Construction of Equilibrium Structures of Biofunctional Amorphous Polymer Using Advanced Sampling Techniques

XF. Li and R. A. Latour

Department of Bioengineering, Clemson University, Clemson, SC 29634

Introduction

- Fundamental studies of the properties of biopolymers require the development of efficient computational methods that are able to handle the huge number of degrees of freedom in such systems in atomistic detail .
- We have developed efficient coarse graining and reverse mapping methods to equilibrate the structure of poly (DTB succinate) [1], poly (methyl MA), poly(butyl MA) and poly(D, L - lactide).
- We have developed a new accelerated sampling method, TIGER3, with which the effective speedup reaches well into the characteristic experimental regime.

Coarse Graining Models for Four Polymers

poly(methyl methacrylate)

poly(butyl methacrylate)

poly(D, L - lactide)

poly(DTB succinate)
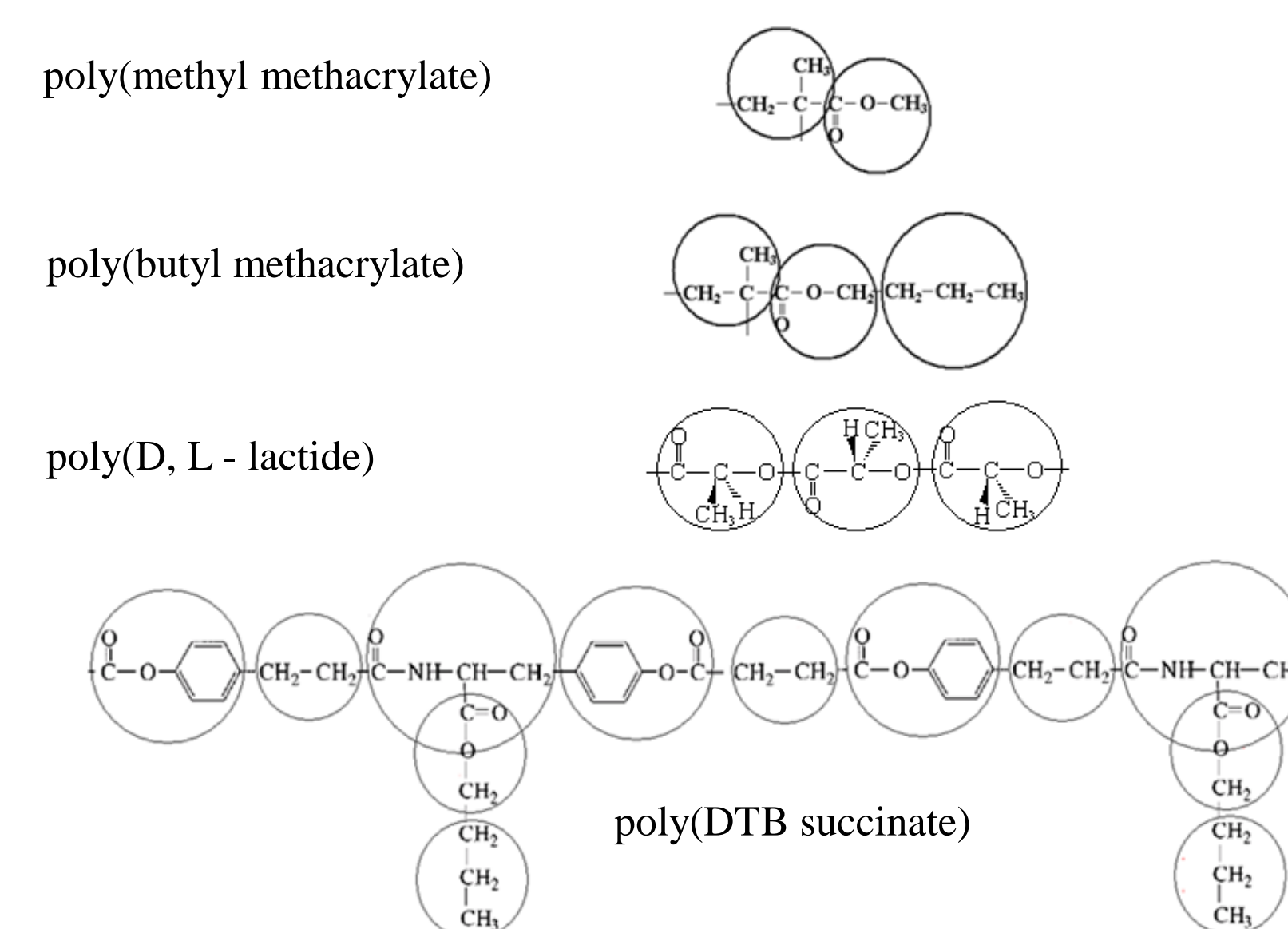
In a coarse graining scheme to map atomistic structure to coarse-grained structure, several atoms are considered as a simple "super-atom" and the interaction energies between super-atoms are obtained in an optimization procedure that reproduces the structural distribution between super-atoms, which is obtained from the atomistic simulations.

Figure 1. Illustration of the mapping method for the four polymers from the atomistic to the coarse grained level.

• Energy Terms Considered in Coarse Graining Procedure

$$E = E_{bonded} + E_{non-bonded} = E_{stretch} + E_{bend} + E_{torsion} + E_{VDW}$$

The potential terms optimized in the order of their relative strength $E_{stretch} \rightarrow E_{bend} \rightarrow E_{vdW} \rightarrow E_{torsion}$.

• Multicentered Gaussian Function for the Parameterization of Bond Stretching and Bending

$$P(x) = \frac{A_1}{w_1}\exp(\frac{-2(x-x_{c1})^2}{w_1^2}) + \frac{A_2}{w_2}\exp(\frac{-2(x-x_{c2})^2}{w_2^2}), \quad A_1, A_2, x_{c1}, x_{c2}, w_1, w_2 \text{ are parameters.}$$

$$E_{stretch} = k_B T\{K_1(x-x_{c1})^2 - \ln[1+K_3\exp[K_1(x-x_{c1})^2 - K_2(x-x_{c2})^2]]\}, \quad K_1=2/w_1^2, \quad K_2=2/w_2^2, \text{ and } K_3 = w_1 A_2/w_2 A_1.$$

• Parameterization of Torsional Interaction

$$E_{dihe}(\phi) = \sum_{n=1}^{3} K_n[1+\cos(n\phi-\delta_n)], \quad K_n \text{ and } \delta_n \text{ are parameters.}$$

• Radial Distribution Function for the Parameterization of van der Waals Interaction

$$E_{vdw} = \varepsilon_{ij}\left[2\left(\frac{\sigma_{ij}}{r_{ij}}\right)^9 - 3\left(\frac{\sigma_{ij}}{r_{ij}}\right)^6\right], \quad \varepsilon_{ij} = 2\sqrt{\varepsilon_i\varepsilon_j}\frac{\sigma_i^3\sigma_j^3}{\sigma_i^6+\sigma_j^6}, \quad \sigma_{ij} = \left(\frac{\sigma_i^6+\sigma_j^6}{2}\right)^{1/6}$$

Iterative Boltzmann-inversion of radial distribution function $g(r)$.

$$E(r) = -k_B T \ln g(r), \qquad E_{i+1}(r) = E_i(r) + k_B T \ln \frac{g_i(r)}{g(r)}$$

$$f = \int e^{-r}[g(r) - g_i(r)]^2 dr \qquad \text{(Convergence condition } f < 0.001)$$

TIGER3 Method

It is conducted in parallel with a number of replicas at different temperatures. Each TIGER3 cycle consists of (1) heating up to target temperature, (2) sampling at the target temperature with a Monte Carlo (MC) scheme with reduced vdW radii, (3) quenching to baseline temperature with recovered radii followed by a relaxation using a hybrid MC/MD scheme, and (4) randomly selecting a quenched replica and comparing it with the baseline replica (without adjustment of radii) based on the Metropolis criterion [2]. The rest of the quenched replicas are reassigned based on their energy levels.

The TIGER3 method leads to fast diffusion of chain segments within the dense system. In actual modeling works, we use a combined scheme of TIGER2 [3] (with normal vdW radii) and TIGER3 (with reduced vdW radii), for instance, a TIGER3 cycle is conducted after every 10 TIGER2 cycles. This scheme can further relax the high energy states resulted from a TIGER3 sampling and increase the successful exchange ratio between the quenched and the baseline replicas.

REFERENCES

[1] Li et al., *polymer*. **50**: 4139 (2009); [2] Metropolis et al.,J Chem Phys **21**, 1087 (1953); [3] Li et al., J Chem Phys **130**, 174106 (2009); [4] MacKerell et al.,J Phys Chem B **102**, 3586 (1998). [5] Maple et al., J Comp Chem, **15**, 162 (1994).

PART II. The Performance of TIGER3

Sampling Efficiency

Tests on amorphous PMMA at 500 K. All Calculations were conducted with CHARMM [4] and PCFF force field [5].
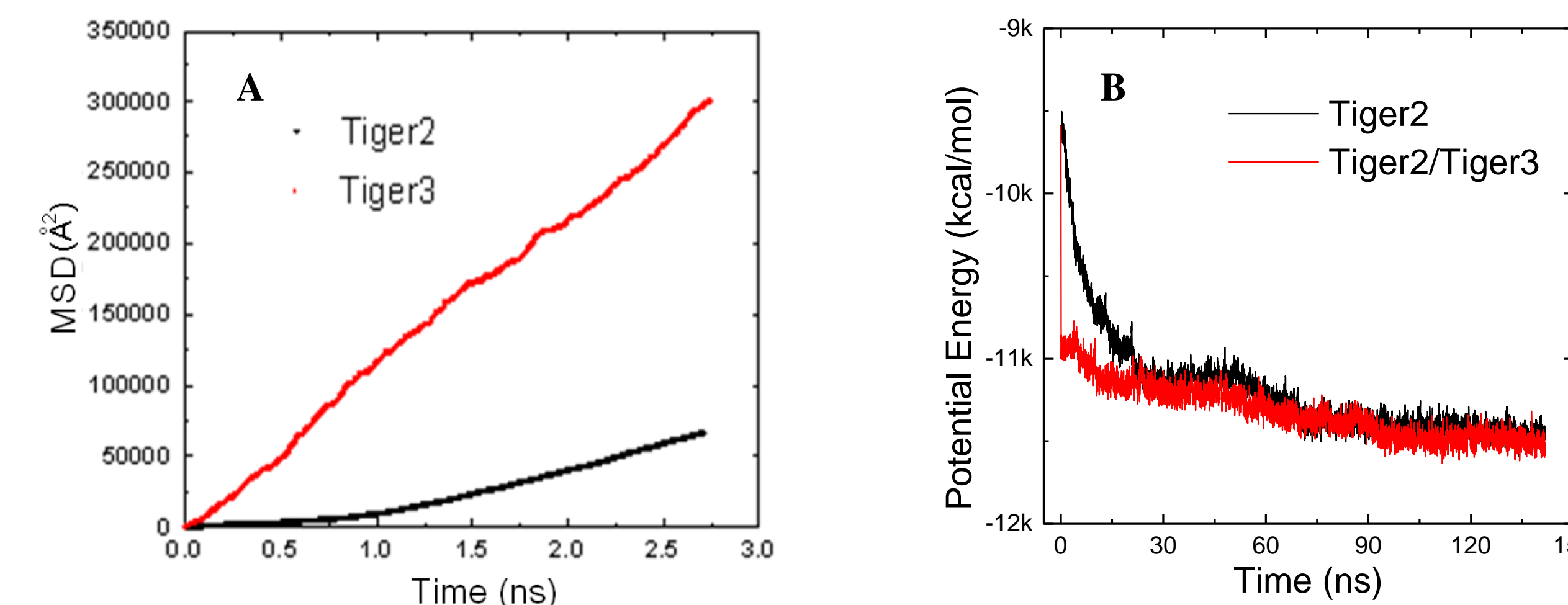

Figure. 2 (A) The mean squared displacements (MSD) calculated for the center of mass of gravity of chains in TIGER2 and TIGER3 simulations. (B) Temporal evolution of the potential energy in a TIGER2 and a 10:1 combined TIGER2/TIGER3 simulations.

Glass Transition Temperature Calculation

Two dense amorphous systems of PMMA and PBMA were generated and equilibrated with the TIGER3/TIGER2 mixed scheme. Started from the equilibrated structures, conventional MD simulation was conducted at various temperatures for 500 ps. The atomic mean squared displacements (MSD, g_0) were calculated from the MD trajectories. An inspection of g_0 at different temperature identifies two diffusion regimes across $400 - 410$ K for PMMA and $300 - 310$ K temperature for PMMA and PBMA, respectively, which corresponds to the glass transition temperature of the two polymers, and are close to the experimental data of about 400 K and 300 K, respectively.
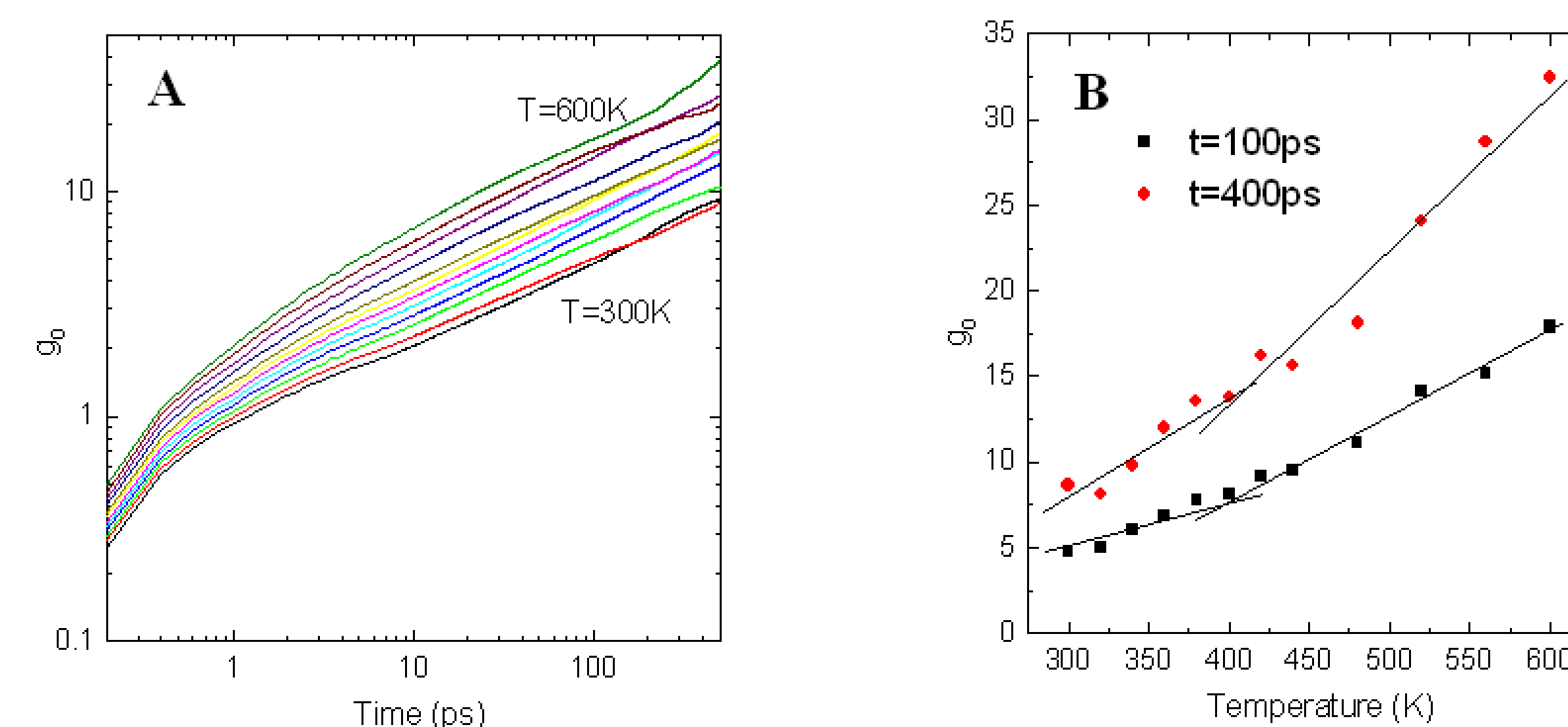

Figure 3. For PMMA, **A**: Change of MSDs following with time at different temperatures. **B**: MSDs as a function of temperature at two observation times. Two diffusion regimes can be identified at temperatures about $400 - 410$ K, from which the glass transition temperature can be estimated.
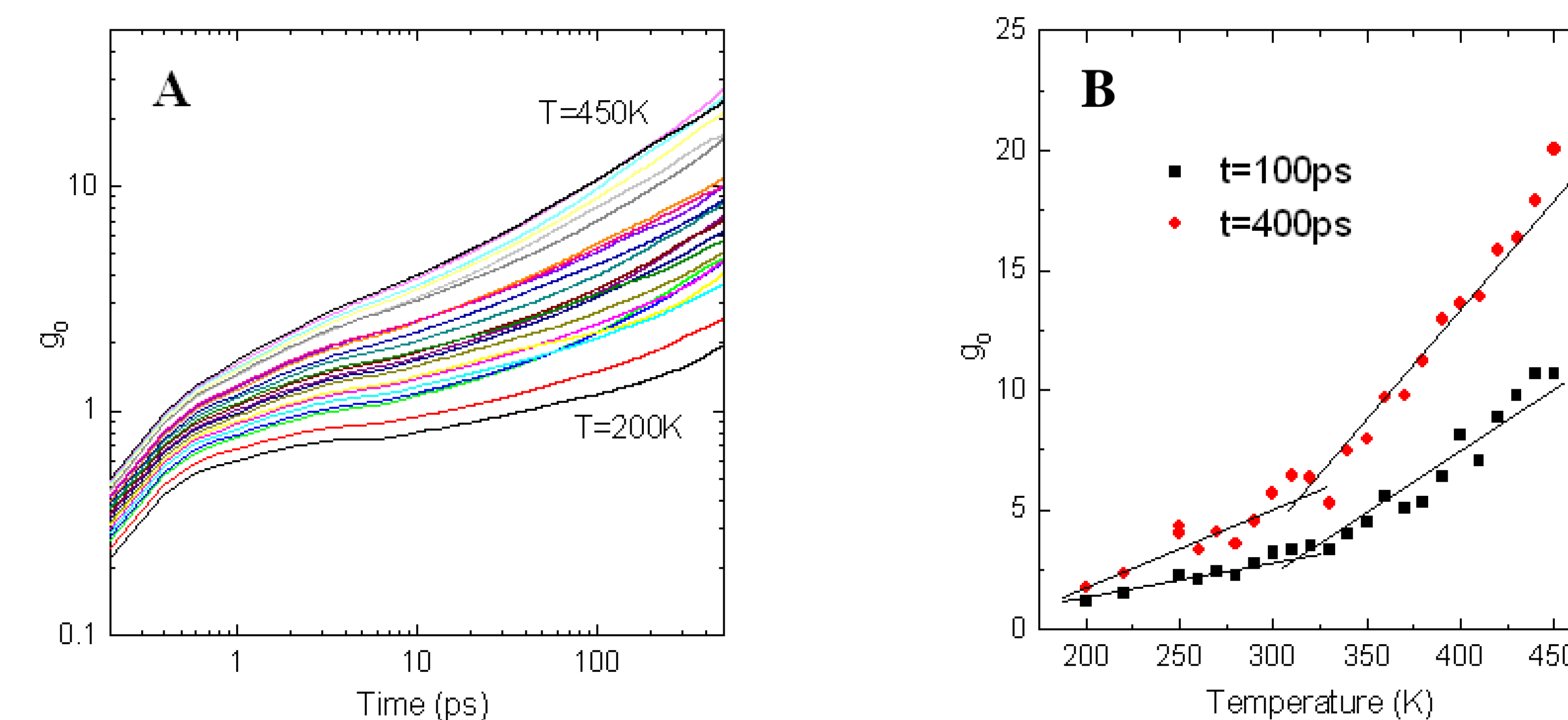

Figure 4. For PBMA, **A**: Change of MSDs following with time at different temperatures. **B**: MSDs as a function of temperature at two observation times. Two diffusion regimes can be identified at temperatures about $310 - 320$ K, from which the glass transition temperature can be estimated.

PART III. Reverse Mapping and Scattering Function Calculation for Atomistic Models

Reverse Mapping Method

- The CG structure determines the contour of the atomistic structure. The position of a CG bead represents the center of mass of the corresponding atomistic unit, and is fixed during reverse mapping.
- Attractive harmonic constraint is imposed between the dummy atoms ($r_{vdW}= 0$) at the open ends of successive atomic units. The introduced atomistic unit is allowed to rotate freely with fixed center of mass.
- ABNR Energy minimization is conducted until the dummy atoms overlap. The dummy atoms are removed, and thus a new bond is formed.
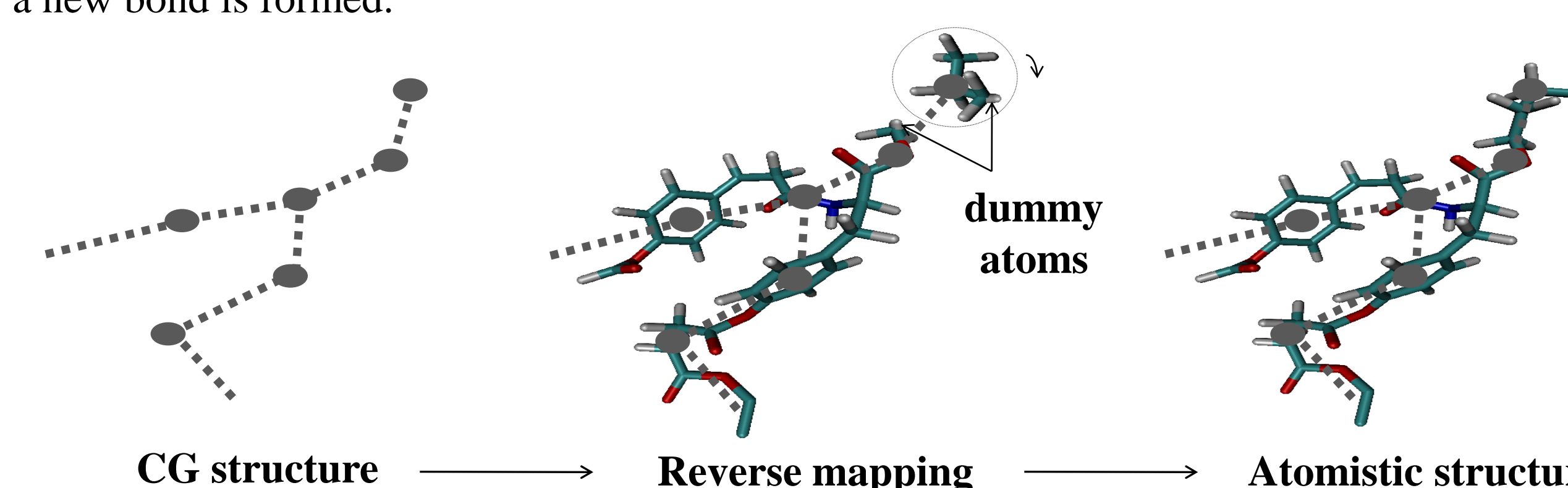

dummy atoms

CG structure $\longrightarrow$ Reverse mapping $\longrightarrow$ Atomistic structure

Figure 5. Schematic illustration of the reverse mapping method.

Recovered Atomistic Structure of DTB Succinate Copolymer
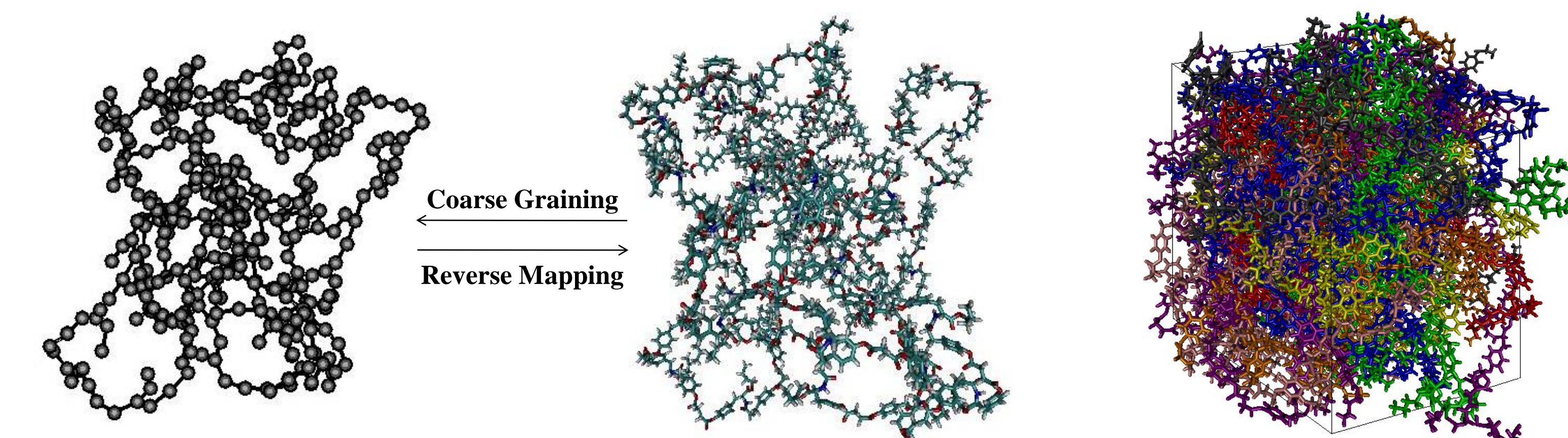

Coarse Graining

Reverse Mapping

Figure 6. LEFT: A CG chain of 50-mer DTB succinate; **MIDDLE:** An atomistic chain obtained by reverse mapping from the CG structure; **RIGHT:** A highly entangled system composed of eight chains of 50-mer DTB succinate.

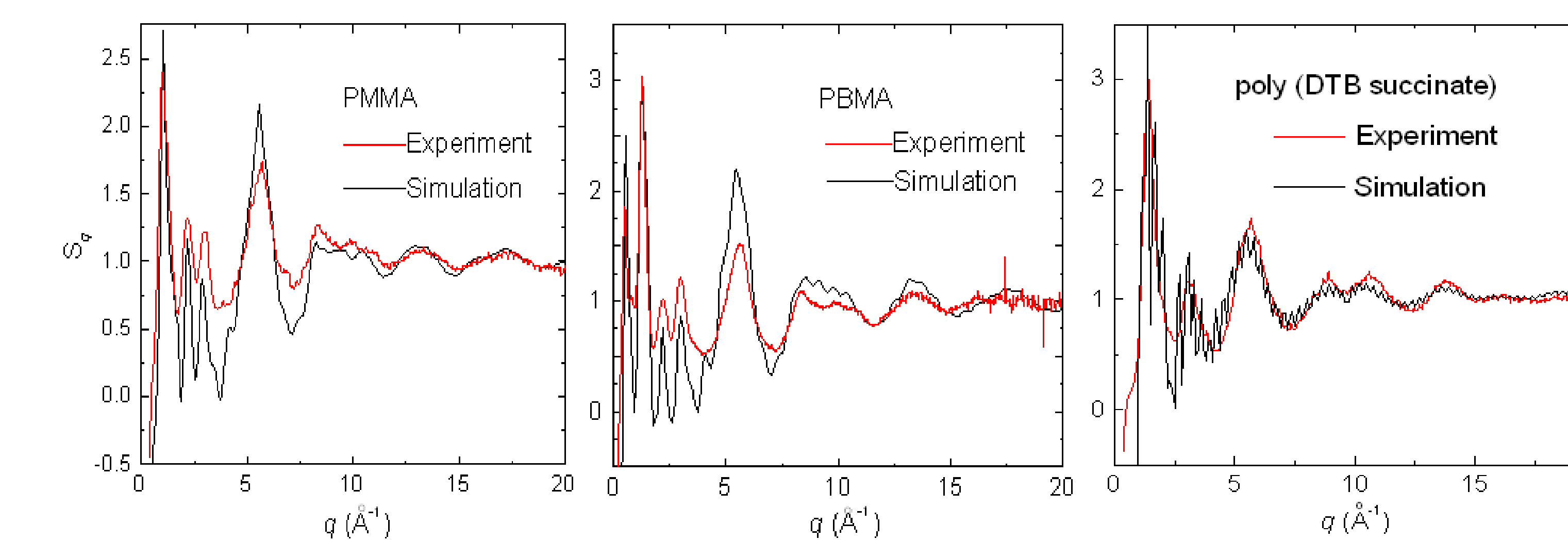### X-Ray Diffraction Structure Factor Calculation

Figure 7: The scattering functions, Sq, calculated for PMMA, PBMA, and poly(DTB succinate) at 295 K temperature showing excellent agreement between predicted and experimental values from x-ray scattering.

CONCLUSIONS

1. The new **TIGER2/TIGER3 scheme combined with coarse-grained model** is able to efficiently equilibrate dense polymer systems.
2. The predictions of the properties of the equilibrated systems are in very good agreement with the experimental observations.