

ADVANCED CONSTITUTIVE MODELLING OF POLYMERS FOR TISSUE BIOPRINTING APPLICATIONS

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Introduction

Modern 3D bioprinting techniques aim at reproducing a specific tissue composition by extruding a bioink, which is a cluster of stem cells embedded into a hosting gel, into the desired pattern. If the extruded structure is fed suitable nutrients, cell differentiation and growth is initiated. However, prior to activating these processes, the gel must first be converted into a polymer construct to provide support and preferential directions to the successive cellular growth phase. There are many ways to accomplish this melt-to-solid transition, most notably photo-polymerisation. The irradiation of a light with suitable intensity and wavelength triggers chemical processes that induce the cross-linking between polymer chains within the printed material, in a time-evolving scheme of structure formation. Controlling this process holds great importance, since cellular motility and nutrient diffusion are greatly affected by the disposition and orientation of the polymer network. As it currently stands, the 3D printing process briefly described above is well known, but in many instances it is not yet adequately optimised and the influence of a variety of parameters hinders a large-scale production basis. For example, the intensity and direction of the UV light has no standard protocol yet, so the definition of an optimal disposition of the light sources can prove essential in minimising the polymerisation times, hence tissue formation times as a whole. This work intends to ground the choice of selected polymerisation parameters to a rational basis.

Methods

To achieve the aforementioned objectives, the relevant Physics of what happens after the melted bio-ink is deposited has been represented through multi-physics Finite Element simulations, where the kinetics of polymer cross-linking has been coupled with finite deformation formulations. Specifically, the curing process may be described by evolution equations of the kind:

$$\begin{aligned}\frac{\partial c_R(x, t)}{\partial t} &= \beta m c_I(x, t) I(x, t) - 2k_T c_R^2(x, t) - k_O c_R(x, t) c_O(x, t) \\ \frac{\partial c_O(x, t)}{\partial t} &= -k_O c_O(x, t) c_R(x, t) \\ \frac{\partial c_I(x, t)}{\partial t} &= -\beta I(x, t) c_I(x, t)\end{aligned}$$

In which c_R, c_I, c_O are the concentrations of radicals, photo-initiators and oxygen respectively, and the light intensity I follows a Beer-Lambert-like diffusion law.

The behaviour during phase evolution follows a well-established mechanical model [1, 2] which recasts the non-linear, finite-elasticity problem associated to each time-dependent crosslink formation into a more convenient equivalent phase.

Viscoelastic behaviour during polymerisation has also been accounted for. More to the point, the constitutive behaviour of the polymer has been divided into an elastic branch, following a Neo-Hookean law:

$$\sigma_{eq} = J_{eq}^{-1} \left(\mu_M J_{eq}^{-\frac{2}{3}} \mathbf{B}'_{eq} + k_M \ln J_{eq} \mathbf{I} \right)$$

Where σ_{eq} is the Cauchy stress, \mathbf{B}'_{eq} is the deviatoric part of the left Cauchy-Green deformation tensor, and μ_M and k_M are the shear and bulk modulus of the cross-linked polymer.

To deal with these highly non-linear differential equations representing the problem, a parametrised custom Finite Element variational formulation has been implemented.

Results

The main results that will be illustrated will address the evolution of the curing (degree of conversion p) as a function of light diffusion within the polymer medium (light intensity I).

Figure and Tables

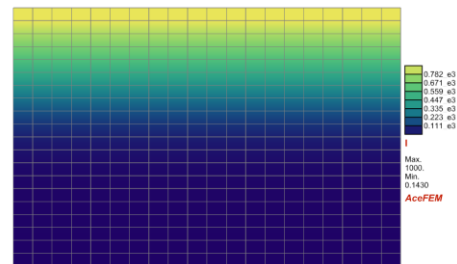


Figure 1: light diffusion inside the medium

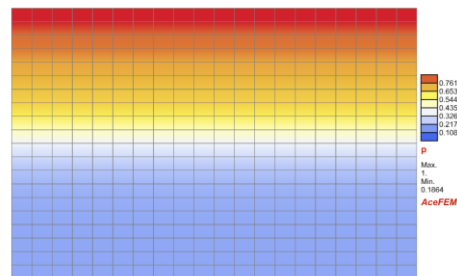


Figure 2: degree of conversion within the analysed medium

References

1. Wu J. et al, J Mech Phys Sol (2018)
2. Long K. N. et al, J Mech Phys Sol (2009).

