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An overview on degradation of biopolymeric scaffolds and the effect on their mechanical properties

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ABSTRACT

In this work we present a brief review of the different methodologies developed to simulate the amorphous polymers fixation devices submitted to hydrolytic degradation. A numerical implementation of the Reaction-diffusion equations proposed by Wang is performed in FreeFem++. We also present a numerical program which performs successive chain scissions in order to obtain the average Young modulus for a scaffold. Afterwards, the young modulus is represented versus the number average molecular weight. The resulting expression is used in the Reaction-diffusion model in order to obtain the Young Modulus distribution inside a scaffold unit. The resulting distribution can be used as an input to simulate further mechanical loads on the device at different degradation times.

INTRODUCTION

In vitro test of polymers are submitted to degradation due to the exposure to water and derivatives. Water molecules are introduced into the polymeric structure through their pores, mainly by attacking the ester bonds of amorphous regions, turning them into shorter water soluble chains [1]. As a consequence, the stiffness of the polymeric matrix decreases during the degradation process and, consequently, the young modulus is reduced. The mechanical properties of the scaffold can be predicted according to the entropy spring model [2]:

$$E=3KNT$$

Where K is the Boltzmann constant, N is the current number of polymeric chains per volume, and T the temperature. Gleadall and his coworkers developed a methodology to perform random and end scissions in order to obtain the current number of chains, excluding the shorter chains that are water soluble [3].

On the other hand, several methods were proposed to predict the surface erosion of polymeric devices, generally using the Monte Carlo method [4], [5]. Recently, a computer algorithm in which the experimental mass loss data set is taken as an input to better fit the experimental results [6].

In this work, a general overview of the most relevant techniques that simulate the hydrolytic degradation of polymeric fixation devices is described. A numerical approach of the Reaction- diffusion equations proposed by Wang et al. [1] by using FreeFem++ software and a computer program to perform successive random and end scissions on a polymer [3], in order to obtain the averaged Young modulus of the polymer[7], [8]. Furthermore, the latter is correlated to the number averaged molecular weight in order to obtain the spatial distribution of the Elastic Modulus along the device.

METHODOLOGY

Several authors developed models to predict the mechanical behavior of Biopolymeric Scaffolds. In order to predict the mechanical properties of the biopolymeric devices, an integrated framework which couples the mechanical properties model with a degradation model proposed by Wang[1].

$$\frac{d\overline{C_m}}{d\bar{t}} = \overline{k_1 C_e} + \overline{C_e C_m^n} + \nabla \cdot \{\overline{D_o}[1 + \alpha(1 - (\overline{C_m} + \overline{C_e})]\nabla(\overline{C_m})\} \quad (1)$$

$$\frac{d\overline{C_e}}{d\bar{t}} = -(\overline{k_1 C_e} + \overline{C_e C_m^n}) \quad (2)$$

Being $\overline{C_e}$ and $\overline{C_m}$ the normalized ester and monomer concentration, $\overline{k_1}$ $\overline{D_o}$ and α are parameters which are adjusted to better fit the experimental results.

On the other hand, there are different methodologies to predict the evolution of the mechanical properties of the biopolymeric devices ([7], [9], [10]). Viera et al defined an empirical model which relates the fracture strength and the molecular weight of PCL-PLA fibers. Wang et al. [7] proposed a model in which the mechanical properties are related to the number of chains whose molecular weight exceeds a critical value, previously defined.

Chain scission

Regarding the chain cleavage, there are two types (Figure 1): **random scission**, which occurs at an arbitrary position within the chain, and **end scission**, where the cleavage occurs at the initial or final bond of the chain. The latter provokes the formation of monomers.

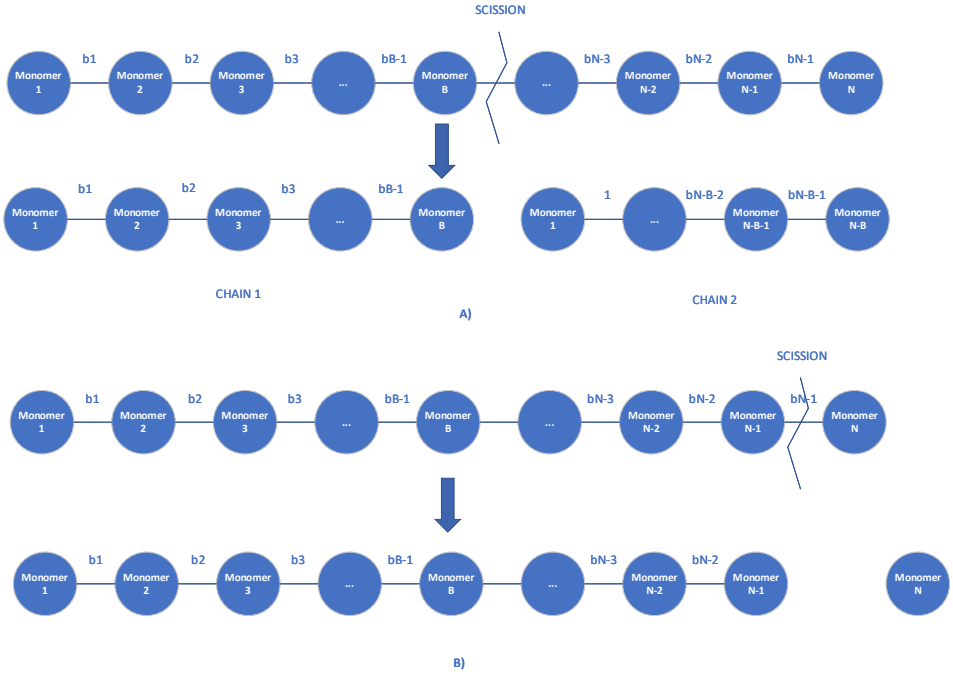

Figure 1. Mechanism of chain cleavage:A)Random Scission; B)End scission.

Framework to predict the Average Young Modulus of a polymer device

In the following diagram(Figure 2.) it can be seen a detailed diagram of the obtaining of the average Young Modulus, based on the methodology proposed by Gleadall et al[3].

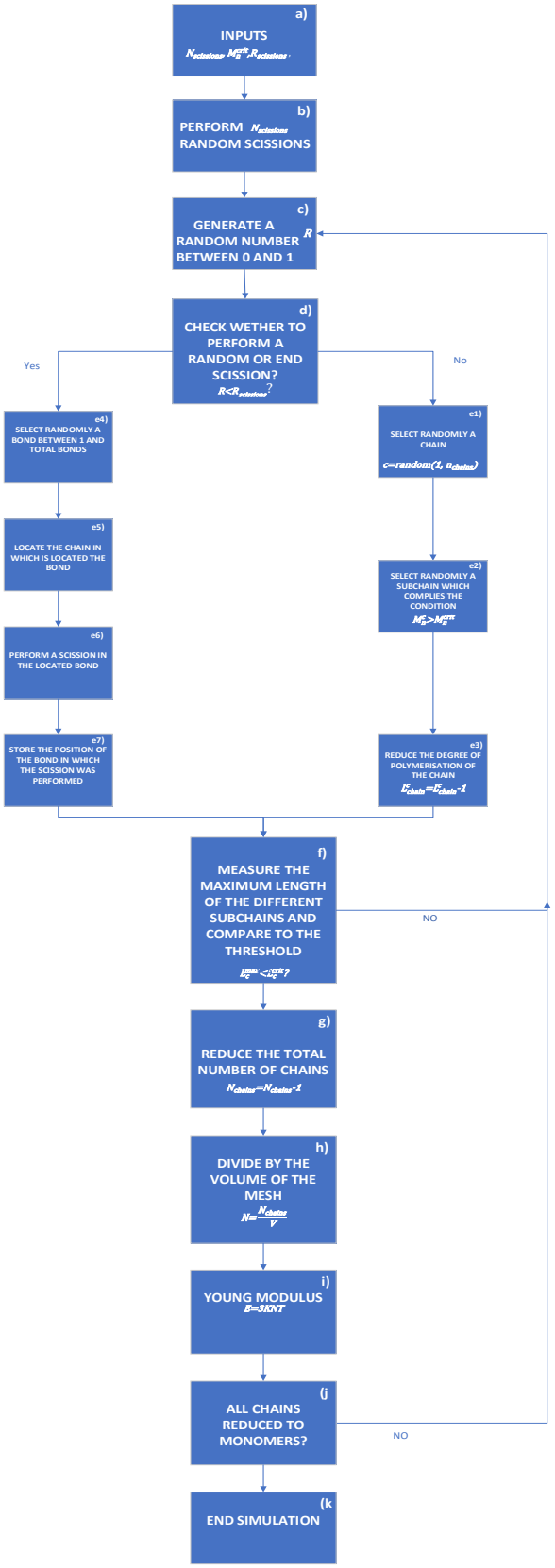

Figure 2. Flow diagram to obtain the average mechanical properties.

The methodology of performing successive chain scissions was implemented in Matlab (R2022a, Copyright 1993-2020 The MathWorks, Inc., Massachusetts, USA). Initially (step a), the critical value of molecular weight must be specified as input parameters, M_n^{crit} , as well as the random to end scission ratio $R_{scissions}$ and the number of initial scissions $N_{scissions}$, to obtain the number of initial chains. In step b), 9999 random cleavages are applied to the initial chain.

In the second part of the process, the type of cleavage to be applied is decided. To do this, a random number r between 0 and 1 is generated (step c). This value is recalculated as a c value, which depends on the previous one:

$$c = \frac{r}{1-r} \tag{3}$$

The value of c is compared with the ratio $R_{scissions}$(step d). **If this falls below, then a random scission will be applied. Otherwise, the scission occurs at the end.**

Random scission.

If scission is produced arbitrarily, a bond is randomly selected on which to apply the cleavage(step e4)).

$$bond = random(1, n-1) \tag{4}$$

Then, the chain which contains the bond is located (step e5)) and the break (e6) is applied. The lengths of the resulting chains are stored in the successive rows of the vector $chain_{array}$

$$chain_{array}(i,:) = (l_{i1}, l_{i2}, \dots, l_{in}) \tag{5}$$

End scission.

To apply end scission, one of the chains that meets the condition of not being a monomer (e1) is randomly selected. Within the chain, the subchain whose length is greater than the threshold value (e2) is arbitrarily selected and its degree of polymerization is reduced by one unit (e3).

$$l_{ij}^{k} = l_{ij}^{k-1}\text{-}1 \tag{6}$$

Once the break is applied, the longest substring is located and compared with the threshold value (f). If the length falls below M_n^{crit} , then the number of chains is reduced(g). If, on the other hand, the condition is not fulfilled, it would return to step (c).

$$n_{chains}^{i} = n_{chains}^{i-1}\text{-}1. \tag{7}$$

Updating of the mechanical properties

Once the number of chains is reduced, it is divided between the total volume:

$$N = \frac{n_{chains}^{i}}{V} \tag{8}$$

The averaged Young Modulus is obtained as follows:

$$E = 3KNT \tag{9}$$

being K the Boltzmann constant($1{,}380649x10^{-23}\ J/K$) and T the absolute temperature in K.

Finally, it is checked if all the chains have been converted into monomers(j). If so, the simulation (k) is terminated. If not, it returns to step c).

Setting input parameters

In this case study, M_n^{crit}, $R_{scissions}$ y $N_{scissions}$ are set to 28800, 1 and 9999, respectively. The number of polymer units is set to $3.66 \cdot 10^7$.

Coupling mechanical properties model with the Reaction Diffusion equations

The number averaged molecular weight is defined by the following expression:

$$M_n = \frac{N_{TOTAL} M_0}{n} \tag{10}$$

Where N_{TOTAL} is the total number of polymer units, M_0 is the molar mass of the polymer and n is the total number of chains present within the polymer.

Number average molecular weight is directly related with the ester concentration:

$$\frac{M_n}{M_n^0} = \frac{C_e}{C_e^0} \tag{11}$$

Once performed the mechanical properties model we can obtain a relationship between the normalized values of young modulus and number average molecular weight (Figure 3):

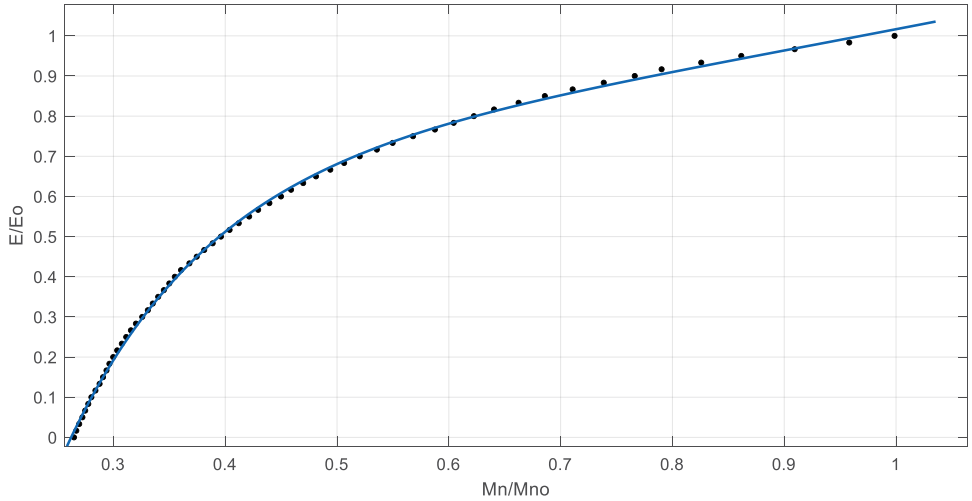

Figure 3. Relationship between the normalized values of young modulus and the number averaged molecular weight.

Calling $\frac{M_n}{M_n^0} = M_n^*$ and $\frac{E}{E_0} = E^*$ The equation which better fits the solution points is a sum of exponential functions:

$$E^* = ae^{bM_n^*} + ce^{dM_n^*} \tag{12}$$

being a=0.6131; b=0.5077; c=-5.408, and d=-7.796, with a goodness of fit RMSE=0.006717.

Implementation in freefem and obtaining of Young Modulus distribution

Once the relationship between the mechanical properties and the molecular weight is obtained, we can solve numerically the equations (1) and (2) using FreeFem++ software. We consider monomer concentration as 0 in those surfaces which are exposed to the liquid. In addition, a Neumann condition of zero gradient monomer concentration is imposed in cross-sectional faces.

The parameters are set to: n=0,5; $\overline{k_1} = 0{,}1$; $\overline{D_o} = 1$; $\alpha = 4{,}5$

Fig 4. shows the evolution of Young Modulus as a function of the coordinates at different normalized time steps.

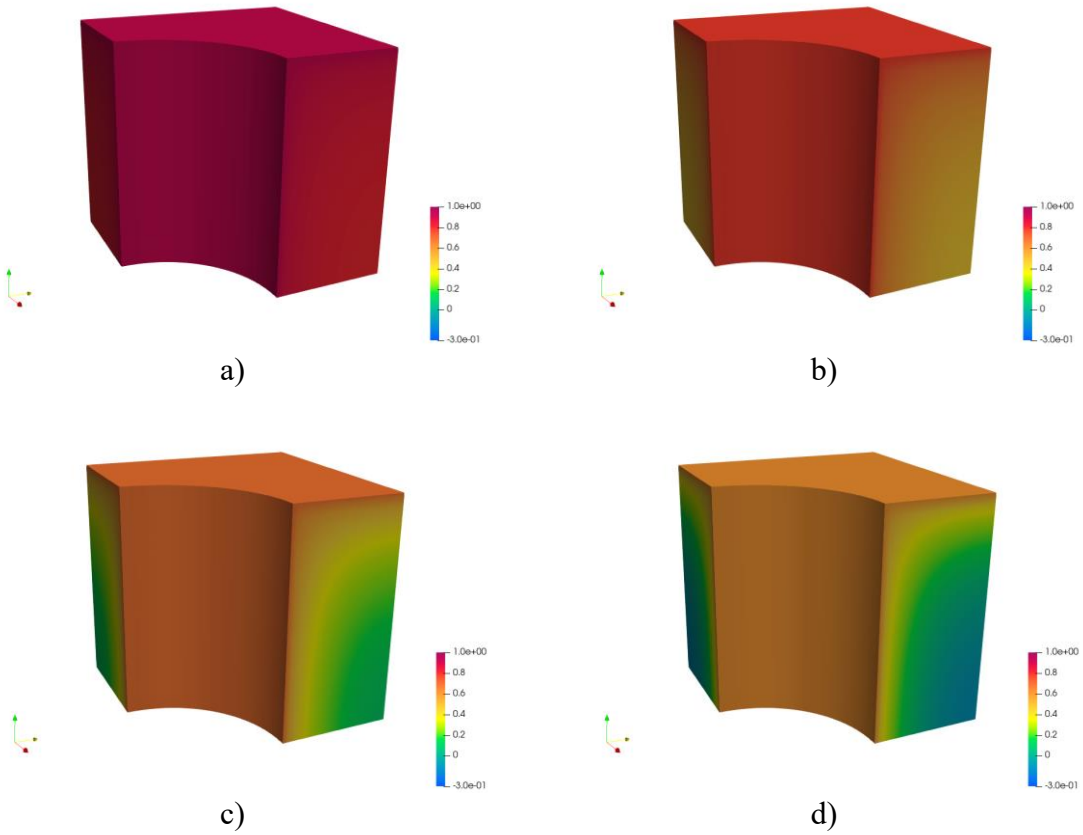

Figure 4. Distribution of Young Modulus on a cell unit at different time steps:t=2(a);t=5(b);t=7(c) and t=8(d)

CONCLUSIONS

In this work, an integrated methodology that predicts the evolution of the mechanical properties of a polymeric device is presented. In this case, pure hydrolytic conditions are assumed for the degradation as well as a constant crystallinity. Once the coupled model that predicts hydrolytic degradation and the loss of mechanical properties has been implemented, the next step will be to complete it, including the effects of surface erosion due to the degree of exposure and the wall shear stress criterion([4], [6], [11]). In this case, the relationship between the value of the normalized elastic modulus will depend on the volumetric relationship between the initial and current volume of the device. On the other hand, it would be useful to evaluate the mathematical model on similar geometries with different porosities [12] and different topologies, such as TPMS surfaces[13], in order to get more general information in the design phase and decide which topology is best suited for a particular case.

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