. Toth R, Santese F, Pereira SP, Nieto DR, Pricl S, Fermeglia M, Posocco P, ize and shape matter! A multiscale molecular simulation approach to polymer nanocomposites, J. Mater. Chem., 2012; 22:5398–5409.

16. Mark F Horstemeyer, Multiscale Modeling: A Review, 2009, in Practical Aspects of Computational Chemistry, Practical Aspects of Computational Chemistry, ed. J. Leszczynski and M.K. Shukla, Springer Science+Business Media, pp. 87–135.

17. Steinhauser MO, Hiermaier S, A Review of Computational Methods in Materials Science: Examples from Shock-Wave and Polymer Physics, Int. J. Mol. Sci., 2009; 10 (12):5135–5216.

18. Curtin WA, Miller RE, Atomistic/continuum coupling in computational materials science, Modelling Simul. Mater. Sci. Eng,, 2003; 11(3):R33–R68.

19. Yeo J, Jung GS, Martín-Martínez FJ, Beem J, Qin Z, Buehler MJ, Multiscale Design of Graphyne-Based Materials for High-Performance Separation Membranes, Adv. Mater, 2019, DOI: 10.1002/adma.201805665.

20. Casalini T, Perale G, From Microscale to Macroscale: Nine Orders of Magnitude for a Comprehensive Modeling of Hydrogels for Controlled Drug Delivery, Gels, 2019; 5:28.

21. Moore G, "IEEE Technical Digest 1975" April 7, 1975, Intel Corp; "Moore's Law in perspective," 2005, Intel information sheet 306971-001US.

22. de Baas AF, What makes a material function? Let me compute the ways…, European Commission, Directorate-General for Research and Innovation, Directorate D - Industrial Technologies, Unit D3 – Advanced Materials and Nanotechnologies, Bruxelles, 2017 (doi 10.2777/417118).

23. McWeeny R, Methods of Molecular Quantum Mechanics, 2nd Edition, Academic Press, Cambridge, 1992.

24. Ercolessi F, Adams JB, Interatomic Potentials from First-Principles Calculations: The Force-Matching Method, Europhys. Lett., 1994; 26:583.

25. Fermeglia M, Ferrone M, Pricl S, Computer simulation of nylon-6/organoclay nanocomposites: prediction of the binding energy, Fluid. Phase. Equilib., 2003; 212:315–329.

26. Vv. Aa., Molecular Simulations and Industrial Applications, ed. K.E. Gubbins and N. Quirke, Gordon & Breach, Amsterdam, 1996.

27. Chen JC, Kim AS, Brownian Dynamics, Molecular Dynamics, and Monte Carlo modeling of colloidal systems, Adv. Colloid Interface Sci., 2004; 112:159–173.

28. Hoogerbrugge PJ, Koelman JMVA, Simulating Microscopic Hydrodynamic Phenomena with Dissipative Particle Dynamics, Europhys. Lett., 1992; 19:155.

29. Groot RD, Warren PB, Dissipative particle dynamics: Bridging the gap between atomistic and mesoscopic simulation, J. Chem. Phys. 1997; 107:4423.

30. Chen S, Doolen GD, Lattice Boltzmann Method for Fluid Flows, Annu. Rev. Fluid Mech., 1998; 30:329-364.

31. Glotzer SC, in Annual Reviews of Computational Physics, ed. Stauffer D, World Scientific, Singapore, pp. 1–46.

32. Fraaije JGEM, van Vlimmeren BAC, Maurits NM, Postma M, Evers OA, Hoffmann C, Altevogt P, Goldbeck-Wood G, The dynamic mean-field density functional method and its application to the mesoscopic dynamics of quenched block copolymer melts, J. Chem. Phys. 1997; 106:4260.

33. Hughes TJR, The Finite Element Method, Prentice-Hall, Englewood Cliffs, 1987.

34. Gusev AA, Numerical Identification of the Potential of Whisker- and Platelet-Filled Polymers, Macromolecules, 2001; 34:3081–3093.

35. Goddard III WA, Cagin T, Blanco M, Vaidehi N, Dasgupta S, Floriano W, Belmares M, Kua J, Zamanakos G, Kashihara S, Iotov M, Gao G, Strategies for multiscale and simulation of organic materials: polymers and biopolymers, Comput. Theor. Polym. Sci., 2011; 11:329–343.

36. McGrother S, Goldbeck-Wood G, Lam YM, Integration of modelling at various length and time scales, Lect. Notes Phys., 2004; 642:223–230.

37. Scocchi G, Posocco P, Fermeglia M, Pricl S, Polymer−Clay Nanocomposites: A Multiscale Molecular Modeling Approach, J. Phys. Chem. B, 2007, 111, 2143–2151.

38. Cosoli P, Scocchi G, Pricl S, Fermeglia M, Many-scale molecular simulation for ABS–MMT nanocomposites: Upgrading of industrial scraps, Microporous Mesoporous Mater., 2008; 107:169–179.

39. Fermeglia M, Pricl S, Multiscale molecular modeling in nanostructured material design and process system engineering, Comput. Chem. Eng., 2009; 33:1701–1710.

www.stijournal.pl

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40. Doi M, Material modeling platform, J. Comput. Appl. Math., 2002; 149:13–25.

41. Milano G, Müller-Plathe F, Mapping Atomistic Simulations to Mesoscopic Models: A Systematic Coarse-Graining Procedure for Vinyl Polymer Chains, J. Phys. Chem. B, 2005; 109:18609–18619.

42. Toth R, Voorn DJ, Handgraaf JW, Fraaije JGEM, Fermeglia M, Pricl S, Posocco P, Multiscale Computer Simulation Studies of Water-Based Montmorillonite/Poly(ethylene oxide) Nanocomposites, Macromolecules, 2009; 42:8260–8270.

43. Ghanbari A, Ndoro TVM, Leroy F, Rahimi M, Böhm MC, Müller-Plathe F, Macromolecules, Interphase Structure in Silica–Polystyrene Nanocomposites: A Coarse-Grained Molecular Dynamics Study, 2012; 45:572–584.

44. Müller-Plathe F, Coarse-Graining in Polymer Simulation: From the Atomistic to the Mesoscopic Scale and Back, Chem. Phys. Chem., 2002; 3:754–769.

45. Fermeglia M, Pricl S, Multiscale modeling for polymer systems of industrial interest, Prog. Org. Coat., 2007; 5:187–199.

46. Posocco P, Fermeglia M, Pricl S, Morphology prediction of block copolymers for drug delivery by mesoscale simulations, J. Mat. Chem., 2010; 20:7742–7753.

47. Posocco P, Gentilini C, Bidoggia S, Pace A, Franchi P, Lucarini M, Fermeglia M, Pricl S, Pasquato L, ACS Nano, 2012; 6:7243–7253.

48. Pengo P, Sologan M, Pasquato L, Guida F, Pacor S, Tossi A, Stellacci F, Marson D, Boccardo S, Pricl S, Posocco P, Gold nanoparticles with patterned surface monolayers for nanomedicine: current perspectives, Eur. Biophys. J., 2017; 46:749–771.