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Mocafe: a comprehensive Python library for simulating cancer development with Phase Field Models

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Abstract

Summary: Mathematical models are effective in studying cancer development at different scales from metabolism to tissue. Phase Field Models (PFMs) have been shown to reproduce accurately cancer growth and other related phenomena, including expression of relevant molecules, extracellular matrix remodeling, and angiogenesis. However, implementations of such models are rarely published, reducing access to these techniques. To reduce this gap, we developed Mocafe, a modular open-source Python package that implements some of the most important PFMs reported in the literature. Mocafe is designed to handle both PFMs purely based on differential equations and hybrid agent-based PFMs. Moreover, Mocafe is meant to be extensible, allowing the inclusion of new models in future releases.
Availability and Implementation: Mocafe is a Python package based on FEniCS, a popular computing platform for solving Partial Differential Equations. The source code, extensive documentation and demos are provided on GitHub at URL: https://github.com/BioComputingUP/mocafe. Moreover, we uploaded on Zenodo an archive of the package, which is available at DOI: https://doi.org/10.5281/zenodo.6366052.
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1 Introduction

Mathematical oncology is an emerging scientific field that exploits mathematical and computational models to predict cancer progression, paving new ways to predictive medicine and our general understanding of the disease. Among different modeling approaches, Phase Field Models (PFMs) have recently shown the capability to describe not only different types of cancer development (Castro *et al.*, 2005; Lorenzo *et al.*, 2016; Cristini *et al.*, 2008), but also other important malignancy-related features, such as angiogenesis (Travasso, Poiré, et al., 2011; Xu et al., 2016, 2020) and extracellular matrix remodeling (Castro *et al.*, 2005). Moreover, PFMs proved their ease of integration with imaging data in 2D and 3D (Lorenzo *et al.*, 2016; Xu *et al.*, 2020), suggesting great opportunities for personalized medicine.
The main idea behind PFMs is to use Partial Differential Equations (PDEs) to describe the evolution of the cancer boundary in the affected tissue (Travasso, Castro, et al., 2011). Even though the study of such equations requires a wise application of scientific software and numerical methods, it is common to find only the mathematical description of PFMs in the literature. The lack of shared and open-source code poses however a consistent limitation to the development and application of PFMs in research (Hong and Viswanathan, 2020). Re-implementing the code to study

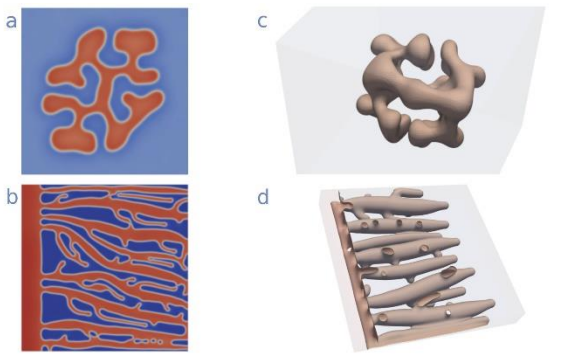

***Figure 1**: Example of simulations obtained with Mocafe: (a, c) prostate cancer PFM described in Lorenzo et al. (2016); (b, d) angiogenesis PFM described in Travasso et al. (2011). The full code to reproduce these results is provided in the Mocafe Demo Gallery, inside the documentation.*

cancer PFMs is not a trivial task even for scientists with a solid mathematical background, especially when an efficient implementation is necessary to achieve a reasonable computational time, e.g., exploiting parallel computing or advanced optimization techniques. This is especially true for hybrid PFMs combining PDEs with agent-based modeling as the libraries traditionally used for studying PDEs are not designed to handle agents and vice-versa.

To overcome these issues, we present a Python package, Mocafe (**Mo**deling **ca**ncer with **FE**niCS), which is an open and extensible implementation of several cancer PFMs available in the literature. The package is based on FEniCS (Logg *et al.*, 2012; Alnæs *et al.*, 2015), an open-source computing platform that is one of the most valuable tools toward a more open approach to PFMs (Hong and Viswanathan, 2020). Moreover, Mocafe is provided with extensive documentation and demos to make cancer PFMs as accessible as possible to any interested researcher.

2 Implementation

Mocafe is a Python package based on the FEniCS computing platform (Logg *et al.*, 2012; Alnæs *et al.*, 2015). We choose FEniCS among other open-source solutions for its excellent balancing between accessibility and efficiency. It provides a Python interface with extensive documentation and a focus on usability. Moreover, its core is composed of efficient data structures and libraries in C++ for solving PDEs. FEniCS code can also exploit parallelization through the Message Passing Interface (MPI) and different finite element shapes and types.

Mocafe is composed of different modules. Some of them are designed to improve user experience and management of simulation data. For instance, with Mocafe it is possible to handle with ease the simulation parameters and to generate reports containing simulation meta-data. However, its true cores are the `angie` and `litforms` sub-packages. `litforms` is a collection of PDE systems for different cancer PFMs, based on the FEniCS Unified Form Language (UFL) (Alnæs *et al.*, 2014). The `angie` sub-package implements a hybrid angiogenesis PFM first presented by Travasso et al. (2011), which shares some features with agent-based models. `angie` includes classes able to efficiently manage agents (representing biological cells) in FEniCS simulations, exploiting parallelization through MPI.

The PFMs implemented in Mocafe have been validated reproducing the results presented in the literature. Moreover, all models can be easily included in any FEniCS script with few lines of code, allowing researchers to integrate cancer PFMs with their own PDE systems. Mocafe is not just an open-source replication of important cancer PFMs, but can serve as a starting point for developing such models and defining new ones. Some examples of the simulations obtained with Mocafe are provided in Figure 1. Notice that each of the implemented models is designed to work just the same in 2D and 3D. The source code to reproduce the simulations, together with the entire Mocafe package and extensive documentation, is freely available on GitHub under a CC BY-NC 4.0 license from URL: https://github.com/BioComputingUP/mocafe.

3 Summary

Mocafe is an open implementation of PFMs for cancer development and angiogenesis. Based on FEniCS, it is designed to be efficient, user-friendly, and compatible with user-defined mathematical models. In line with the FEniCS' philosophy, all implemented models and classes support parallelization through MPI and work both in 2D and 3D. While it is not the first reproduction of the PFMs we implemented (Barbosa *et al.*, 2017; Vilanova *et al.*, 2013), it is to the best of our knowledge the first open-source implementation of these models. The modular design of Mocafe allows to easily embed additional models and developments of the models already included, e.g., different isoforms for the angiogenic factors (Travasso, Poiré, *et al.*, 2011), blood flow (Moreira-Soares *et al.*, 2018), and tumors' mechanics (Lorenzo *et al.*, 2019). Moreover, Mocafe provides useful methods to manage simulations' data and meta-data. Mocafe is an effort to make cancer PFMs more accessible and reproducible, and to stimulate the development of better PFMs. Finally, we commit to long-term maintenance and encourage feature requests, feedback, and contributions from the scientific community.

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