4m Slithering Polymers and Migrating Cells: Application of Computational Methods to Problems in Polymer Physics and Cell Organization

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A. RHEOLOGY OF POLYMER MELTS

The rheological responses of LLDPE (linear low-density polyethylene), which has a linear architecture, and conventional LDPE (low-density polyethylene), which has a "comb"-like architecture with side chains along the linear backbone, are dramatically different. For example, a minute degree of long-chain branching (LCB), of the order of one side branch per 10,000 backbone carbon atoms, can enhance the zero-shear viscosity of a linear chain by a factor of 100 [1]. Today, LCB can be administered and controlled via metallocene-based catalysts. LCB endows LDPE with superior processing properties like shear-thickening, that make it resistant to tear during film blowing. However, the threshold of conventional methods of chemical analysis like spectroscopy and chromatography in detecting sparse structural details like low concentrations of LCB is far below a level that can be considered adequate from an industrial perspective. The sensitivity of rheology to molecular architecture and branching details has spawned the notion of analytical rheology - the idea that linear viscoelastic measurements can be used to probe the underlying molecular structure of polymers.

Accurate linear-viscoelastic models are a prerequisite to implement analytical rheology. In principle, these viscoelastic models may be mathematically inverted to infer structures responsible for a particular rheological response. The span of important time scales in the relaxation of polymer melts ranges from nanoseconds to a few seconds. To make industrially relevant predictions, we need a multi-scale modeling approach, where assumptions placed on a coarse grained model are justified by a more fine-grained model. A typical modeling hierarchy in the order of increasing detail is as follows:

1.Mean-Field Tube Models 2.Simplified Slip-Link Models 3.Real-space Slip-Link Models 4.Lattice Monte Carlo Methods like the Bond-Fluctuation Model 5.Molecular Dynamics

For example, during my PhD, motivated by the inability of mean-field models to capture branch-point motion, I used a simple virtual-space slip-link formulation to probe where and why tube models based on dynamic dilution are most likely to fail [2]. The simple slip-link model, in turn, employed a quadratic potential energy term, which was justified using the bond-fluctuation model and molecular dynamics simulations. The results of these fine-grained simulations suggest ways in which the mean-field tube theory may have to be modified. Currently, I am interested in how chain and sub-chain level mechanisms manifest and control the parameters used in the mean-field description. The cross-talk between various levels of modeling, will shape future directions of inquiry.

B. MODELING OF TISSUE ENGINEERING SCAFFOLDS

Coaxing cells to produce functional tissue, demands their cultivation and organization on 3D substrates, or scaffolds. These scaffolds act as a surrogate for the extra-cellular matrix found in the human body. A wide range of materials and manufacturing methods for the synthesis of 3D scaffolds have been developed. However, the development of scaffolds is beset with a variety of challenges, including tissue ingrowth that is limited to the exterior of the scaffold due to insufficient nutrient and product transport, and loss of cellular phenotype due to improper cell-matrix, cell-cell contacting/signaling. Recently, highly uniform and organized tissue engineering scaffolds possessing inverted-colloidal crystal (ICC) geometry, which are inexpensive to manufacture and do not suffer from material constraints, have been developed [3].

Due to the regularity of these ICC scaffolds, computational modeling functions as an important tool to explore the vast available design space and to earmark regions of interest. For example, simplified Brownian Dynamics models have been used to characterize the transport of nutrients/metabolic products through the porous ICC scaffolds, and to quantify the extent of cell-matrix contacting. These studies may be used to optimize scaffold geometry.

Currently I am trying to develop models that reflect some the complexity and richness inherent in biological systems. For instance, cells have highly anisotropic shapes and cell-cell and cell-matrix interactions are usually highly specific. In addition, cells exhibit a wide range of phenomena like adhesion, migration, growth, division, chemotaxis etc. To incorporate these phenomena, current and future research is focused on developing cellular automata and agent-based models.

REFERENCES

[1] Wood-Adams et al., Macromolecules, 33, 7489 (2000) [2] Shanbhag et al., Phys. Rev. Lett., 85, 1995502 (2001) [3] Kotov et al., Langmuir, 20(19) 7887 (2004)