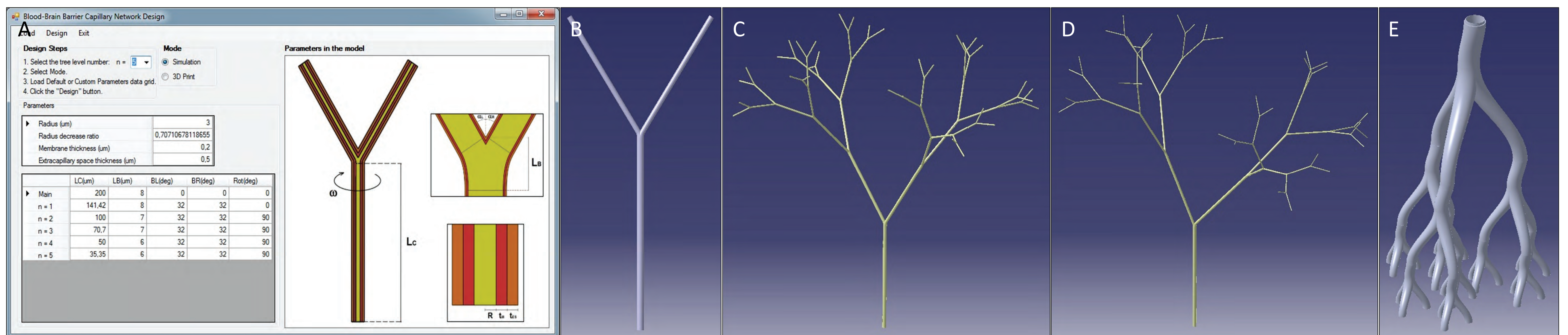


F. García Polite<sup>1</sup>, A.A. García-Granada<sup>2</sup>, J. J. Molins Vara<sup>1</sup>, M. Balcells<sup>3</sup>

Department of <sup>1</sup>Chemical and <sup>2</sup>Industrial Engineering, IQS School of Engineering, Universitat Ramon Llull, Barcelona, Spain, <sup>3</sup>Harvard-MIT Biomedical Engineering Center, Massachusetts Institute of Technology, Cambridge, MA, USA

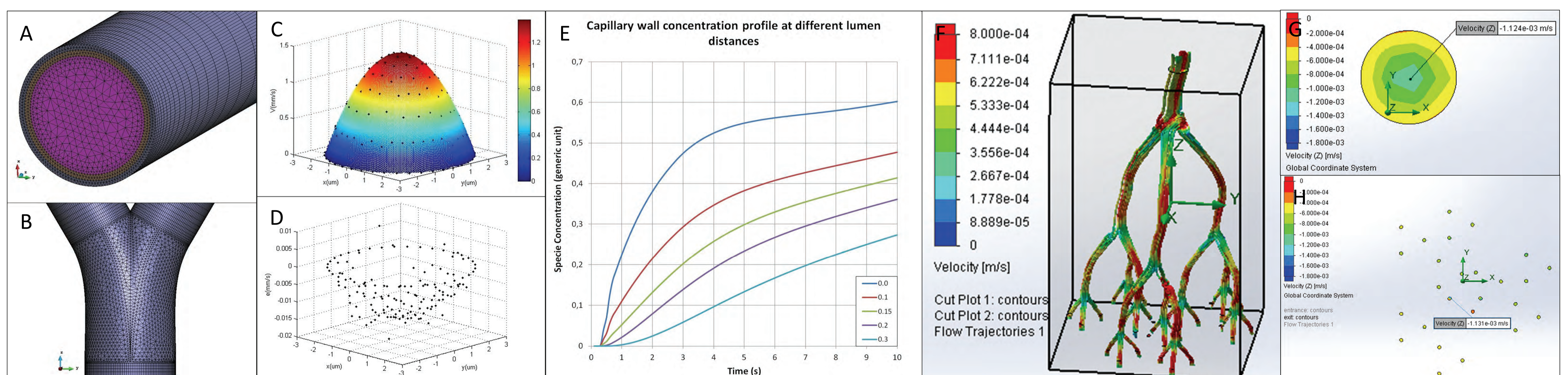
## ABSTRACT

In order to facilitate the preparation and execution of simulation of blood flow and diffusion through the membrane in brain capillary networks, a software has been developed as a macro that accelerates the generation of the starting geometry. By designing the base geometry and input the most relevant considered parameters, a code has been generated that saves time and effort when drawing the desired structure. The steps followed in developing the program are based on the choice of a model capillary network, as a Blood-Brain Barrier model, from which the user selects the parameters of interest. Capillaries were drawn first following different stable strategies. Macros were recorded for different stages of the drawing process and the associated code was analyzed in order to be a parametric design. A final version was developed based on Microsoft Visual Basic 2010 Express<sup>®</sup> and CATIA<sup>®</sup> respectively. The initial design considered straight cylinders with a diameters around 6.0 $\mu$ m, which are divided into branches, following multifractal patterns and reaching diameters of few micrometers. With the use of this software, in few steps a new CAD (Computer Aided Design) is generated to study the influence of relevant parameters, such as initial radius, branching patterns or bifurcation angles. The CAD data is automatically transferred to simulate FEM (Finite Element Method) simulations with CFD (Computational Fluid Dynamics) techniques and to generate prototypes with additive manufacturing techniques.



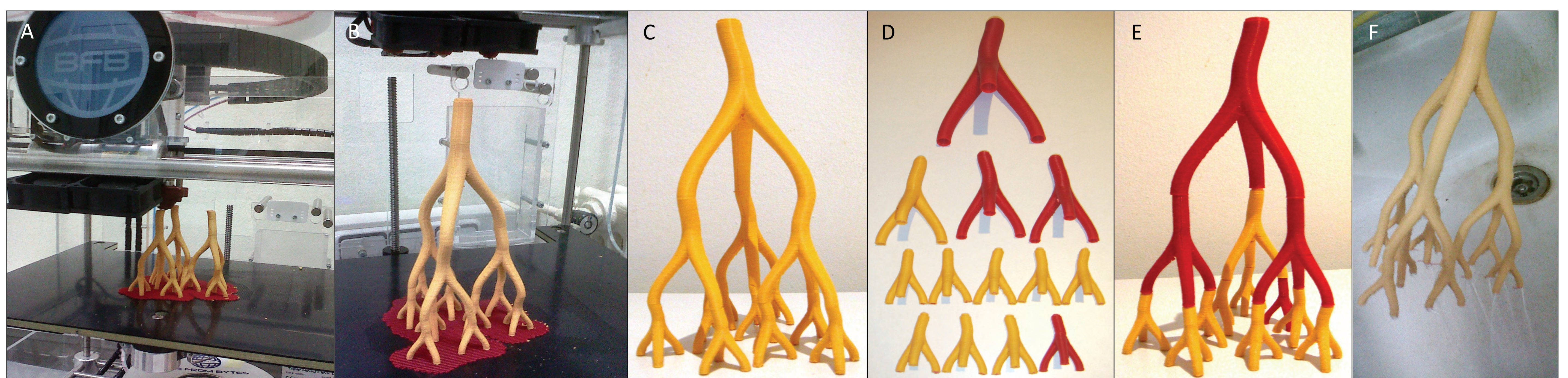
**Figure 1. Computational Platform for Blood-Brain Barrier Capillary Network Design**

A Blood-Brain Capillary Network model has been extracted by combining and applying multi-fractal and graph theory concepts. A capillary tree-like structure has been designed with editable parameters in each of the tree levels, such as capillary lengths and radius, bifurcation and rotation angles and capillary wall. A user-friendly computational platform (A), implemented on Microsoft Visual Basic 2010 Express<sup>®</sup>, allows the load of parameter data files, as text files previously defined by the user, and the generation of a CATIA script file corresponding to the design operations that construct the model. The script file obtained can additionally save the model as IGS or STL files for computational fluid dynamics simulations or 3D-printing processes respectively. The CAD drawing procedure is based on straight cylinders with bifurcated children branches (B). The structure is repeated as many times as the number of branching levels selected. The free selection of geometrical parameters allows the generation of either symmetrical (C) or asymmetrical (D) tree structures. Further improvements of the platform pretend to extract editable parameters from curved structures in order to obtain more realistic capillary networks (E).



**Figure 2. Computational Fluid Dynamics (CFD) and Preliminary Passive Diffusion Simulations**

Geometrical models obtained with our computational interface have been exported and pre-processed with Tdyn<sup>®</sup>. The IGS files were imported and fluid and diffusion conditions were assigned to different regions in the geometry. In order to proceed with numerical resolutions, based on the Finite Element Method (FEM), geometries were discretized with combined meshes. Capillary segments and bifurcation regions were discretized with semi-structured prismatic elements (A) and unstructured tetrahedral elements (B) respectively. Parabolic flow profile, as Poiseuille's law, was evaluated (C) and verified (D), obtaining numerical errors lower than 1.2%. Additional simulations on complex curved capillary networks (F) provided equivalent results (G)(H). Preliminary passive diffusion simulations provided precise concentration profiles along the capillary wall (E). Truthful performance of both concerned phenomena allow higher detailed CFD simulations where the effect of geometrical parameters in the model proposed will be tested.



**Figure 3. 3D-Printing of Capillary network prototypes**

A material prototype of a scaled curved capillary network has been generated with 3D-Printing technologies (A)(B). The final shape was obtained as a single entity (C) and as a set of individual network sections outlining the whole structure (D) and allowing rotation possibilities (E). Post-printing steps included flow tests inside the prototype (F). 3D-Printing process needs to be optimized so as to obtain smaller models with 3D-bioprinters for in vitro experimentation.

More information at:

<http://personales.ya.com/meaagg/BBB/BBB.html>

