Simulation of ε-Caprolactone Enzymatic Ring-Opening Polymerization using the Finite Element Method

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ABSTRACT

Poly-ε-caprolactone (PCL) is a highly versatile polymer with significant biomedical and industrial applications. This paper focuses on simulating the enzymatic ring-opening and step-growth mechanisms of ε-caprolactone polymerization. Tracking the polymer chain length typically requires solving large systems of ordinary differential equations (ODEs), which can be computationally prohibitive. To overcome this limitation, this study compares a fully discrete chemical species model with a reduced-grid approach based on the finite element method. The main results demonstrate that, at a specific grid refinement level, the continuous finite element approach can reproduce the dynamic behavior of the discrete model with Mean Average Percentage Error of 0,03 % in terms of Weight Average Molecular Weight. Ultimately, the finite element approach proves to be a robust alternative that drastically reduces simulation time without compromising thermodynamic rigor and global mass balance.

Keywords: Simulation; Poly(ε-caprolactone); Ring-opening polymerization; Finite elements.

1 Introduction

In the 21st century, there is a growing trend toward the renewable monomers production that offers the same potential as current petroleum-derived counterparts (Vilela et al., 2014). Driven by the impending depletion of fossil resources and fluctuating oil prices, biobased alternatives have emerged as a viable option to challenge the multi-billion-dollar petrochemical industry (Mooney, 2009). Among these materials, polyesters synthesized from renewable sources stand out due to their biodegradability. Furthermore, the biobased monomers required to produce these polyesters are relatively accessible compared to those of other polymer classes (Vilela et al., 2014).

Within the broader category of biobased polyesters, polylactones represent a highly significant class. Although polylactones can be synthesized via traditional step-growth polycondensation, ring-opening polymerization (ROP) remains the main route for achieving high-molar mass polymers (Albertsson and Varma, 2002). Currently, poly-ε-caprolactone (PCL) is the most commercially representative polylactone. However, despite its well-known biodegradability, its industrial production is still heavily reliant on petroleum-based precursors (Zhang et al., 2021). To address this paradox, recent studies have explored an alternative biobased route to synthesize ε-caprolactone (ε-CL) from hydroxymethylfurfural (HMF), a platform chemical readily derived from D-fructose (Buntara et al., 2011; Nicklaus et al., 2013).

Enzymes are highly efficient natural catalysts that drive and regulate numerous biological processes. Naturally occurring macromolecules—such as polysaccharides, polynucleotides, proteins, and polyesters—are fundamental to the existence of all living organisms (Gross et al., 2001). The biogenesis of these complex structures typically proceeds through in vivo biocatalytic chain-growth polymerization, utilizing activated precursors generated via intracellular metabolic pathways (Gross et al., 2001). Owing to their vast structural diversity and inherent sustainability, these microbial-derived catalysts are increasingly being investigated as highly viable candidates to replace conventional materials across various industrial sectors (Moradali and Rehm, 2020).

The study most closely related to—and which partially inspired—the present work was conducted by Johnson et al., 2011. The authors developed a mathematical kinetic model for the enzymatic ring-opening polymerization of ε-CL, proposing specific reaction pathways. Their methodology employs a discrete species approach, accounting for every chemical species in the reaction medium by solving the corresponding system of Ordinary Differential Equations (ODEs). Therefore, the present paper aims to introduce a more computationally efficient alternative

by solving these population balance equations using the continuous finite element method, thereby enabling the application of the model to control and optimisation purposes.

2 Methodology

2.1 Reaction Medium

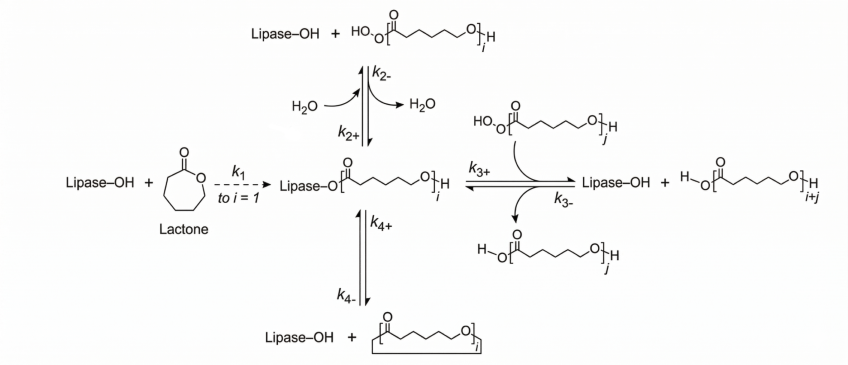
The composition of the reaction medium evolves dynamically over time under strictly isothermal conditions. At the onset of the polymerization ($t = 0$), the system comprises solely the monomer (ε-CL), the immobilized biocatalyst (CALB), and water. This initial water content is predominantly introduced via the residual moisture present in both the monomer and the enzyme preparation.

2.2 Reaction Mechanism

The kinetic framework underlying the present model is based on the reaction pathways proposed by (Johnson et al., 2011) for the enzymatic ring-opening polymerization (e-ROP) of ε-CL (Figure 1). Initially, the enzyme catalyzes the ring-opening of ε-CL, forming an acyl-enzyme intermediate (active chain) of size one (EP_1). Following this initiation step, the complex can undergo three distinct nucleophilic attacks:

- **Hydrolysis:** Trace water in the reaction medium attacks the acyl-enzyme complex, cleaving the ester bond to release a linear dead polymer of size i (P_i) and regenerating the free enzyme.
- **Propagation/Polycondensation:** The terminal hydroxyl group of an existing dead polymer chain (P_j) attacks the acyl-enzyme complex (EP_i). This intermolecular reaction forms a new ester bond, elongating the chain to yield P_{i+j} while regenerating the biocatalyst.
- **Cyclization (Backbiting):** An intramolecular nucleophilic attack occurs between the ends of the active chain (EP_i), cleaving the complex to release a cyclic macrolactone (C_i) and the free enzyme.

Figure 1: e-ROP Reaction Mechanism of PCL



Source: Johnson et al., 2011 (Adapted)

Furthermore, the model accounts for chain-length-dependent kinetics to accurately reflect the decreasing reactivity of longer macromolecules (Table 1). Mathematically, this physical dependence is incorporated into the population balance equations by scaling the intrinsic kinetic rate constants by the respective chain length (j or i) raised to a negative fractional exponent (Johnson et al., 2011).

Table 1: Kinetic Rate Constant with Chain Length Dependence

Chain Length Dependence	**Kinetic Rate Parameter** (k_0)
$k_1 = k_{1,0}$	150 x 10^{-5} L/mol/s
$k_{2+} = k_{2+,0}\, j^{-0.5}$	36000 x 10^{-8} L/mol/s

Chain Length Dependence	Kinetic Rate Parameter (k_0) (Continued)
$k_{2-} = k_{2-,0}\, j^{-0.5}$	4000 x 10^{-5} L/mol/s
$k_{3+} = k_{3+,0}\, j^{-0.5}$	3000 x 10^{-7} L/mol/s
$k_{3-} = k_{3-,0}\, j^{-0.5}$	3000 x 10^{-7} L/mol/s
$k_{4+} = k_{4+,0}\, i^{-1.5}$	1500 x 10^{-11} 1/s
$k_{4-} = k_{4-,0}\, j^{-0.5}$	4000 x 10^{-7} L/mol/s

Source: Johnson et al., 2011 (Adapted)

2.3 Mathematical Methods

To solve systems of ODEs that are involved in mass balances, some mathematical strategies can be used. In this paper, the Discrete Chemical Species and Finite Element methods were investigated. The focus behind this application is reducing the dimensionality of the ODE system (de Oliveira, 2006), Table 2 exemplifies generically the number of equations based on the number of the chain length or the number of grid nodes.

Table 2: Number of ODEs by Method

Mathematical Method	Number of ODEs
Discrete Chemical Species	$4 + 3{\cdot}N$
Finite Element	$4 + 3{\cdot}dn$

N: maximum chain length, dn: number of grid nodes

Source: Autor

2.3.1 Discrete Chemical Species Model

The Discrete Chemical Species (DCS) approach represents the highest theoretical level of discretization. In this framework, every individual species in the reaction medium is governed by its own ODE, explicitly translating the population balance equations. As a result, this method serves as a rigorous benchmark that accurately captures the complete molecular mass distribution (de Oliveira, 2006). The population balance equations are represented from (1) to (7).

$$\frac{d[\varepsilon\text{-CL}]}{dt} = -k_1[\varepsilon\text{-CL}][E] \tag{1}$$

$$\frac{d[\mathrm{H_2O}]}{dt} = -k_{2+}\sum_i [\mathrm{EP}_i][\mathrm{H_2O}] + \sum_j k_{2-}[\mathrm{P}_j][\mathrm{E}] \tag{2}$$

$$\frac{d[\mathrm{C}_i]}{dt} = k_{4+}[\mathrm{EP}_i] - k_{4-}[\mathrm{C}_i][\mathrm{E}] \tag{3}$$

$$\frac{d[E]}{dt} = -\frac{d[\varepsilon\mathrm{CL}]}{dt} - \frac{d[\mathrm{H_2O}]}{dt} + \sum_i\sum_j k_{3+}[\mathrm{EP}_i][\mathrm{P}_j] - \sum_j k_{3-}[\mathrm{P}_j][E] + \sum_m \frac{d[C_m]}{dt} \tag{4}$$

$$\frac{d[\mathrm{EP}_1]}{dt} = -\frac{d[\varepsilon\mathrm{CL}]}{dt} - k_{2+}[\mathrm{EP}_1][\mathrm{H_2O}] + k_{2-}[E][P_1] + \sum_{m=2} k_{3-}\frac{[P_m]}{m-1}[E] - k_{3+}[\mathrm{EP}_1]\sum_j [P_j] \tag{5}$$

$$\left.\frac{d[\mathrm{EP}_i]}{dt}\right|_2^{175} = -\frac{d[C_i]}{dt} - k_{2+}[\mathrm{EP}_i][\mathrm{H_2O}] + k_{2-}[E][P_i] - \sum_j k_{3+}[\mathrm{EP}_i][P_j] + \sum_{m=i+1} k_{3-}\frac{[P_m]}{m-1}[E] \tag{6}$$

$$\left.\frac{d[\mathrm{EP}_i]}{dt}\right|_{176}^{1000} = -k_{2+}[\mathrm{EP}_i][\mathrm{H_2O}] + k_{2-}[E][P_i] - \sum_j k_{3+}[\mathrm{EP}_i][P_j] + \sum_{m=i+1} k_{3-}\frac{[P_m]}{m-1}[E] \tag{7}$$

In this kinetic model, the transfer and cleavage reactions demand specific statistical considerations. As observed in the terms associated with the rate constant k_{3-}, the concentration of a dead polymer $[P_m]$ is divided

by $(m-1)$. This statistical factor accounts for the fact that a polymer chain of length m possesses exactly $m-1$ cleavable ester bonds, ensuring that the probability of enzymatic attack is proportional to the chain size. A critical feature of this model is the physical constraint applied to intramolecular cyclization (backbiting), which is evident in the transition between Equations (6) and (7). The formation of cyclic macrolactones (C_i) is thermodynamically hindered by entropic penalties as the chain length increases. Therefore, the cyclization terms are strictly active for chains up to a length of 175, after which the probability of the active chain end finding its own tail becomes negligible, and the mechanism proceeds exclusively via linear propagation and intermolecular transfer. Finally, it is essential to emphasize the scale of this discrete approach. To accurately capture the molecular weight distribution up to a chain length of $n = 1000$, the model requires the simultaneous numerical integration of over 3000 highly coupled and stiff ordinary differential equations. This exponential growth in dimensionality inherently leads to severe computational bottlenecks.

2.3.2 Finite Element

To overcome the computational burden of the discrete method, the finite element (FE) approach is introduced as a efficient alternative. This technique reduces the dimensionality of the system through mathematical interpolation. The interpolation strategy employs a basis function that accurately captures the expected physical distribution of the intermediate chain lengths (S_i) (Equation (8)) that are not explicitly integrated (de Oliveira, 2006). By constructing a discretized grid of representative chain sizes (ξ), the model avoids tracking every individual chemical species in the reaction medium, restricting the rigorous integration solely to the predetermined grid points.

This interpolation strategy is applied to the active chains (EP_i), dead polymers (P_i), and cyclic species (C_i). To accurately capture the early stages of chain growth, the grid is constructed using a hybrid discretization approach. The first 10 nodes are explicitly discretized with a step size of one. Beyond this point, the nodes are geometrically distributed up to the maximum truncated chain length (de Oliveira, 2006)(Equation (9)).

$$S_i = \left(S^{(k+1)}\right)^{\left(\frac{i-\xi_k}{\xi_{k+1}-\xi_k}\right)} \cdot \left(S^{(k)}\right)^{\left(\frac{\xi_{k+1}-i}{\xi_{k+1}-\xi_k}\right)} \quad \text{com} \quad \xi_k \leq i < \xi_{k+1} \tag{8}$$

$$\begin{cases} \xi_k = k & \text{para } k = 1,2,\ldots,10 \\ \xi_k = (i_{\text{maximo}})^{\frac{k}{N}} & \text{para } k = 11,12,\ldots,N \end{cases} \tag{9}$$

3 Results

The simulations were conduced by a maximum chain length of 150 in 7200 s by an initial condition of 9,4 x 10^{-3} mol, 3,0 x 10^{-3} mol and 6,3 x 10^{-3} mol of ε-CL, enzyme, and water, respectively. The simulated mass profiles of the reacting species demonstrate robust physical consistency throughout the process. As established by mass conservation, the total enzyme concentration remains strictly constant, while the ε-CL monomer is fully depleted, and water participates in a dynamic cycle of consumption and regeneration (Figure 2). The product formation kinetics accurately reflect a high polymer yield (Figure 3). Furthermore, the temporal evolution of the molar mass distribution confirms that, upon reaching high conversions, the chain length population approaches a classical Flory distribution (Figure 4). Remarkably, both the DCS and FE methods yielded perfectly convergent concentration profiles. This agreement validates that the finite element strategy drastically reduces the system's dimensionality (number of ODEs) and CPU time without compromising reaction parameters such as Mn and Mw (Table 3).

Table 3: Simulation Parameters

Mathematical Method	Number of ODEs	CPU Time (s)	Mn	Mw
Discrete Chemical Species	454	43,4	1290,67	1916,91
Finite Element	154	4,0	1290,46	1916,55

Source: Autor

Figure 2: Evolution of Reactant Masses during Batch e-ROP of ε-CL

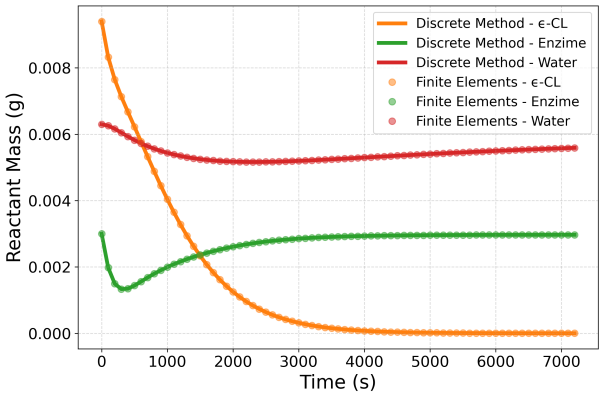


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Figure 3: Evolution of Polymer Yield during Batch e-ROP of ε-CL

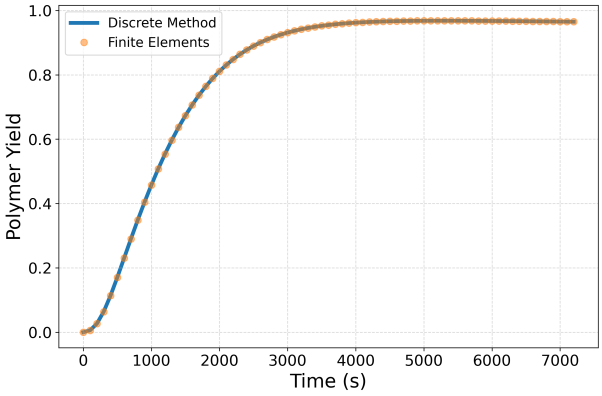

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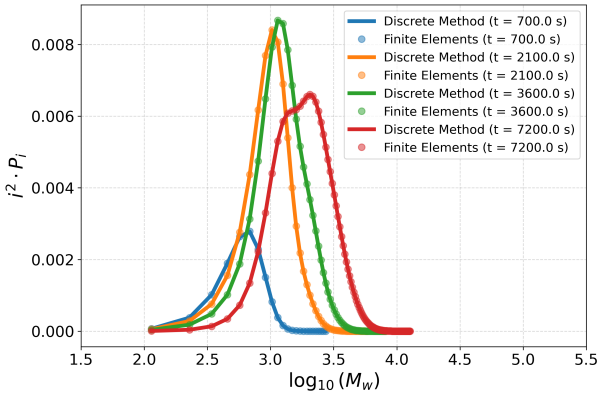
Figure 4: Evolution of Chain Length Distribution during Batch e-ROP of ε-CL



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4 Conclusion

The present study successfully developed and compared two mathematical modeling approaches for the enzymatic ring-opening polymerization (e-ROP) of ε-caprolactone. While the Discrete Chemical Species (DCS) model provided a rigorous baseline by tracking every individual polymer chain, it inherently suffered from high computational costs. To overcome this, a Finite Element (FE) approach utilizing a hybrid logarithmic grid was implemented. The results demonstrated that the FE method accurately reproduced the kinetic profiles, the mass conservation of the catalyst, and the final molar mass distribution obtained by the DCS model.

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