Molecular Modelling of Polymers and Nanocomposites

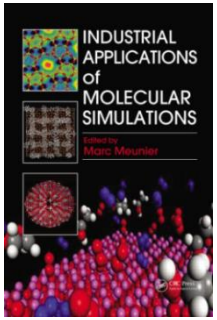
Dr MARC MEUNIER
Principal Application Scientist & Fellow
BIOVIA, Cambridge, U.K.

3DEXPERIENCE

BIOVIA

DASSAULT SYSTEMES | The 3DEXPERIENCE Company

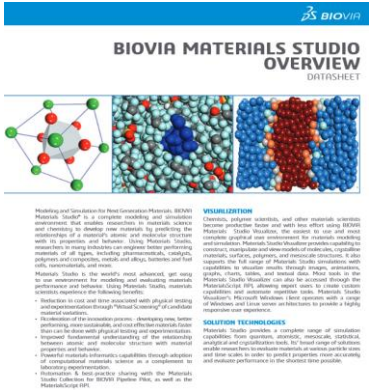
Agenda



	Dassault Systèmes BIOVIA
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

| Virtual BioSphere and Materials

accelrys® becomes BIOVIA

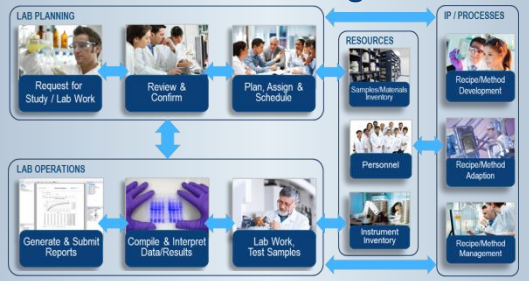


BIOVIA provides a **scientific** collaborative environment for advanced biological, chemical and materials experiences.
The sophisticated enterprise system of modelling, simulation, laboratory and quality management enables **innovation** for science-based industries.

The Laboratory Workflow

BIOVIA

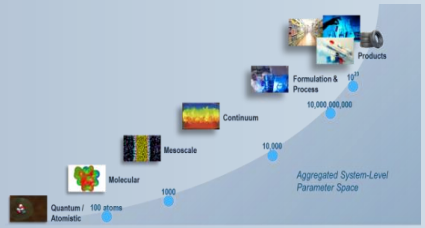
Unified Lab Management



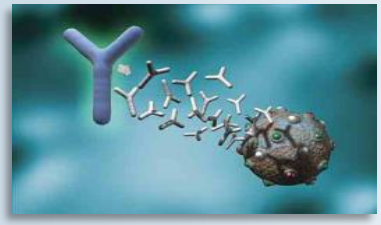
Process Production Operations

Quality and Regulatory

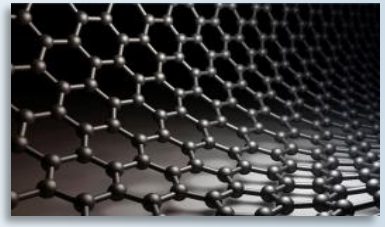
Collaborative Science



Predictive Models

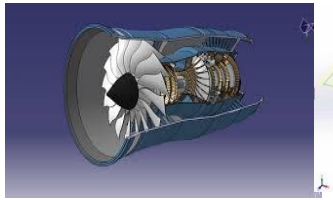


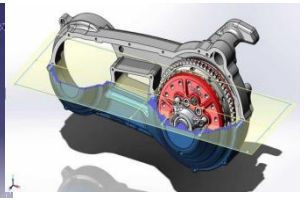
Novel Therapeutics

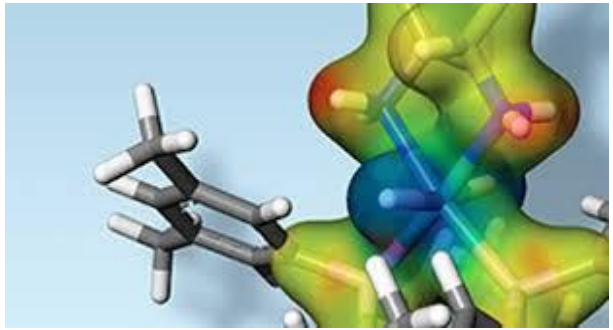


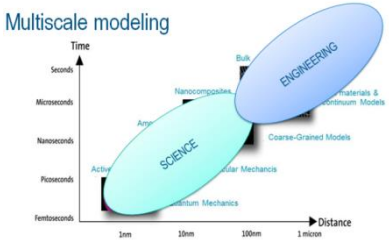
Engineered Materials

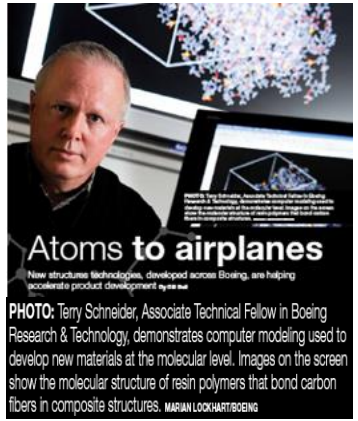
Chemicals & Formulations



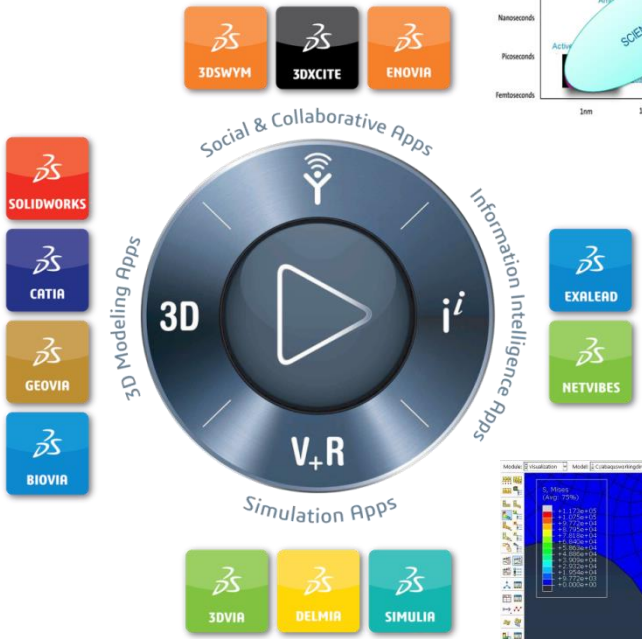


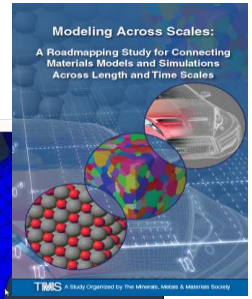


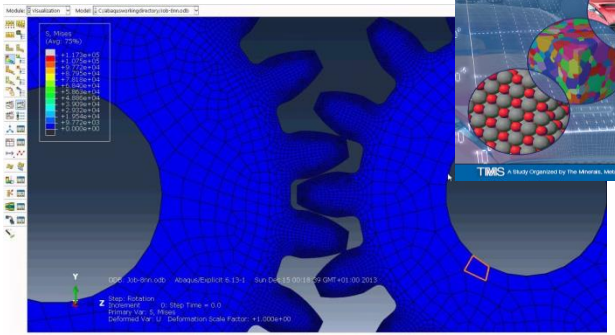


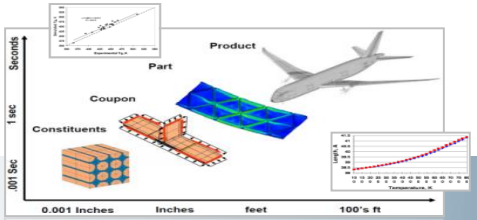


BOEING Frontiers 2010









BIOVIA

DASSAULT SYSTEMES | The 3DEXPERIENCE Company

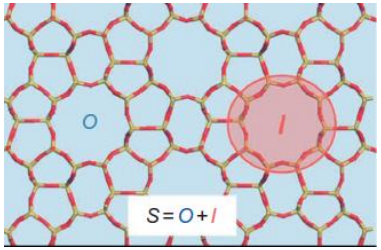
Multi-Scale Simulations

The Nobel Prize in Chemistry 2013

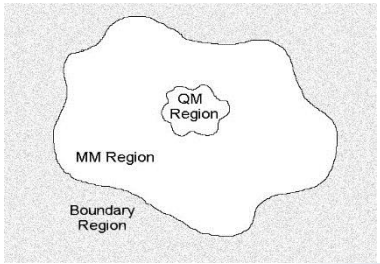
Martin Karplus, Michael Levitt and Arieh Warshel

"for the development of multiscale models for complex chemical systems"

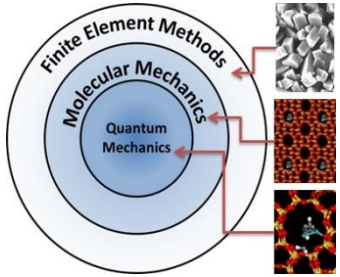
Hybrid: *Mixture* (e.g. QM/MM)

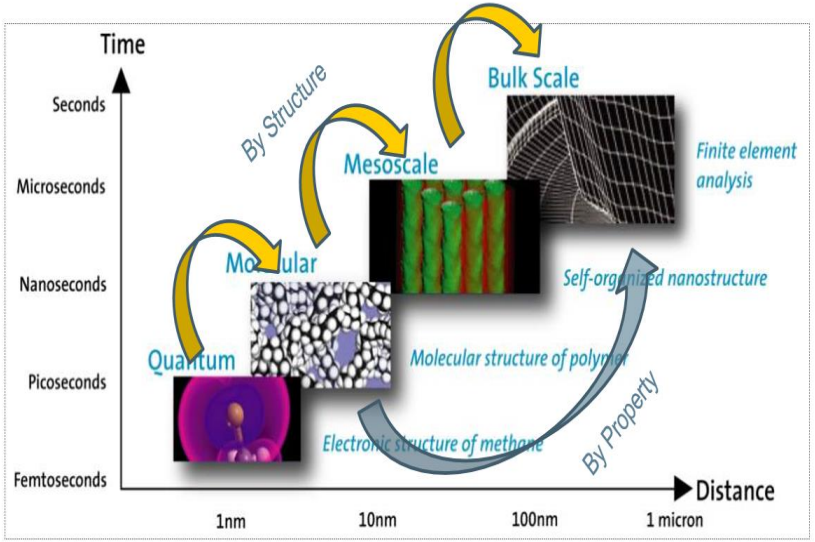


$$E_{tot} = E_{QM} + E_{MM} + E_{QMMM}$$



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





Multiscale modeling of nanomaterials: recent developments and future prospects

1

G. Fitzgerald[1], J. DeJoannis[2], M. Meunier[3]

[1]Accelrys, Inc., San Diego, CA, USA; [2]Accelrys, Inc., Burlington, MA, USA; [3]Accelrys Limited, Cambridge, UK

Multiscale Modeling in Additive Manufacturing

Time(s)

10^{3}

10^{0}

10^{-3}

10^{-6}

10^{-9}

10^{-12}

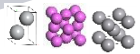
Alloy Atomistic Structure

Substance Microstructure

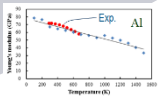
Constituent Bulk Properties

Materials Performance

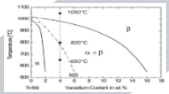
Pure metal properties
- Mechanical/Thermal



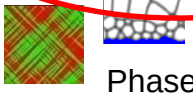
Alloy properties
- Mechanical/Thermal



Phase diagram



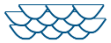
Process dependent structure
- Polycrystal/Phase transformation

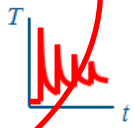


Phase Field / Homogenization

Material properties(1)

Process induced structure
- Lepidic pattern

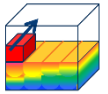


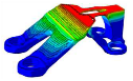


Temperature profile

Material properties(2)

AM simulation





Post-processing
- Annealing

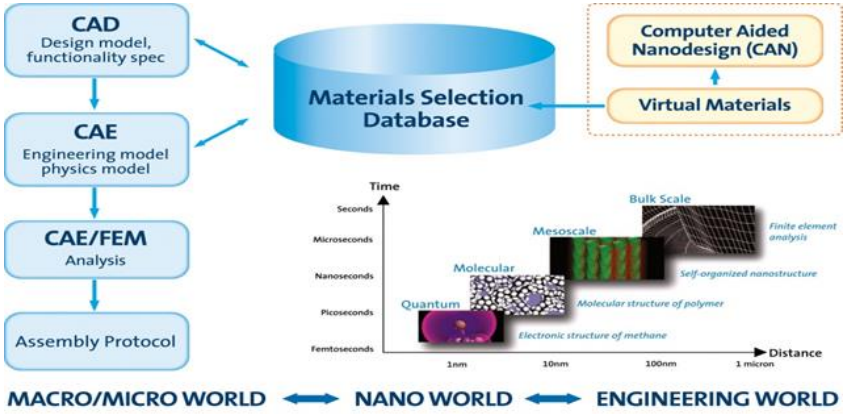
SIMULIA Abaqus

BIOVIA Materials Studio

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

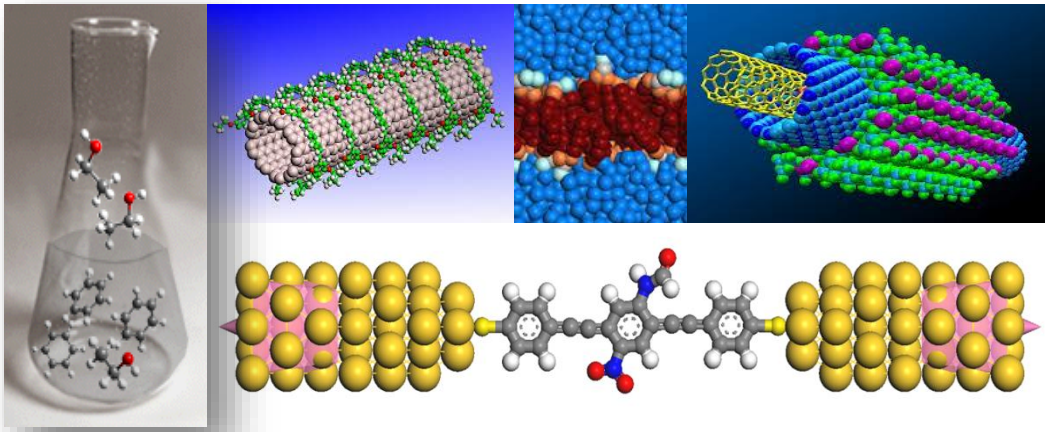
Predictive Materials Science

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



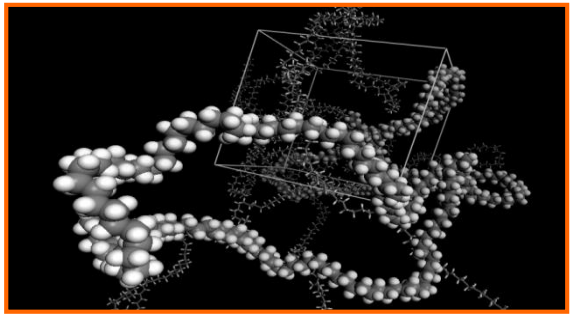
There is a wide variety of computational tools:

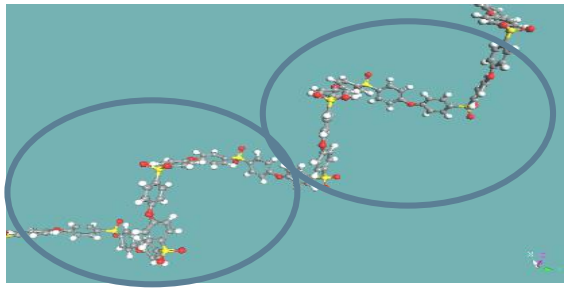
1. Visualization
2. Quantum Mechanics
3. Classical Mechanics
4. Mesoscale
5. Crystallisation
6. QSAR & Statistics…

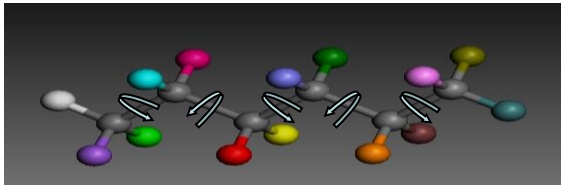


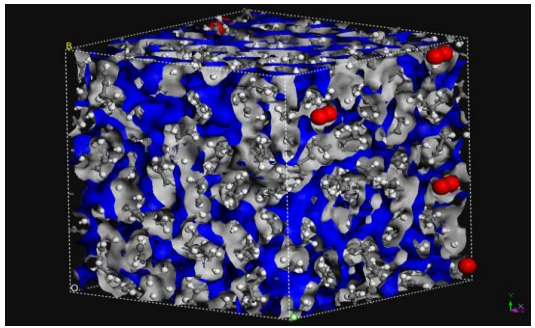
POLYMERS MODELLING

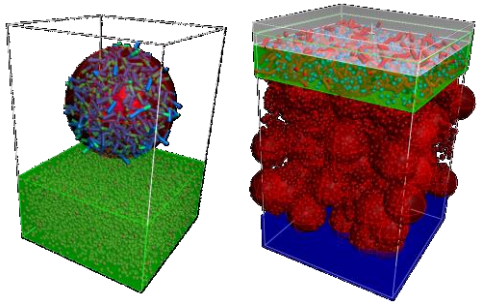
- Comprehensive tools for model building and simulating
- Modelling bulk amorphous systems, mixtures, blends, liquid crystals, etc.

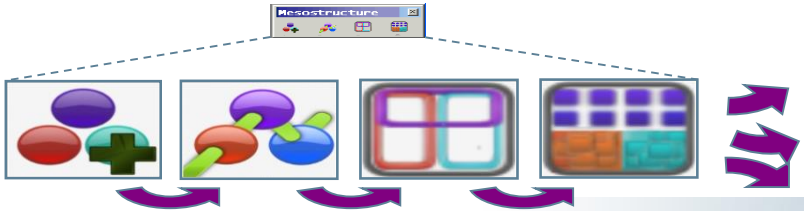




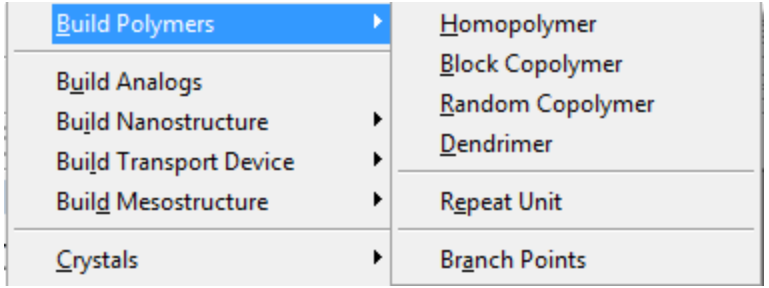






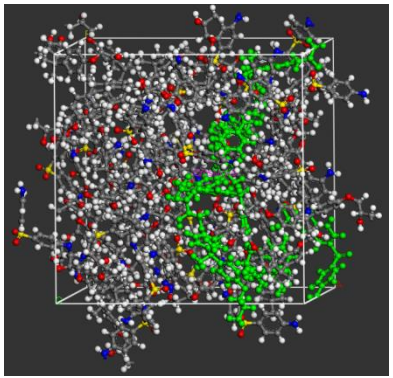


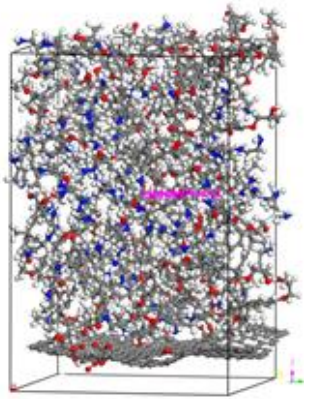
Polymer Builder



- 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**”)





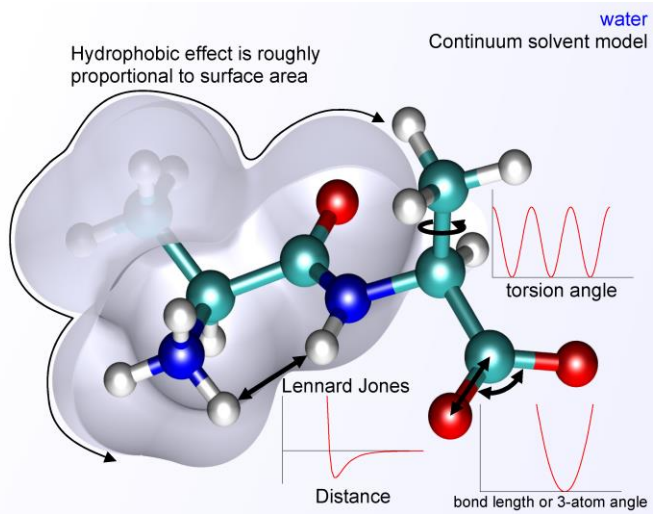
Atomistic Simulations

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

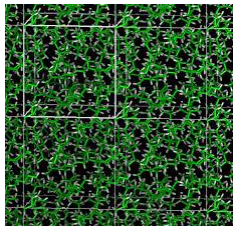
Applications include nanocomposites, coatings, lubricants, food packaging, gels, and adhesives…

LIMITS:

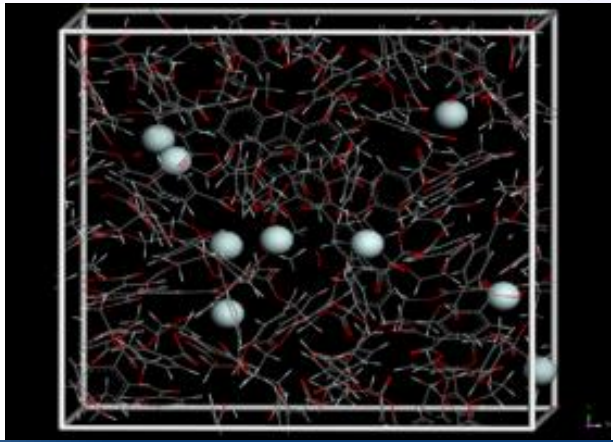
- Force fields are valid for a 'limited' type of material (e.g. organics or zeolites)
- Size of system ~ 10^4 atoms or a few nanoseconds



$$V(R) = \sum_b D_b\left[1 - e^{-a(b-b_0)}\right]^2 + \sum_\theta H_\theta(\theta-\theta_0)^2 + \sum_\phi H_\phi[1 - s\cos(n\phi)] + \sum_\chi H_\chi\chi^2 + \sum_b\sum_{b'} F_{bb'}(b-b_0)(b'-b'_0) + \sum_\theta\sum_{\theta'} F_{\theta\theta'}(\theta-\theta_0)(\theta'-\theta'_0) + \sum_b\sum_\theta F_{b\theta}(b-b_0)(\theta-\theta_0) + \sum_\phi F_{\phi\theta\theta'}\cos(\theta-\theta_0)(\theta'-\theta'_0) + \sum_\chi\sum_{\chi'} F_{\chi\chi'}\chi\chi' + \sum_i\sum_{j>i}\left[\frac{A_{ij}}{r_{ij}^{12}} - \frac{B_{ij}}{r_{ij}^{6}} - \frac{q_i q_j}{r_{ij}}\right]$$



$$-\frac{dV}{dr_i} = m_i\frac{d^2r_i}{dt^2}$$



COMPASS II Forcefield

J Mol Model (2016) 22:47
DOI 10.1007/s00894-016-2909-0

ORIGINAL PAPER

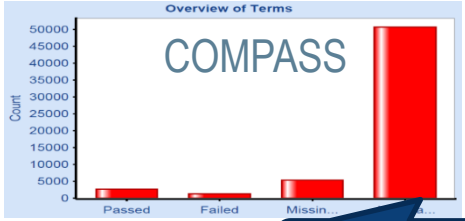
COMPASS II: extended coverage for polymer and drug-like molecule databases

Huai Sun[1] · Zhao Jin[1] · Chunwei Yang[1] · Reinier L. C. Akkermans[2] · Struan H. Robertson[2] · Neil A. Spenley[2] · Simon Miller[2] · Stephen M. Todd[2]

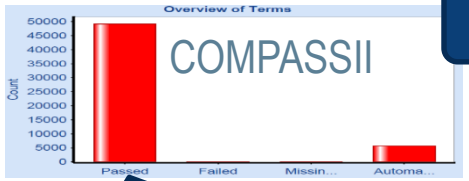
- Extensions to COMPASS (I) include:
  - Maybridge screening database
    - Heterocyclics, sulphur containing molecules
  - Ionic liquids
    - NIST database
  - Improved parameters for oximes, azo bonds etc.
- Maintains quality of original forcefield
- Developed in collaboration with Prof Huai Sun (SJTU)

COMPASS force field (J Phys Chem B 102(38):7338–7364, 1998)

Maybridge Screening DB



Unknown quality parameters



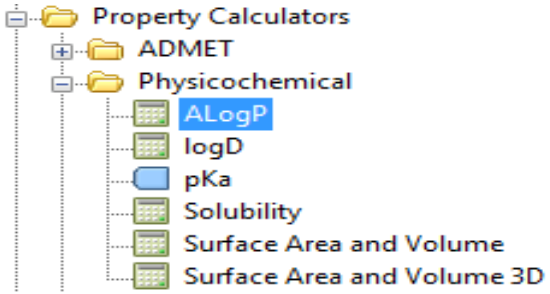
Fully parameterized

Table 1
Theoretical methods used for the calculation of physicochemical properties of compounds

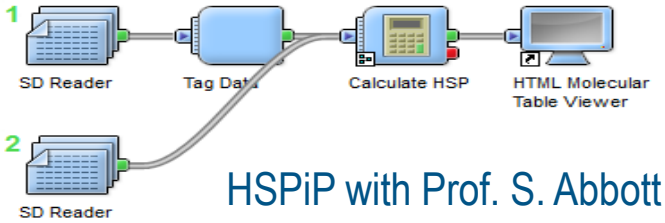
Theoretical relations	Component symbols	Refs
Solubility parameter		31,48
$^{a}HIL = \frac{E_{coh}}{V} = \sqrt{CED}$ (1a)	δ_{HIL}, Hildebrand solubility parameter E_{coh}, cohesive energy V, total volume CED, cohesive energy density	
$^{a}HAN = \left(\delta_d^2 + \delta_p^2 + \delta_h^2\right)$ (1b)	δ_{HAN}, Hansen solubility parameter δ_d, partial dispersion component δ_p, partial dipole-dipole component δ_h, partial hydrogen-bonding component	49
$4(\delta_{d1}-\delta_{d2})^2 + (\delta_{p1}-\delta_{p2})^2 + (\delta_{h1}-\delta_{h2})^2 \le R_0^2$ (1c)	R_0, radius of interaction sphere in Hansen space 1 or 2 – (subscript) indicates compound 1 or 2, respectively	
$\delta = \frac{E_{coh}}{V} = \frac{(E_{vac}-E_{bulk})C}{V} = \sqrt{CED}$ (1d)	δ, solubility parameter E_{coh}, cohesive energy E_{vac}, energy of molecule in vacuum state E_{bulk}, energy of molecule in amorphous state V, total volume C, unit conversion factor CED, cohesive energy density	31
Flory-Huggins interaction parameter		
$\chi_{FH} = \frac{\Delta H_{mix}}{kTN_1\phi_2}$ (2a)	χ_{FH}, Flory-Huggins interaction parameter ΔH_{mix}, enthalpy change upon creation of a binary mixture k, Boltzmann constant. T, absolute temperature N_1, number of molecules of solvent φ_2, volume fraction of polymer	55
$\chi_{FH} = \frac{V_{ref}(\phi_1 CED_1 + \phi_2 CED_2 - CED_{12})}{RT}$ (2b)	χ_{FH} – Flory-Huggins interaction parameter V_{ref} – molar volume of the smaller molecule in the binary mixture φ_i – volume fraction of compound i in the binary mixture CED – cohesive energy density 1 or 2 – (subscript) indicates compound 1 or 2, respectively	58,59
$\chi_{FH} = \frac{VA_{12}}{RT} + \beta$ (2c) $A_{12} = (\delta_1 - \delta_2)^2$ or $A_{12} = (\delta_{d1} - \delta_{d2})^2 + 0.25(\delta_{p1} - \delta_{p2})^2 + 0.25(\delta_{h1} - \delta_{h2})^2$ β = 0 or 0.34 when Hansen and Hildebrand solubility parameters are used, respectively	χ_{FH} – Flory-Huggins interaction parameter V – the molar volume of the solute R – gas constant T – absolute temperature δ_i – Hildebrand solubility parameter of compound i δ_d – partial dispersion component (Hansen) δ_p – partial dipole-dipole component (Hansen) δ_h – partial hydrogen-bonding component (Hansen) β – correction to the Flory combinatorial entropy 1 or 2 – (subscript) indicates compound 1 or 2, respectively	31,49, 55
Enthalpy		
$\Delta H_{mix} = \chi_{FH} RT \phi_1 \phi_2$ $\Delta H_{mix} = H_{12} - n_1 H_1 - n_2 H_2$ (2d)	ΔH_{mix}, enthalpy change upon creation of a binary mixture χ_{FH}, Flory-Huggins interaction parameter R, gas constant T, absolute temperature φ_1, volume fraction of component i n_1, mole fraction of component i H_1, enthalpy of component i at pure-state H_{12}, enthalpy of mixture of component 1 and 2 1 or 2 – (subscript) indicates compound 1 or 2, respectively	53, 55-57
Lipophilicity		
$\log P = \sum_{i=1}^{n} a_i \cdot f_i + \sum_{i=1}^{M} k_i \cdot C_m$ (3)	P, partition coefficient n, functional groups of the molecule f_i, hydrophobic fragmental constant a_i, incidence of functional group Cm, the Correction factor (CM = 0.219) K_i, the frequency of Cm	28,65,66
Radius		
Flory's theory: $R_g = \frac{R}{\sqrt{6}}$, where : $R = aN^{\alpha}$ (4)	R_g, radius of gyration of linear polymer R, end-to-end distance a, bond length of monomer N, degree of polymerization of polymer α, swelling exponent	55,70

SOLUBILITY PREDICTION

Group Contributions:
$\log S = \Sigma a_i n_i + a_0$

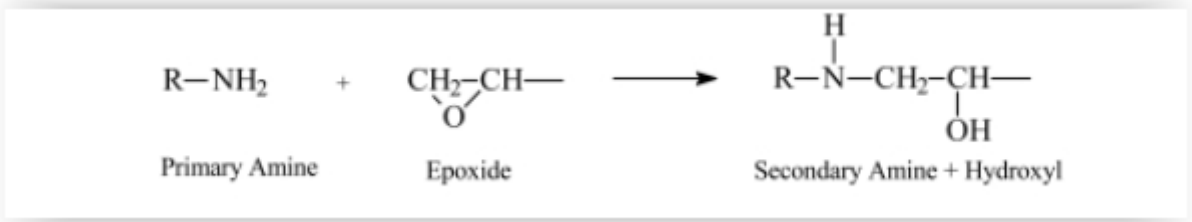


PP Chemistry Collection



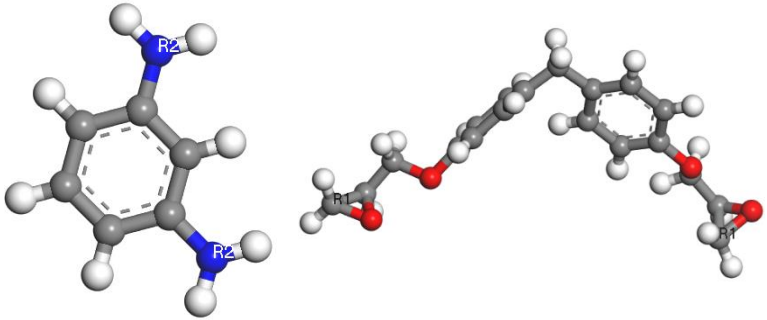
HSPiP with Prof. S. Abbott

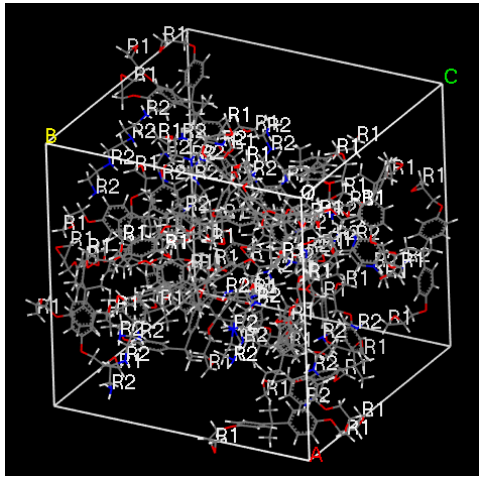
Building Polymer Networks

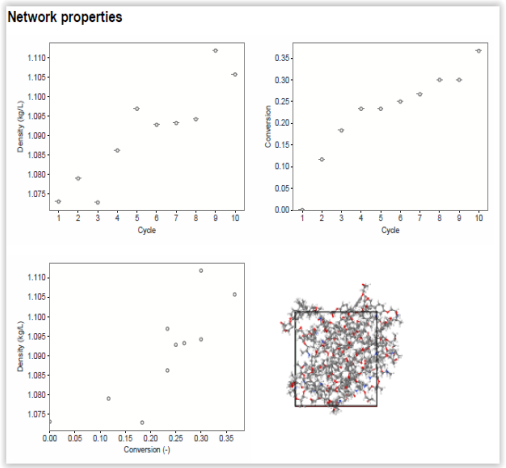


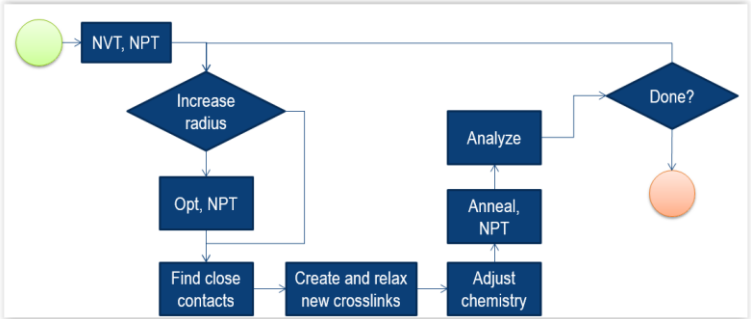
Step 1: Build a 3D model of the mixture

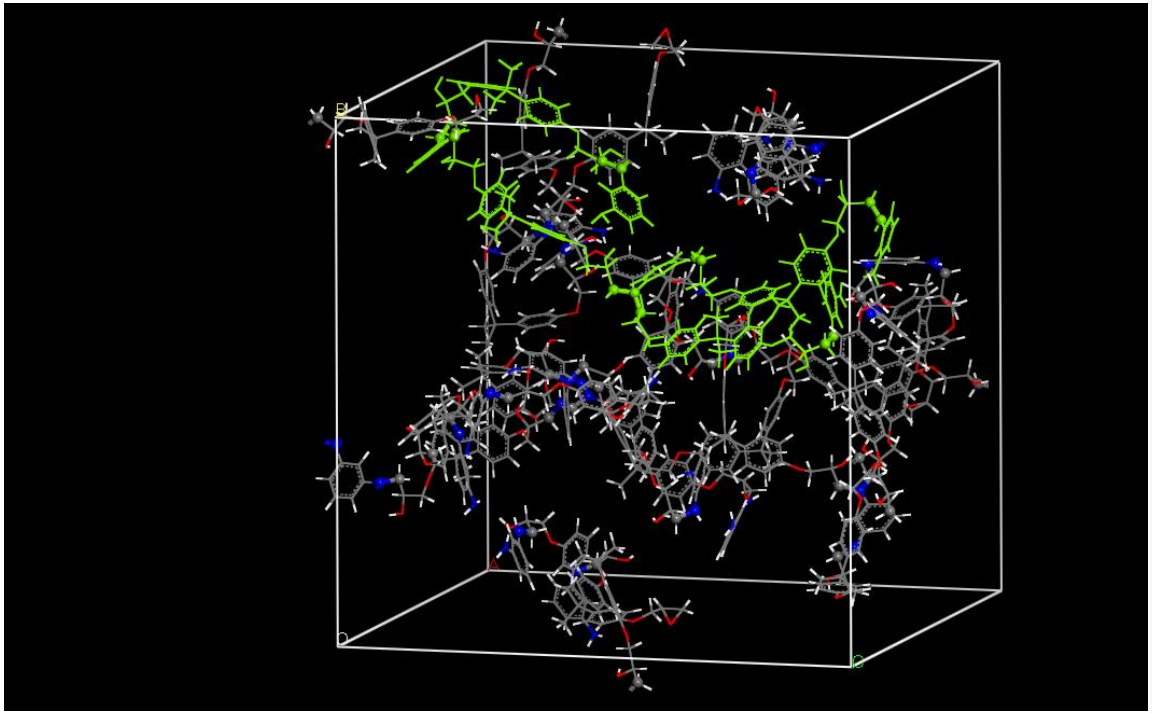
Step 2: Allow for cross-linking reactions to happen whilst running successive MDs simulations

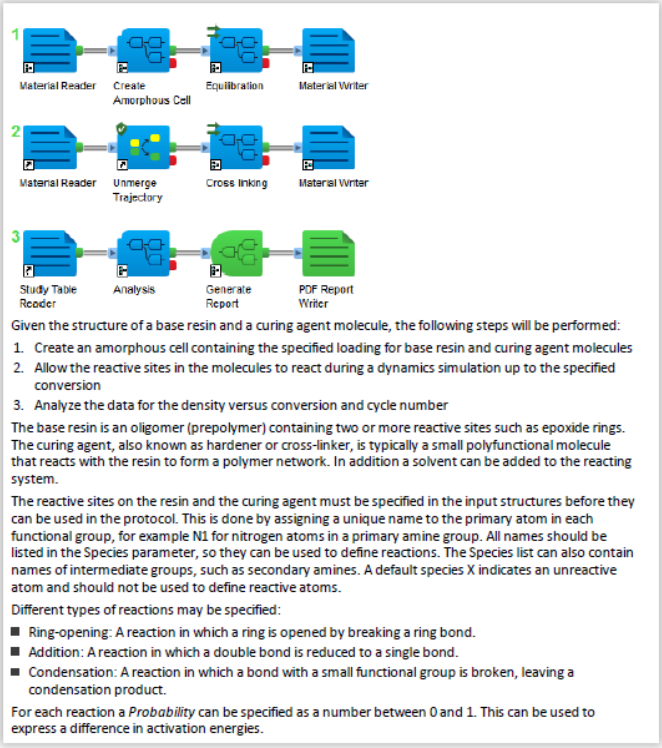












Given the structure of a base resin and a curing agent molecule, the following steps will be performed:

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 dynamics 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:

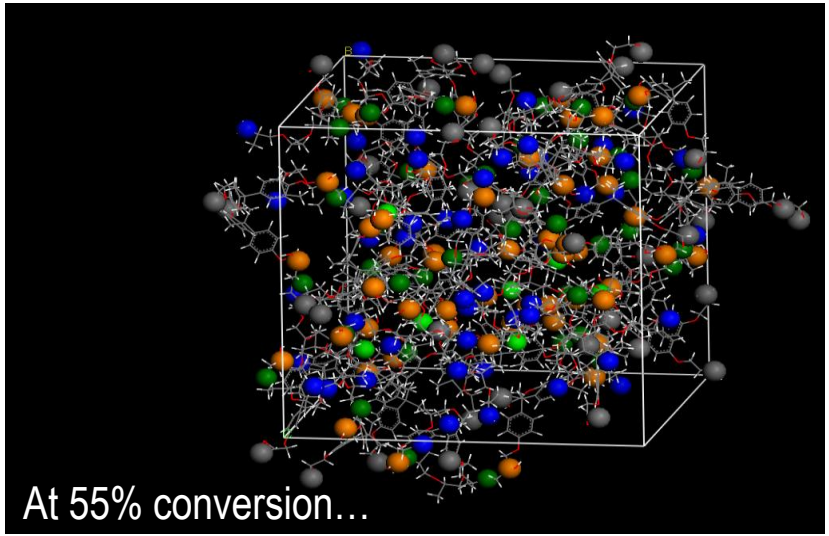
- Ring-opening: A reaction in which a ring is opened by breaking a ring bond.
- Addition: A reaction in which a double bond is reduced to a single bond.
- Condensation: A reaction in which a bond with a small functional group is broken, leaving a condensation product.

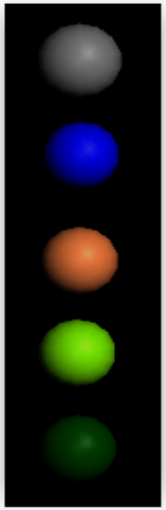
For each reaction a *Probability* can be specified as a number between 0 and 1. This can be used to express a difference in activation energies.

SIMULATING THE CURING OF AN EPOXY POLYMER NETWORK

BIOVIA MATERIALS STUDIO

[Polymer Network]





Unreacted Epoxy ring

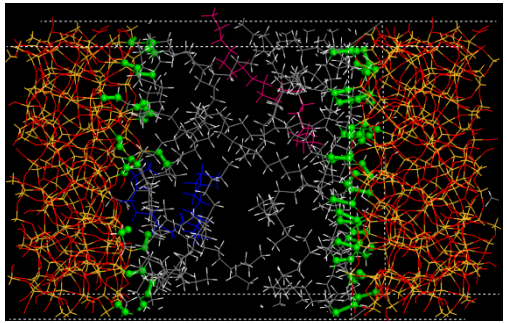
Primary Amine

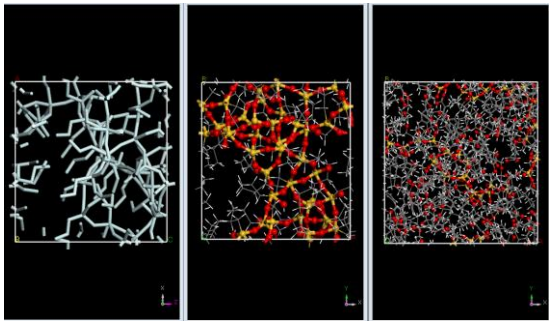
Crosslinked Epoxy

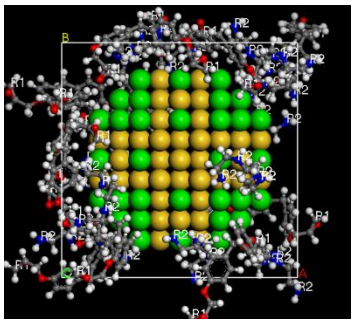
Tertiary Amine

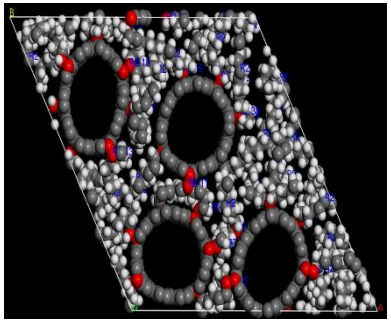
Secondary Amine

Other ‘networks’









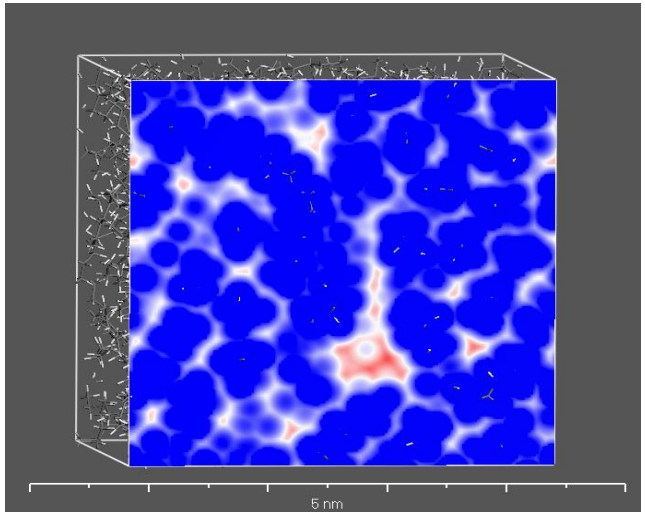
Environmental Stress Cracking of Polymers

- 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(1-2v) and
  - bulk $K = \frac{8.04(e_{coh}+x_c\Delta H_m)}{V}$
- So that, $E \sim e_{coh} / V = \delta_{HIL}$
- “the solubility parameter affects both the modulus and the surface energy and has a major role in ESC mechanism”

D. Alperstein and M. Meunier. *Atomistic simulations of environmental stress cracking in polymers. Molecular Simulation, ICMS 2016 Special Issue – submitted.*

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"*



Polyethylene model with water (1.2 wt%) - free volume display (2D slice, blue is highly dense, red: low density or free volume).

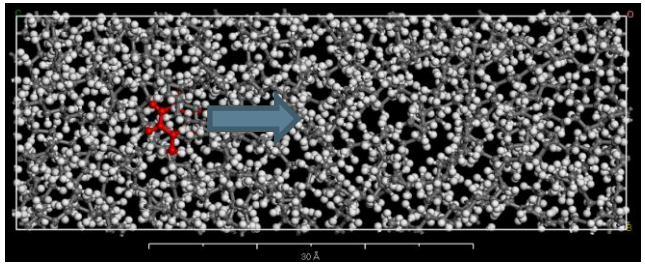


Figure 2: Toluene molecule (red) in amorphous PE, the blue arrow indicates the direction of the applied external force.

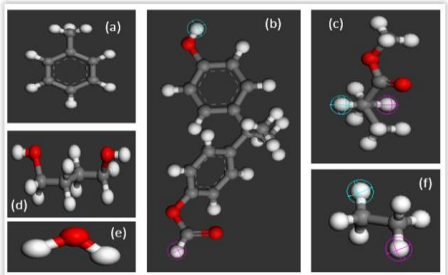


Figure 1: Atomistic models used in the simulations: (a) Toluene (b) PC repeat unit (c) PMMA repeat unit (d) 1,4 Butane diol (e) Water (f) Polyethylene repeat unit.

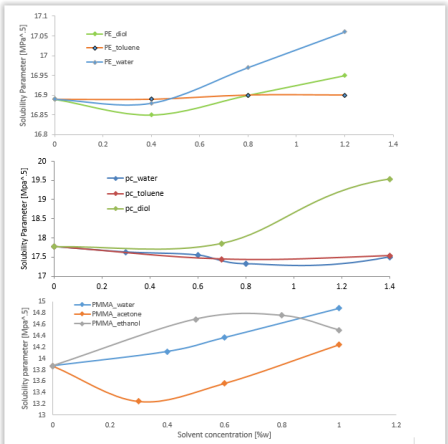
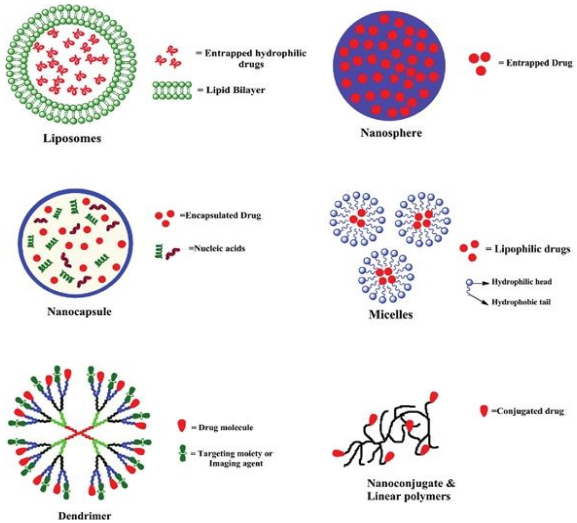


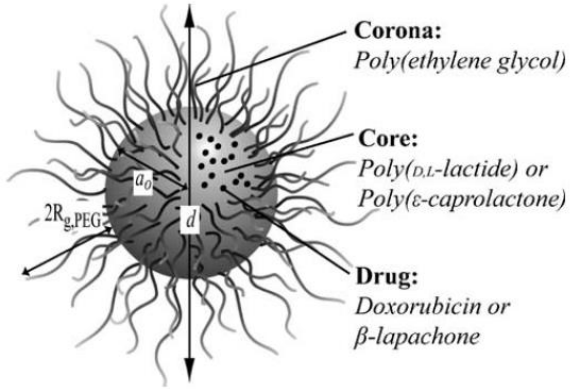
Figure 3: Solubility parameters of the polymer-ESC fluids mixtures versus ESC fluids concentration (wt%).

D. Alperstein and M. Meunier. *Atomistic simulations of environmental stress cracking in polymers. Molecular Simulation, ICMS 2016 Special Issue – submitted.*

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.





Predicting drug loading in PLA-PEG nanoparticles

M. Meunier*[1], 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

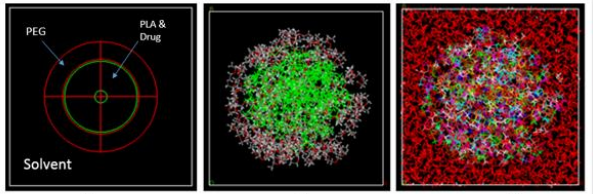


Figure 2: Schematic display of the PLA-PEG nanoparticle (a) micelles regions (b) unsolvated atomistic micelle model (c) solvated atomistic micelle model.

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

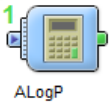
Methodology

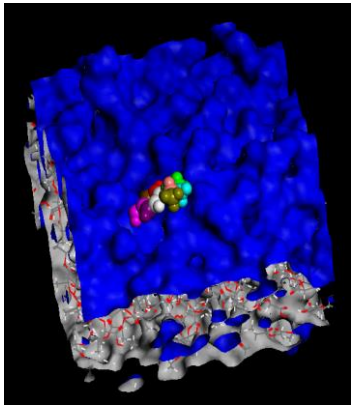
- **Literature analysis reports many predictive approaches:**
  1. Combination of molecular dynamics simulations and docking (Monte-Carlo)
  2. Using Solubility parameters: $\delta = \sqrt{\frac{\Delta H_v - RT}{V_m}}$
     1. Flory-Huggins Chi (χ) parameter calculation $\chi = \frac{V}{RT}(\delta_i - \delta_j)^2$
     2. Hansen Solubility Parameters

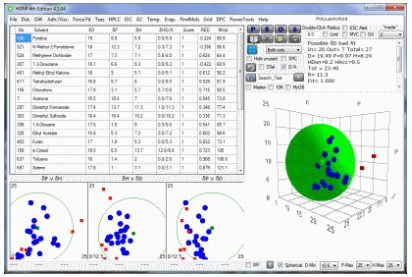
$$\delta^2 = \delta_D^2 + \delta_P^2 + \delta_H^2$$

$$(Ra)^2 = 4(\delta_{d2} - \delta_{d1})^2 + (\delta_{p2} - \delta_{p1})^2 + (\delta_{h2} - \delta_{h1})^2$$

  3. QSAR
     1. Log P





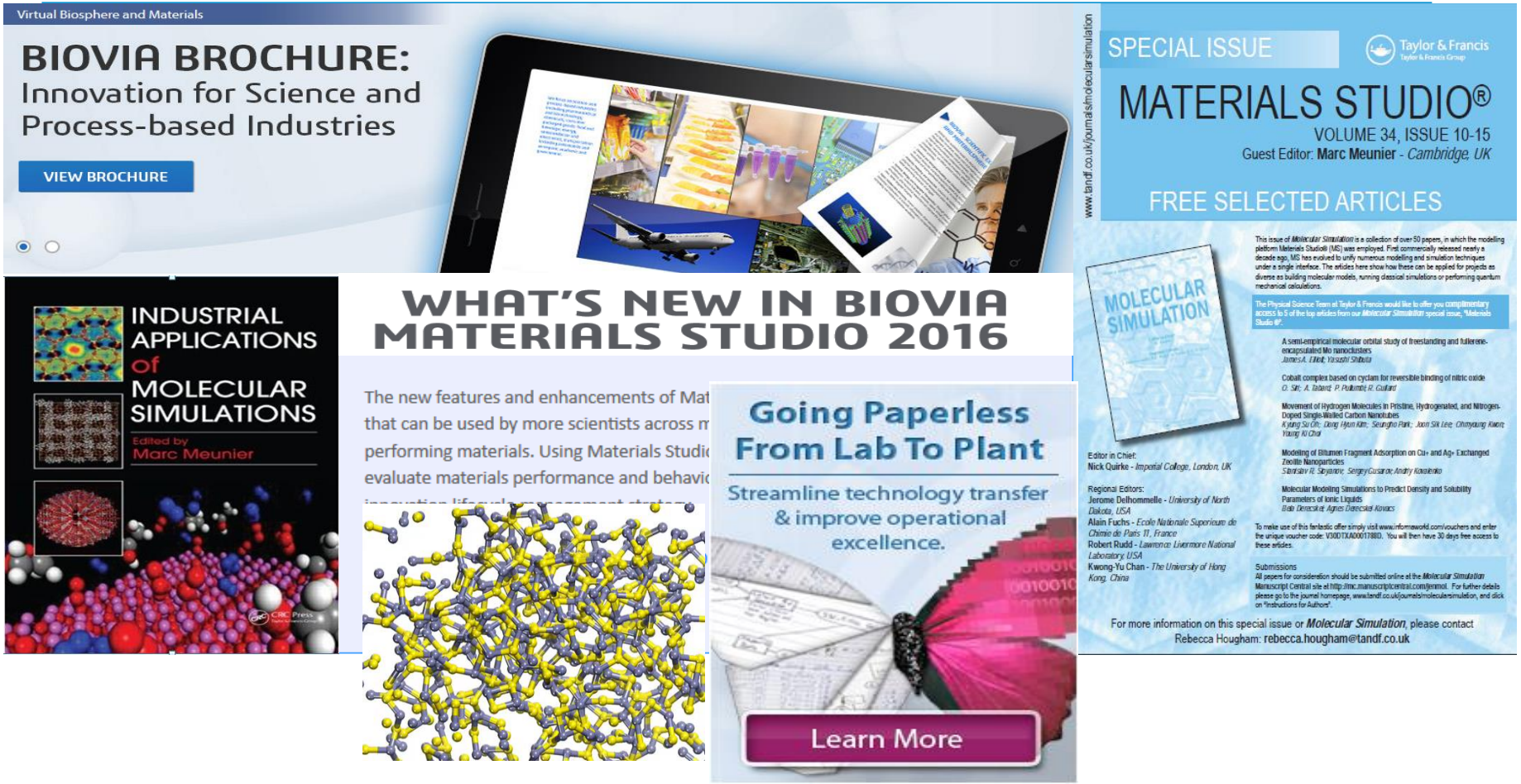


HSPiP

- **Compare results from different simulations methods with experimental results of drug loading**

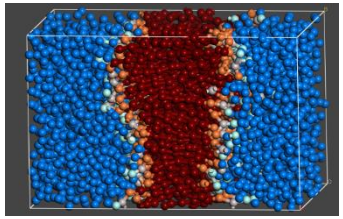
More Information

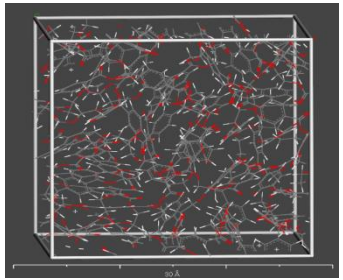
www.accelrys.com

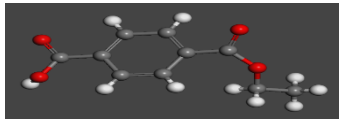


Multiscale modeling of nanomaterials: recent developments and future prospects

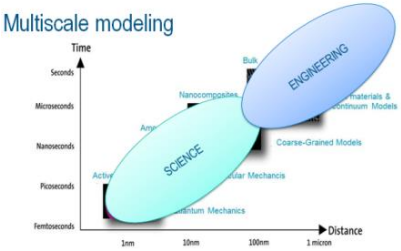
G. Fitzgerald[1], *J. DeJoannis*[2], *M. Meunier*[3]
[1]Accelrys, Inc., San Diego, CA, USA; [2]Accelrys, Inc., Burlington, MA, USA; [3]Accelrys Limited, Cambridge, UK

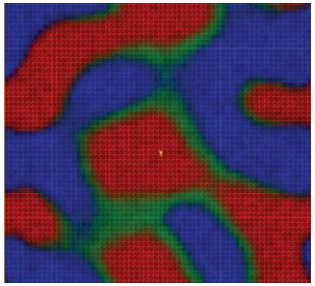


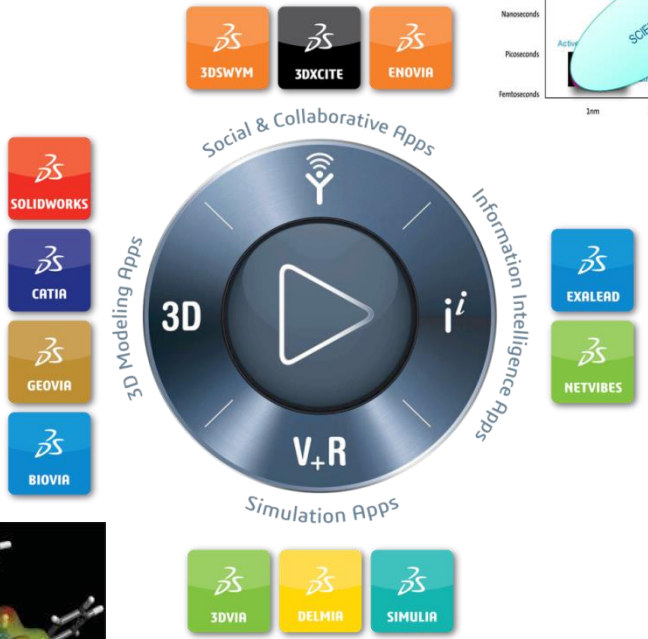


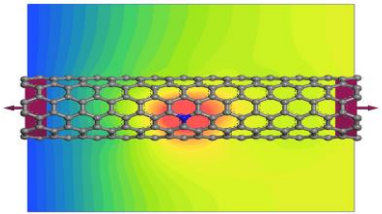


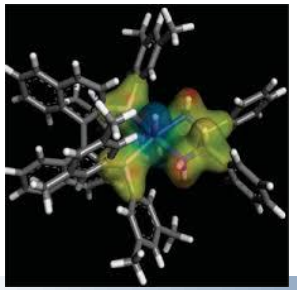
1 Multi-Scale at DS BIOVIA

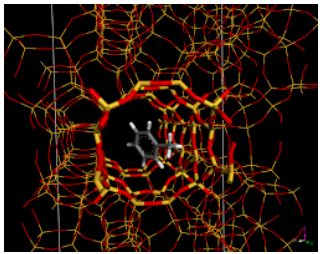












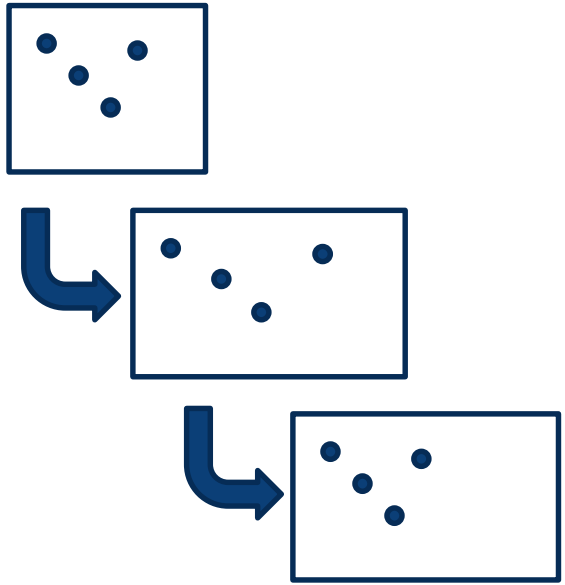
Extended Mechanical Properties

- 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]

0K

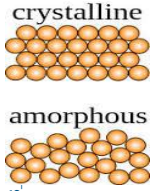
- Stress fluctuation
  - Relates stiffness tensor to fluctuations in stress
  - NVE - adiabatic elastic constants
  - NVT – isothermal elastic constant
  - Requires trajectory

>0K

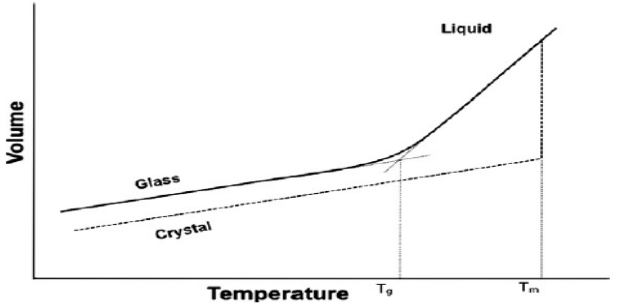


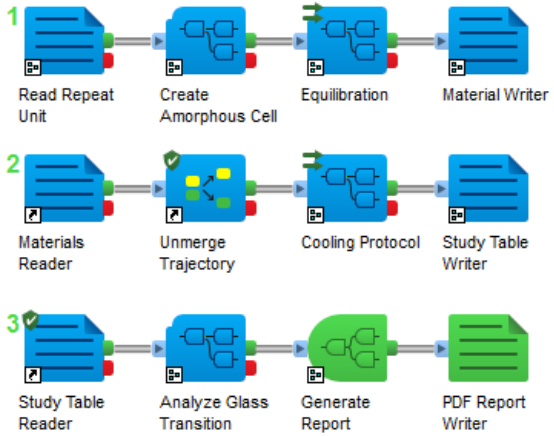
Energy and derivatives are recomputed by Mechanical Properties task. Hessian need not be precomputed (unlike Vibrational Analysis)

Glass Transition Temperature Prediction



- The glass transition temperature (Tg) 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 Tg (water acting as a plasticizer).





Dilatometric Analysis

Property	Value
Glass transition temperature (K)	534.07 ± 11.06
Specific volume at Tg (L/kg)	1.03 ± 0.29
Thermal expansion in glass state (1/10³K)	0.41 ± 0.72
Thermal expansion in rubber state (1/10³K)	3.24 ± 0.72
Transition temperature range (K)	2.68 ± 276.95