Molecular Modelling of Polymers and Nanocomposites

Dr MARC MEUNIER
Principal Application Scientist & Fellow
BIOVIA, Cambridge, U.K.
Agenda

1. Multi-scale modelling
2. Polymer modelling
3. Epoxy Networks: modelling cross-linking reactions
4. Environmental Stress Cracking of polymers
5. Polymer Nanoparticles for Drug Delivery
BIOVIA provides a **scientific** collaborative environment for advanced biological, chemical and materials experiences. The sophisticated enterprise system of modelling, simulation, laboratory and quality management enables **innovation** for science-based industries.
Multi-Scale Simulations

Hybrid: *Mixture* (e.g. QM/MM)

Hierarchical: One method at a time going up (or down) scale

\[ E_{\text{tot}} = E_{\text{QM}} + E_{\text{MM}} + E_{\text{QMMM}} \]
Multiscale Modeling in Additive Manufacturing

- **Time (s)**
  - $10^{-12}$ to $10^{-9}$
  - $10^{-9}$ to $10^{-6}$
  - $10^{-6}$ to $10^{-3}$
  - $10^{-3}$ to $10^{0}$
  - $10^{0}$ to $10^{3}$

- **Length (m)**
  - $10^{-1}$ to $10^{-2}$
  - $10^{-2}$ to $10^{-3}$
  - $10^{-3}$ to $10^{-4}$
  - $10^{-4}$ to $10^{-5}$
  - $10^{-5}$ to $10^{-6}$
  - $10^{-6}$ to $10^{-7}$
  - $10^{-7}$ to $10^{-8}$
  - $10^{-8}$ to $10^{-9}$
  - $10^{-9}$ to $10^{-10}$

- **Materials Performance**
- **Constituent Bulk Properties**
- **Substance Microstructure**
- **Alloy Atomistic Structure**

- **Pure metal properties**
- **Mechanical/Thermal**

- **Alloy properties**
- **Mechanical/Thermal**

- **Phase diagram**

- **Process dependent structure**
  - Polycrystal/Phase transformation

- **Process induced structure**
  - Lepidic pattern

- **Materials**
  - **Performance**
  - **Constituent**
  - **Bulk**
  - **Properties**

- **Phase Field / Homogenization**

- **AM simulation**
  - **Material properties(1)**
  - **Material properties(2)**

- **Post-processing**
  - **Annealing**

- **Temperature profile**

- **BIOVIA Materials Studio**

- **SIMULIA Abaqus**
Predictive Materials Science

Molecular modelling tools allow for the simulation of chemicals and materials and to predict their properties and behaviour.

There is a wide variety of computational tools:

1. Visualization
2. Quantum Mechanics
3. Classical Mechanics
4. Mesoscale
5. Crystallisation
6. QSAR & Statistics…
POLYMERS MODELLING

- Comprehensive tools for model building and simulating
- Modelling bulk amorphous systems, mixtures, blends, liquid crystals, etc.
Polymer Builder

- Build Polymers from existing library of Repeat-Units or sketch your own.
- Build one or more chains, select Tacticity, Chain Length, etc.
- Then, use Monte-Carlo based approach to ‘mix’ models together (Additives, solvent, nanomaterials, etc.)
  - Build a new phase
  - Build ‘into’ an existing phase (“Packing”)
Atomistic Simulations

Atomistic Simulations: allows you to construct and characterize models of isolated chains or bulk polymers, either crystalline or amorphous, and predict key properties.

Applications include nanocomposites, coatings, lubricants, food packaging, gels, and adhesives...

LIMITS:

- Force fields are valid for a ‘limited’ type of material (e.g. organics or zeolites)
- Size of system ~ $10^4$ atoms or a few nanoseconds
COMPASS II Forcefield

- Extensions to COMPASS (I) include:
  - Maybridge screening database
    - Heterocyclics, sulphur containing molecules
  - Ionic liquids
    - NIST database
  - Improved parameters for oximes, azo bonds etc.

- Maintains quality of original forcefield

- Developed in collaboration with Prof Huai Sun (SJTU)

SOLUBILITY PREDICTION

Group Contributions:

\[ \log S = \sum a_i n_i + a_0 \]
Building Polymer Networks

Step 1: Build a 3D model of the mixture

Step 2: Allow for cross-linking reactions to happen whilst running successive MD simulations
Given the structure of a base resin and a curing agent molecule, the following steps will be performed:

1. Create an amorphous cell containing the specified loading for base resin and curing agent molecules.
2. Allow the reactive sites in the molecules to react during a dynamic simulation up to the specified conversion.
3. Analyze the data for the density versus conversion and cycle number.

The base resin is an oligomer (prepolymer) containing two or more reactive sites such as epoxide rings. The curing agent, also known as hardener or cross-linker, is typically a small polyfunctional molecule that reacts with the resin to form a polymer network. In addition, a solvent can be added to the reacting system.

The reactive sites on the resin and the curing agent must be specified in the input structures before they can be used in the protocol. This is done by assigning a unique name to the primary atom in each functional group, for example, N1 for nitrogen atoms in a primary amine group. All names should be listed in the Species parameter, so they can be used to define reactions. The Species list can also contain names of intermediate groups, such as secondary amines. A default species X indicates an unreactive atom and should not be used to define reactive atoms.

Different types of reactions may be specified:
- Ring-opening: A reaction in which a ring is opened by breaking a ring bond.
- Addition: A reaction in which a double bond is reduced to a single bond.
- Condensation: A reaction in which a bond with a small functional group is broken, leaving a condensation product.

For each reaction, a probability can be specified as a number between 0 and 1. This can be used to express a difference in activation energies.
At 55% conversion…

Other ‘networks’

Unreacted Epoxy ring
Primary Amine
Crosslinked Epoxy
Tertiary Amine
Secondary Amine
Environmental Stress Cracking of Polymers

- Environmental Stress Cracking (ESC) is one of the most common causes of unexpected brittle failure of thermoplastic (especially amorphous) polymers.

- ESC is linked to the polymer Moduli:
  - elastic: \( E = 3K(1-2\nu) \) and
  - bulk \( K = \frac{8.04(e_{coh} + x_c\Delta H_m)}{V} \)

- So that, \( E \sim \frac{e_{coh}}{V} = \delta_{HIL} \)

- “the solubility parameter affects both the modulus and the surface energy and has a major role in ESC mechanism”

ESC of Polymers

- Atomistic simulations (MD) allow for the computation of:
  - Free Volume
  - Fluids Diffusion
  - Solubility parameters (w%) 
  - Solvation Free Energies

- "a general efficiency approach that combines all results into a single efficiency number could distinguish between an ESC fluid and a non ESC fluid in all the systems tested"
In silico modelling to predict drug affinity to PLA-PEG nanoparticle core

- Intended to be a “virtual screening” for potential drug
- Focus only on non-covalent encapsulation.

M. Meunier*, A. Goupil** and P. Lienard*

* Dassault Systèmes Biovia, 334 Milton Road Science Park, Cambridge CB4 0WN U.K.

** Dassault Systèmes Biovia, 10, rue Marcel Dassault, Velizy-Villacoublay 78140 France

& Sanofi. 13 Quai Jules Guesde, 94400 Vitry-sur-Seine, France

M. Meunier, A. Goupil and P. Lienard. Predicting drug loading in PLA-PEG nanoparticles. To be submitted.
Methodology

- Literature analysis reports many predictive approaches:
  1. Combination of molecular dynamics simulations and docking (Monte-Carlo)

2. Using Solubility parameters:
   1. Flory-Huggins Chi ($\chi$) parameter calculation
   \[ \chi = \frac{V}{RT} (\delta_i - \delta_j)^2 \]
   2. Hansen Solubility Parameters
   \[ \delta^2 = \delta_D^2 + \delta_P^2 + \delta_H^2 \]
   \[ (Ra)^2 = 4(\delta_{d2} - \delta_{d1})^2 + (\delta_{p2} - \delta_{p1})^2 + (\delta_{h2} - \delta_{h1})^2 \]

3. QSAR
   1. Log P

- Compare results from different simulations methods with experimental results of drug loading
More Information
Multiscale modeling of nanomaterials: recent developments and future prospects

G. Fitzgerald¹, J. Delboeuf², M. Meunier³
¹Accelrys, Inc., San Diego, CA, USA; ²Accelrys, Inc., Burlington, MA, USA; ³Accelys Limited, Cambridge, UK
## Extended Mechanical Properties

- **Constant Strain**
  - Apply several different small finite strains, measure stress
  - Plot stress Vs strain
- **Static method (using Hessian)**
  - Assumes that energy is quadratic in neighbourhood of current configuration
  - Faster than constant strain
  - Requires well optimized structure
- **Stress fluctuation**
  - Relates stiffness tensor to fluctuations in stress
  - NVE - adiabatic elastic constants
  - NVT – isothermal elastic constant
  - Requires trajectory
**Glass Transition Temperature Prediction**

- The glass transition temperature ($T_g$) of an amorphous solid is a critical physical property which can dramatically influence its physical stability and viscoelasticity properties.
- Study the effect of humidity on $T_g$ (water acting as a plasticizer).