Molecular Dynamics Simulation of Thermal Degradation of Bioresorbable Polymers

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Statement of Purpose: "Bioresorbable Biomaterials" is the buzzword in the field of biomaterials due to their inherent property of *in vivo* resorption over time. This makes polymers like poly(lactic acid) (PLA), poly(glycolic acid) (PGA) etc. attractive biomaterials for regenerative medicine and tissue engineering applications. However, the same useful property of hydrolytic degradation is a major concern from a manufacturer's stand point. Studies have shown the influence of melt-processing parameters on the resorption behavior of these biomaterials. For example, higher residual moisture causes rapid hydrolytic degradation during processing[1], higher processing temperatures lead to depolymerization resulting in process induced monomers, which catalyze the degradation process[2], and the extrusion rate also affects the degradation profile. Thus, one needs to determine the optimum processing conditions for bioresorbable polymers in order to achieve the desired properties in extruded fibers while preventing excess degradation during processing. Here, we propose the use of Molecular Dynamics (MD) simulation to understand thermal degradation of PLA at the molecular level. This will help in designing resorbable implants with precise *in vivo* resorption behavior.

Methods: MD simulation is a powerful tool to study the behavior of a material at the molecular level. We used a newly developed force-field ReaxFF[3] in LAMMPS (MD code developed at Sandia Lab.). First of all, PLA polymer chains were created using Materials Studio (Accelrys®). Ten polymer chains, each with 10 repeat units, were packed in an amorphous cell (21.4 Å x 21.4 Å x 21.4 Å) with density 1.25 g/cc (Fig.1).

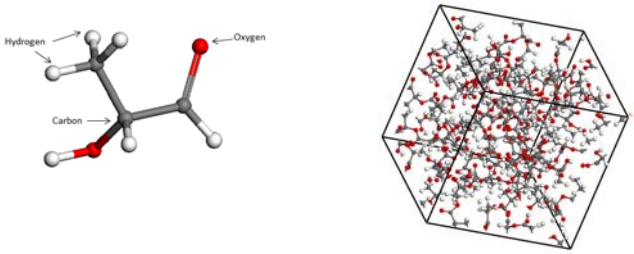

Fig 1. PLA Monomer & its Packing into Amorphous Cell

The system was then equilibrated in LAMMPS at 300 K for 1 nanosecond (ns) using NVT ensemble and periodic boundary conditions which resulted in the final density of 1.15 g/cc (Fig.2). The equilibrated system was then used with ReaxFF force-field to study degradation of the polymer chain with the increasing temperature. The simulation was carried out for 5 ps with a time-step of 0.25 fs and the rate of increase in temperature was 300 K/ps. The final temperature at the end of the simulation was 1800 K. VMD (molecular visualization program) was used to view the polymer chains and the fragments resulting from the thermal degradation.

Results: Fig. 2 shows the energy minimization in the system after relaxation at room-temperature. While there is no change in the kinetic energy, the potential energy and thus the total energy of the system reduces due to chain relaxation. This relaxed configuration also results in a slightly lower final density (1.15 g/cc) as compared to the packing density (1.25 g/cc).

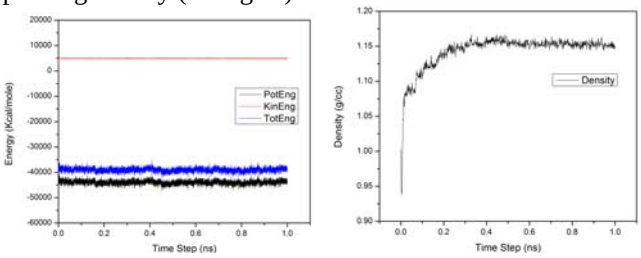

Fig 2. System Equilibration at Room Temperature and Final Density after Chain Relaxation

Fig. 3 shows the behavior of one of the many PLA chains that are subjected to thermal degradation. At room temperature, PLA chain is relaxed and complete with 10 repeat units. However, after 5 ps and at 1800 K, the chain breaks into smaller PLA fragments and forms compounds like CO_2, CO, and free radicals like CHO, CH_3, OH, COOH, Oxygen ion and Hydrogen ion. Although not very stable, the free radicals and monomers could potentially catalyze the degradation of the polymer chain.

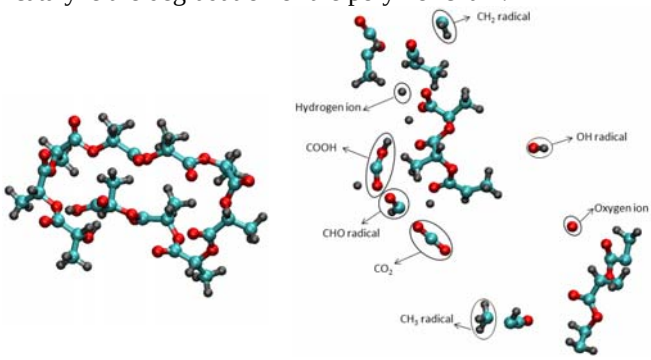

Fig 3. Single PLA Chain at Room Temperature vs. Chain Fragments and Radicals after Thermal Degradation

Conclusions: This preliminary study shows that MD simulation can be used to study the resorption behavior of biomaterials. Further work is being planned to validate the results of this computational study with experimental data. Future work also includes extending the computational tools to simulate other processing parameters and their influence on the resorption profile of biomaterials. The ultimate goal is to get better understanding of process induced pre-mature degradation. This will help to design resorbable biomaterials (such as scaffolds) with better predictability of their *in vivo* performance. Moreover, with better understanding, the processing parameters themselves could be used to precisely modulate the resorption behavior of these biomaterials.

References: [1] Oepen R. Clin Mater. 1992;10:21-28 [2] Ella V. J. Appl. Polym. Sci. 2011;5:2996-3003 [3] van Duin A. J. Phys. Chem. 2001;105;9396-9409