Modeling Degradation of Bioresorbable Polymers and Devices

Jingzhe Pan, Xiaoxiao Han, Ruoyu Huang and Ying Wang
Department of Engineering, University of Leicester, Leicester, UK. (jp165@leicester.ac.uk)

Introduction: Bioresorbable polymers, poly(glycolide) and poly(lactide) and their copolymers for example, are being used in controlled drug delivery, orthopaedic fixation, tissue engineering and many other biomedical applications to provide various temporary functions inside human body. However the device development has been entirely based on trials and errors. This is very problematic because the typical degradation time can be several months to several years. The lack of a mathematical model for the biodegradation process makes it difficult to extrapolate experience and data obtained in one device to another. This talk presents a mathematical framework for modelling the degradation of bioresorbable devices, taking into account of the interplay between hydrolysis reaction, monomer diffusion and degradation-induced crystallisation.

The Model: A bioresorbable polymer is simplified as being consisted of (a) amorphous polymer molecules, which can hydrolyse but are too large to diffuse, (b) monomers, which are the product of the hydrolysis reaction and can diffuse; (c) polymer crystals, which nucleate and grow as chain cleavage occurs, and (d) water molecules, which are abundant anywhere in the device. The governing equations for the concentrations of the monomers and amorphous polymer, and the degree of crystallinity are developed. This is a set of partial differential and integration equations which can only be solved numerically. Furthermore a model for the change in the Young's modulus of the amorphous polymer phase is developed. The model relates the change in the Young's modulus to the change in the average molecular weight of the amorphous polymer.

Model Validation and Applications: Firstly the governing equations are solved for thin plates and films using a finite difference method. A large amount of experimental data has been collected for a range of bioresorbable polymers using thin plate or film samples. The numerical solutions are compared with the experimental data. It is shown that the model can fit all the experimental data very well, including the well known thickness effect for PLA films. Secondly a concept of biodegradation map is proposed. Biodegradation involves several underlying processes including (a) diffusion of the monomers out of the device, (b) non-autocatalytic and autocatalytic hydrolysis reactions and (c) crystallization. The biodegradation map is a graphical means of showing which process is in control for a particular set of degradation conditions. The maps were obtained by varying the material and geometry parameters in the governing equations. It then becomes clear that most of the existing data published in the literature are in the "fast diffusion" zone on the map. Despite being extremely valuable, these data provide little information on the rate of the auto-catalytic reaction which is vitally important when modeling the device degradation. Thirdly a computer programme is developed to solve the governing equations using the finite element method for sophisticated three-dimensional devices. This is necessary because there is no commercial computer package available that can solve our governing equations. The finite element analysis can predict the spatial distribution and temporal evolution of average molecular weight, degree of crystallinity and Young's modulus in a bioresorbable device.

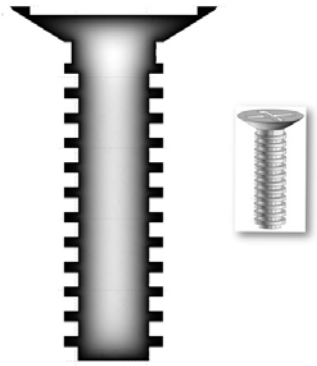

Fig 1. A finite element model for biodegradation

The small figure in Fig 1 shows a 3-dimensional finite element model for a bioresorbable screw, often used in orthopedic surgeries. The large figure shows predicted molecular weight distribution in the cross-section of the screw at a particular degradation time. The brighter region inside the screw indicates lower molecular weight while darker region on the boundary indicates higher molecular weight. The heterogeneous nature of the biodegradation process can be clearly observed. Finally a reverse engineering technique is being developed to back-calculate the material data in the governing equations from degradation data of an existing bioresorbable device (the screw shown in Fig 1 for example). These data can then be used to predict the degradation behavior of a different device made of the same polymer.

Conclusions: The trial and error approach in device development is problematic. Many experience and degradation data have been collected for existing devices. The mathematical model developed here can be used to back-calculated the material parameters which can then be applied to new device design using the same polymers. This is a powerful approach which will accelerate the development of various biodegradable devices.

References: Part of this work has been published in the following papers:

Wang Y, Pan J, Han X, Sinka C, Ding L. Biomaterials. 2008;29: 3393-3401.

Han X, Pan J. Biomaterials. 2008; in press, DOI 10.1016/ j.biomaterials.2008.10.001.