



# A simplified theory of crystallisation induced by polymer chain scissions for biodegradable polyesters

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## ABSTRACT

A simplified theory for the crystallisation of biodegradable polyesters induced by polymer chain scissions during biodegradation is presented following a theory developed by Han and Pan. The original theory is greatly simplified so that it becomes very straightforward to use and the number of material parameters is significantly reduced. Furthermore it is demonstrated that the spherulite structure widely observed in polymers can be taken into account using the theory. The simplified theory is fitted to the experimental data of poly-L-lactic acids (PLLAs) obtained from literature. It is shown that the simplified theory is equally able to fit the data as the original one. It is also shown that the theory can fit degradation data for PLLAs of different initial degrees of crystallinity with spherulite structures.

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## 1. Introduction

Bioresorbable polymers such as poly-L-lactic acid (PLLA) have been widely used for various temporary interventions inside the human body. Fixation screws, drug-eluting stents and tissue engineering scaffolds are some typical examples. These bioresorbable polymers have been the subject of extensive experimental testing giving details on average molecular weight, crystallinity and mechanical properties as functions of time. A clear degradation pathway has been established [1–10]. Water diffuses into the devices relatively quickly and then the polymer chains react slowly with water molecules (hydrolysis) leading to chain cleavage. The chain scissions provide the polymer chains with extra mobility so that they crystallise leading to a gradual and significant increase in the degree of crystallinity. It is very important to be able to predict how crystallinity changes during the degradation process because crystallinity affects both the degradation rate and mechanical properties of the devices [3,7,11]. Pan and his co-workers summarised the existing experimental observations and understanding into a set of mathematical models for polymer degradation [12–14]. In particular they developed a theory for chain scission induced crystallisation [12,13] by extending the classical Avrami theory [15–17]. Their original theory, however, involves both

differential and integrational equations which are difficult to use. The objective of this paper is to show that the theory can be greatly simplified. The integration equation can be eliminated and the number of material parameters in the theory can be reduced. Furthermore it is shown that the spherulite structure widely observed in semi-crystalline bioresorbable polymers can be taken into account in the theory.

## 2. A simplified theory for crystallisation induced by polymer chain scission

In the model developed by Han and Pan [12,13], the rate of polymer chain scission due to hydrolysis reaction is given by

$$\frac{dR_s}{dt} = k_1 C_e + k_2 C_e \left( \frac{C_{ol}}{1 - X_c} \right)^{0.5} \quad (1)$$

in which  $R_s$  ( $\text{mol m}^{-3}$ ) is the molar number of scissions per unit volume,  $k_1$  ( $\text{day}^{-1}$ ) and  $k_2$  ( $[\text{mol}^{-1} \text{m}^3]^{0.5} \text{day}^{-1}$ ) are the reaction constants for the non-catalytic and auto-catalytic hydrolysis reactions respectively,  $C_e$  ( $\text{mol m}^{-3}$ ) is the molar concentration of ester bonds in the amorphous polyester chains, and  $X_c$  is the degree of crystallinity (volume fraction). Water is assumed to be abundant hence its concentration does not appear in the rate equation. The polymer chains have a distribution in length. In order to make the model traceable, Wang and Pan [14] made a key simplification in their original model – the polymers chains are divided into two

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groups: long polymer chains that are water insoluble and cannot diffuse, and short chains, referred to as oligomers, that are water soluble and can diffuse. In the degradation model, this distinction is important because the oligomers can diffuse away to reduce the local acidity and reduce the degradation rate. On the other hand the actual distribution of the chain length does not have a major effect on the degradation rate. If a chain scission occurs near either end of the chain, then an oligomer is produced. The molar number of ester bonds in oligomers per unit volume,  $C_{ol}$  ( $\text{mol m}^{-3}$ ), is calculated based on the concentration of scissions according to the following empirical relation [12,13]:

$$\frac{C_{ol}}{C_{e0}} = \alpha \left( \frac{R_s}{C_{e0}} \right)^\beta \quad (2)$$

in which  $\alpha$  and  $\beta$  are empirical parameters (no units), and  $C_{e0}$  ( $\text{mol m}^{-3}$ ) is the initial value of  $C_e$ . The values of  $\alpha$  and  $\beta$  can be adjusted to reflect the probability of scissions creating oligomers, thereby allowing the model to be suitable for degradation ranging from end scission to random scission. For crystallisation, Han and Pan [12,13] assume that each chain scission has a probability of nucleating a crystal which gradually grows to a maximum size. Because crystals are nucleated at different times of the degradation process, the current degree of crystallinity is history dependent for which an integrational equation over time is required. In fact the individual crystals are all nano-sized [18] and the time taken to form these crystals are much shorter than the typical time taken by the hydrolysis reaction. In the current paper, it is assumed that each chain scission has a probability,  $p$  (no units), of nucleating a crystal which immediately grows to a finite volume of  $V_c$  ( $\text{m}^3$ ). The extended degree of crystallinity,  $X_{\text{ext}}$  (volume fraction), which assumes the crystals do not impinge on each other, is then given by

$$X_{\text{ext}} = p\eta_A R_s V_c \quad (3)$$

in which  $\eta_A$  is Avogadro's constant ( $\text{mol}^{-1}$ ). Following the Avrami theory [15–17], we assume that the actual and extended degrees of crystallinity are related by

$$\frac{dX_c}{dX_{\text{ext}}} = X_{\text{max}} - X_c \quad (4)$$

in which we have introduced a maximum degree of crystallinity,  $X_{\text{max}}$  (volume fraction), as a model parameter. Finally following Han and Pan [12,13] the consumption of amorphous polymer chains by the oligomer production and crystallisation leads to

$$\frac{dC_e}{dt} = -\frac{dC_{ol}}{dt} - \frac{\omega dX_c}{dt} \quad (5)$$

in which  $\omega$  is the inverse molar volume ( $\text{mol m}^{-3}$ ) of the crystalline phase. The number-averaged molecular weight ( $\text{g mol}^{-1}$ ) is given by

$$M_n = \frac{(C_e + \omega X_c)M_0}{N_{\text{chains}0} + (R_s - (C_{ol}/m))} \quad (6)$$

in which  $N_{\text{chains}0}$  ( $\text{mol m}^{-3}$ ) is the initial molar concentration of the polymer chains,  $M_0$  ( $\text{g mol}^{-1}$ ) is the molar mass of a lactic acid unit, and  $m$  (no units) is the average number of repeating units of the oligomers. The term on the top of Eq. (6) is the total weight of the crystalline and amorphous phases in the calculation unit excluding oligomers due to the assumption that oligomers are too small to be measured experimentally. The term on the bottom is the total number of polymer chains excluding oligomers in which  $(R_s - (C_{ol}/m))$  is the number of new chains produced by chain scission excluding oligomers. Eqs. (1)–(6) completely define the simplified model for simultaneous degradation and crystallisation of polyesters. Here the oligomer diffusion is ignored in order for us

to focus on the new elements of the crystallisation theory. The diffusion equation used by Pan et al. [12–14] can be readily added to the above equations to accommodate oligomer diffusion.

In the original model by Han and Pan [12,13], the changing rate of molar concentration of nucleation sites,  $N$  ( $\text{mol m}^{-3}$ ), is calculated as

$$dN = -\xi N dt - \frac{N}{1 - X_c} dX_c + p dR_s \quad (7)$$

The extended degree of crystallinity is given by

$$X_{\text{ext}} = \int_0^t \alpha_0 r_{\text{max}}^3 \left( 1 - e^{-(G/r_{\text{max}})(t-\tau)} \right)^3 \xi N(\tau) \eta_A d\tau \quad (8)$$

in which crystal growth is integrated from the time since their nucleation,  $\tau$  (day), to the current time  $t$  (day). The model parameters  $\xi$  ( $\text{day}^{-1}$ ),  $\lambda$  (no units),  $\alpha_0$  (no units),  $r_{\text{max}}$  (m), and  $G$  ( $\text{m day}^{-1}$ ) have been removed in the simplified theory. The actual and extended degrees of crystallinity are related by

$$\frac{dX_c}{dX_{\text{ext}}} = \left[ \left( 1 - \frac{C_{ol}}{C_{e0}} \right) - X_c \right]^\lambda \quad (9)$$

A minor correction is made in Eq. (9) to that used by Han and Pan to ensure mass conservation.

### 3. Validation of the theory using data obtained by Weir et al.

Weir et al. [4,5] carried out a set of degradation experiments for PLLA in phosphate buffer solution (PBS) with pH 7.4 at three temperatures: 37 °C, 50 °C, and 70 °C. Compression-moulded samples of 0.8 mm in thickness were used. Measurements of average molecular weights, mass loss, crystallinity, and thermal and mechanical properties were taken at various follow-up times during degradation. Weir et al. [4,5] found that their molecular weight data can be fitted to a hydrolysis model using a single activation energy despite testing at temperatures on both sides of the glass transition temperature. This was later confirmed by Han et al. [13] who fitted both the molecular weight and crystallinity data to the original model. Here the following parameters are assumed to be temperature dependent according to Arrhenius relation:

$$k_1 = k_{10} e^{-(E_{k1}/RT)}, \quad k_2 = k_{20} e^{-(E_{k2}/RT)}, \\ G = G_0 e^{-(E_G/RT)}, \quad \xi = \xi_0 e^{-(E_\xi/RT)}, \quad X_{\text{max}} = X_{\text{max}0} e^{-(E_{X_{\text{max}}}/RT)} \quad (10)$$

in which  $k_{10}$  ( $\text{day}^{-1}$ ),  $k_{20}$  ( $[\text{mol}^{-1} \text{m}^3]^{0.5} \text{day}^{-1}$ ),  $G_0$  ( $\text{m day}^{-1}$ ),  $\xi_0$  ( $\text{day}^{-1}$ ), and  $X_{\text{max}0}$  (no units) are pre-exponential constants,  $E_{k1}$ ,  $E_{k2}$ ,  $E_G$ ,  $E_\xi$ , and  $E_{X_{\text{max}}}$  (all  $\text{J mol}^{-1}$ ) are the corresponding activation energies,  $R$  ( $\text{J K}^{-1} \text{mol}^{-1}$ ) is the gas constant and  $T$  (K) is the absolute temperature.

In order to quantitatively indicate how well a model can fit the experimental data, a root mean square error is used in the following discussion which is defined as

$$\text{RMSE} = \sqrt{\frac{\sum (x_i - y_i)^2}{n}} \quad (11)$$

where  $x_i$  are the calculated values from the model,  $y_i$  are the measured values, and  $n$  is the number of data points.

Fig. 1 shows the best fit between our theories and the experimental data obtained by Weir et al. [4,5]. The solid lines represent

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