AN UNDERGRADUATE COURSE IN MODELING AND SIMULATION OF MULTIPHYSICS SYSTEMS

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Abstract

An overview of a course on modeling and simulation offered at the Nanotechnology Engineering undergraduate program at the University of Waterloo is presented in this paper. The motivation for having this course in the undergraduate nanotechnology curriculum, the course structure and its learning objectives are discussed. Further, one of the computational laboratories covered in the course, a relatively simple drug release model, is presented in this work. This computational laboratory is designed to expose the students to the modeling and simulation of a macroscopic model, given in the form of an ODE, coupled with one of the boundary conditions of the system's microscopic behavior, given in the form of a PDE. The implementation of the proposed drug release model is performed in COMSOL, a commercial software application suitable to train students in the modeling and simulation of micro and nano systems.

Keywords: modeling and simulation, drug release, computational laboratory

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. Introduction

A mathematical model is an abstraction of a physical system, i.e. a mathematical image of the reality. These models are of great importance in engineering because they can provide relevant information about the system being modeled which may not be available from experiments, e.g. a model can explain variations in the measurable macroscopic properties of a physical system using accurate information from the microscopic level, which cannot be usually measured in a laboratory. Also, mathematical models help engineers to make decisions and to improve the quality of a process. On the other hand, mathematical models can lead to wrong decisions or conclusions about the system under study if they are not validated with experimental work. Therefore, a complete study of a physical system should integrate modeling, simulation and experimental work.

The process modeling fundamentals are usually introduced to the engineering students in one or two courses on transport phenomena. Although there are textbooks available in the field of transport phenomena[1-5], most of them present the momentum, energy and mass transport phenomena as independent subjects. This limits the application of the concepts learned in transport phenomena courses to practical systems where different laws of physics may occur simultaneously, e.g. the unsteady mass transport of a chemical flowing, with a given velocity profile, through a non-isothermal tubular reactor with an asymmetric geometry. It has been widely recognized that the study of fluid dynamics, heat and mass transfer in a unified framework constitute one of the keystones in fundamental engineering sciences and contribute to the development of new emerging fields in engineering such as nanotechnology[1,6]. Therefore, it is important to expose undergraduate engineering students to the modeling and simulation of physical processes

that involve the study of two or more laws of physics, this has been referred to as *multiphysics modeling*. The multiphysics modeling of a physical process may involve not only the simultaneous solution of different laws of physics occurring at the same time but also the coupling of two or more phenomena occurring at different length or time scales. The latter class of systems, also referred to as *multiscale systems*, are of increasing interest in engineering since they can be used to describe the macroscopic properties of a physical system by modeling and simulating the microscopic behavior of the physical process [7,8]. Although a sound background in numerical techniques may be desirable for simulating the type of processes previously described, the use of commercial software may prove very valuable for accomplishing this task, especially for those who are just becoming familiar with the subject of modeling and simulation.

In the Fall of 2008, the Micro and Nano Systems Computer-Aided Design (CAD) course, NE-336, was offered for the first time to the third-year students of the Nanotechnology undergraduate program at the University of Waterloo. The goal of this course is to study the process modeling fundamentals and to train the students in the modeling and simulation of multiphysics models that are relevant in the field of nanotechnology. Also, the students are exposed to conventional numerical techniques available for solving both ordinary and partial differential equations (ODEs and PDEs, respectively). Since the course deals with the modeling and simulation of micro and nano systems, one of the most important goals of the course is to train the students in the implementation of multiphysics models. For this purpose, they have to perform different computational laboratories which provide them with practical hands-on experience in the simulation of micro systems. These laboratories are intended to provide a clear physical understanding

of the systems being simulated. Since the course is mainly focused on the modeling and numerical simulation of multiphysics systems, only an introduction to the electronic and atomistic simulations required to model nano systems are discussed by the instructor in the last section of the course (see course structure in section 2.1). The goal of this paper is to give a general overview of the NE-336 course and to present one of the computational laboratories covered in the course. The laboratory presented in this work corresponds to a drug delivery system where the macroscopic properties of the system depend upon the variations at the microscopic system level.

The rest of this paper is organized as follows: in section 2, an overview of the NE-336 course is presented. Section 3 presents a computational laboratory that addresses the release of a drug in a storage tank. The mathematical model used to describe the behavior of this system, the challenges posed by this problem and the laboratory tasks performed by the students on this lab are discussed in this section. Section 4 presents the evaluation made by the students regarding the learning experience in this course. Concluding remarks are presented in section 5.

2. Course Description

Micro and Nano Systems Computer-Aided Design is one of the core courses in the Nanotechnology Engineering curriculum at the University of Waterloo. This course, NE-336, is composed of 3 weekly hours of lecture, 1 weekly hour of tutorial and 3 biweekly hours of computational laboratory. Lectures are used by the course instructor to provide the essential course material. Tutorial sessions are used to reinforce the concepts presented in the lectures, to solve sample problems and as a pre-laboratory session.

Laboratory sessions are used to help students to gain practical experience on the implementation of multiphysics models in an application software, on its simulation, and on the analysis of the simulation results. The course grading is based upon a midterm exam, laboratory reports and assignments, hand-written quizzes, a laboratory quiz and a final exam that covers the complete course content. The course is suitable for those students who are already familiar with classical thermodynamics and the traditional analytical methods for solving ODEs and PDEs.

The course objectives can be summarized as follows:

i) Learn how to derive first-principle models for simple physical systems that involve fluid dynamics, heat and mass transfer.

ii) Present the basic numerical techniques available to solve ODEs and PDEs.

iii) Train the students in the use of COMSOL, a widely used commercial software based in Finite Element Analysis (FEA).

iv) Stress the multiphysics nature of real systems and highlight the complexity of the solutions of multiphysics models describing specific micro and nano systems.

v) Solve illustrative case studies where the coupling between different mathematical models is implemented.

2.1 Course Structure

Based on the learning goals specified for this course, the course content has been divided as follows:

i) *Physics modeling process.* This section covers first-principle modeling and empirical modeling. Here, the basic concepts used to model physical systems that follow the laws

of classical mechanics, i.e. conservation of mass, energy and momentum, are applied to simple physical systems. The basic steps in the modeling process, the different approaches used to obtain a first-principle model and the traditional methods used to perform empirical modeling are discussed. Each of the above topics is supported with practical examples, e.g. cooling of a fluid flowing through a circular section of a tube, analysis of a plug flow reactor and flow in a circular tube. The books by Bird et al.[1] and Tosun[3] are the basic sources for this section of the course.

ii) *Numerical methods for solving ODEs and PDEs.* This section presents the traditional numerical methods available to solve initial value problems, such as Euler and Runge-Kutta methods, boundary value problems, the shooting method, and eigen-value problems for solving ODEs. Similarly, methods used in the solution of PDEs like the finite difference method, the method of lines and an introduction to the finite element method are discussed. In this section of the course, a detailed discussion on truncation and discretization errors in numerical analysis are presented. For example, the students are made aware of the errors generated by the use of approximate functions in the different terms of the PDEs containing the variable to be solved. Here, it is also shown that the errors depend on several factors, such as the truncation of Taylor series to form a particular finite difference scheme, e.g., first and second order, the order of a Lagrange polynomial to form a shape function in finite element and the size of the mesh elements. Also, comparisons between analytical solutions and that obtained by finite difference methods, i.e., forward, backward and centered finite difference, are discussed in the course. Moreover, comparisons between finite element and finite difference methods for regular and irregular geometries are also discussed on this part of the course.

Furthermore, a grid convergence analysis is evaluated by solving a particular system using different grid sizes. From this analysis, the students realize that meshing the domain of the physical system is a key step in the numerical set-up of the problem that would have a direct effect on the numerical solution. A formal grid convergence analysis that involves the use of relatively complex and time consuming algorithms to deal with stiff multiphysics systems is beyond the scope of this undergraduate course. The basic references for this part of the course are Chapra and Canale[9] and Chadrupatla and Belegundu[10].

iii)*Introduction to multiphysics models.* The goal of this section is to expose the students to physical systems that can be modeled using two or more laws of physics (multiphysics approach) and to train them in the implementation of such models in the application package used in the course, i.e. COMSOL. The examples provided in this section span from the modeling of the Joule heating effect in a section of a pipeline to the modeling of the mass transport of an incompressible fluid in a non-isothermal reactor. Other illustrative examples are used by the course instructor to show the importance of sensitivity analysis and the effect of parameter uncertainty on the simulation results. Most of the topics presented in this section are taken from Zimmerman[6], Bird et al.[1], Tosun[3] and the COMSOL library[11].

iv) *Advanced topics in multiphysics models.* The last part of the course is used to model physical systems where the coupling between the different mathematical equations appears at one boundary condition, i.e., extended multiphysics systems. Also, the implementation of multiphysics models with periodic boundary conditions is discussed. Likewise, this last section of the course is used to introduce the students to the traditional

methods used in the modeling of systems at the atomistic, molecular and coarse-grained level. This section of the course is supported with the COMSOL library [11], Zimmerman[6] and Hung et al.[7].

2.2 Computational Laboratories

The computational laboratories are a key component of the NE-336 course. In the laboratory sessions, the students are able to use MATLAB and COMSOL, which are the application packages used in this course. The first of these software packages is primarily used to solve those systems that can be modeled using ODEs, whereas the second one is used to model physical systems that involve PDEs or a combination or PDEs with ODEs (see case study in section 3).

The first laboratory session, laboratory zero, presents the students with an overview of the laboratories to be performed throughout the course. During this session, the course instructor implements, simulates and analyzes two simple models on each application package. The model implemented in MATLAB corresponds to a simple non-isothermal mixing tank process modeled using 2 ODEs, whereas the model implemented in COMSOL describes the unsteady Joule heating effect of a micro-resistor beam. The learning goals of the first and the second laboratories are to introduce the students to both of the application packages used in the course. In the first laboratory, the students learn the basic syntax required to execute ODEs in MATLAB, whereas in the second laboratory they learn the basic steps in the modeling process in COMSOL. For these laboratories, the physics of the models implemented on each application package are relatively simple. The third laboratory addresses the implementation of a drug delivery

model in COMSOL, which is presented in the next section. The fourth and the fifth laboratories cover an electro-migration model and a micro cantilever beam model, respectively. These models require the application of different laws of physics that makes the problem challenging to the students. The last laboratory session of the term, a laboratory quiz, is used to evaluate the students in their ability to implement models in both application packages. This quiz is of great significance for this course since it evaluates the abilities and skills learned by the students in the laboratory sessions.

Each of the laboratory manuals are divided in three sections: Section 1 contains a brief introduction of the physical system to be studied as well as the most significant aspects of its implementation in the corresponding application package. Section 2 covers basic questions regarding the implementation of the model. Section 3 lists questions that require additional simulations of the model, model analysis and parametric sensitivity analysis. The students must submit at the end of the laboratory session their responses to Section 2. This portion of the laboratory is used to evaluate the student's performance on the laboratory. Section 3 of the laboratory manual is submitted by the students a week after the laboratory session is completed. This is because the questions posed on this section require an in-depth analysis of the model and additional computational simulations. This portion of the laboratory (section 3) is considered as an assignment for the course.

3. Case Study: Drug Release in a Batch Process

This computational laboratory deals with the transient release of a drug in a mixing storage tank. The learning objective of this computational experiment is to show the

students the modeling and simulation of a system described by an ODE coupled with a PDE at one of the boundary conditions. This kind of mathematical modeling, also referred to as extended multiphysics problems, is very common in chemical processes where the multiple scale modeling of the physical phenomena occurs [6]. The physical description of the process is shown in Figure 1. The system sketched on this figure is widely used to study the drug release kinetics in biological systems (Tan et al.[12,13]). The drug is placed into a drug reservoir, assumed to be a solid sphere of radius δ, which is encapsulated by a polymer substance, e.g. a nano-gel. The encapsulating layer is used to control the drug delivery rate. As shown in Figure 1, the nano-particle, i.e. the nano-gel and the drug reservoir, are assumed to form a solid sphere of radius *R*. A mixing storage tank is assumed to be filled with a large number of nano-particles, *Np*. The tank is used to mimic the drug concentration profiles in a given system, e.g. a human body. The system is assumed to be isothermal and well stirred. Also, the density of the fluid, i.e. the fluid on the side of the tank, is considered to be constant.

Due to the educational nature of the present laboratory, several simplifications were made regarding some other considerations that can be involved when dealing with the modeling of a drug delivery system. The drug particles are considered to be appropriately described by an average particle behavior regarding their mass transport properties. That is, classical continuum transport equations are assumed to apply to the presented drug delivery system, which is comprised of both the drug particles and the fluid inside the tank. In principle, atomistic dynamic simulations may be required to model the dynamic behaviour of each particle in the system. However, these simulations may be lengthy and

may increase the complexity of the present educational laboratory. Since the objective of this computational laboratory is to present the modeling and simulation of an extended multiphysics system such as the drug release problem, molecular simulations of the drug particles are outside the scope of the present laboratory. Moreover, in a more realistic scenario the drug reservoir may consist of a polymeric matrix that can experience swelling and erosion[14,15]. Further, a constant drug release rate may be sought if the solution inside the drug reservoir is oversaturated (since the maximum concentration of drug should be constant and correspond to the saturation concentration[14]).

The transport of the drug through the drug reservoir and the polymeric material is controlled by the unsteady diffusion within the sphere. This diffusion process is mathematically described as follows (microscopic model):

$$r^2 \frac{\partial C_A}{\partial t} = D \frac{\partial}{\partial r}\left(r^2 \frac{\partial C_A}{\partial r} \right) \qquad (1)$$

where C_A is the drug concentration in the nano-particle (mol/m^3); r, the radius of the solid sphere (m); and D is the diffusion coefficient (m^2/s) in either layer one (D_r) or layer two (D_p). The boundary conditions (BCs) and the initial condition (IC) assumed for this microscopic process are as follows:

- BC1: at r=0, C_A is finite, i.e. $\frac{\partial C_A}{\partial r} = 0$
- BC2: at $r=\delta$, $-D_r \left.\frac{\partial C_A}{\partial r}\right|_{r=\delta} = -D_p \left.\frac{\partial C_A}{\partial r}\right|_{r=\delta}$
- BC3: at r=R, $-D_p \left.\frac{\partial C_A}{\partial r}\right|_{r=R} = k_c \left(C_A^l \big|_{r=R} - C_A^\infty \right)$
- IC: at t=0, C_A=C_{A0}

where the term k_c represents the mass transfer coefficient (m/s) which accounts for the diffusion on the fluid side; $C_A^l\big|_{r=R}$ is the drug concentration on the surface of the sphere on the fluid side; C_A^∞ is the concentration of the drug in the tank, i.e. a point in the tank that is assumed to be far away from the surface of the particle; and C_{A0} is the initial drug concentration in the drug reservoir.

Figure 2 shows the interface between the surface of the nano-particle and the fluid. As shown, it is evident that a relationship must be given to relate the interfacial compositions $C_A^l\big|_{r=R}$ and $C_A\big|_{r=R}$. One alternative is to assume equilibrium across the interface, that is,

$$C_A^l\big|_{r=R} = K\, C_A\big|_{r=R} \qquad (2)$$

where K represents an equilibrium constant. The unsteady drug concentration in the mixing tank is defined as follows (macroscopic model):

$$V\,\frac{dC_A^\infty}{dt} = NpA_{\,p}\,kc\left(C_A^l\big|_{r=R} - C_A^\infty\right) \qquad (3)$$

where V is the tank's volume (m^3) and A_p is surface area of the particles (m^2). The initial concentration of the drug in the tank is assumed to be zero.

The present educational laboratory presents the students with the challenge of coupling the drug transport in the nano-particle and its distribution in the storage tank. This is because the drug concentration in the bulk depends on the drug's concentration at the surface of the nano-particle. Thus, the students must solve a PDE (equation 1) and an ODE (equation 3) simultaneously. Since the coupling between the drug transport in the nano-particle and the concentration of the drug in the bulk occurs at the surface of the nano-particle (BC3), this case study is considered to be an extended multiphysics

problem[16]. The solution of this system of equations (equations 1 and 3) requires the implementation of numerical techniques. Thus, this type of problem is suitable to exemplify the capabilities of COMSOL in solving practical engineering problems.

The proposed model is built-up in COMSOL in two sequential steps. First, only the drug's transport in the nano-particle is modeled according to equation 1 without considering the coupling of this equation with equation 3, i.e., C_A^{∞} is assumed to be negligible (C_A^{∞} =0 in equation 3). For this laboratory, the students use the 2D unsteady mass transport by diffusion module in COMSOL[11] to account for the transient behavior of the drug concentration throughout the nano-particle, described by equation 1. It is important to mention that equation 1 can also be implemented using a 1D model given the symmetry of the sphere. In this laboratory however, the choice of using a 2D model is made because the step-up of this type of model is simpler than the one corresponding to a 1D model, especially given the two different materials of which the nano-particle is composed. Also, when implementing a 2D model, the variation of the drug concentration can be obtained for a complete cross section of the sphere, giving a clear physical meaning of the variation of the drug concentration in the sphere at specific times. A representative solution for the first part of the laboratory is the drug concentration profile as a function of the radius of the nano-particle for different times ranging from 600 to 1000 s (Figure 3). The model parameters used to generate the results presented in this paper are shown in Table I. As shown in Figure 3, there are two different profiles (for each fixed time value) in the nano-particle. One profile corresponds to the diffusion of the drug inside the drug's reservoir and the other corresponds to the diffusion of the drug through the nano-gel. From this plot, the students can observe that different nano-gel and

drug's reservoir materials will have an effect on the drug's diffusion rate. Thus, in the actual computational laboratory, the students are requested to test this model using different drug's reservoirs and nano-gel materials.

Once the nano-particle model has been implemented, the second step in the modeling process consists of coupling the diffusion model with the variations of the drug in the storage tank described by equation 3 (macroscopic model). The 1D PDE coefficient form module in COMSOL[11] was used to represent the macroscopic ODE model. Thus, a single line of arbitrary length is used to represent the variation of the drug concentration in the storage tank (equation 3). Since the coupling between the microscopic model (equation 1) and the macroscopic model (equation 3) occurs at one boundary condition (BC3), the line representing the storage tank's model must intersect with the external surface of the nano-particle, i.e. at $r=R$. Then, the variable that represents the drug concentration at the surface on the nano-particle side is made available in the 1D macroscopic model using the variable extrusion option in COMSOL[11]. This is the most challenging part in the implementation of this model in COMSOL. The laboratory manual includes hints in this section to assist the students with the coupling of the microscopic and the macroscopic model. Also, the students can seek help from the laboratory assistants. Once the drug release model has been completely implemented, the students are requested to simulate this process under different scenarios. The base case scenario assumes that the concentration of the drug at the radius of the nano-particle is the same on both the fluid and the nano-particle sides, i.e. $K=1$ in equation 2. Figure 4 shows the time evolution of the drug concentration in the storage tank for this scenario. The students must submit a plot like that shown in Figure 4 at the end of the laboratory

session. The rest of the scenarios considered in the laboratory were designed to provide an in-depth knowledge of the drug delivery process. This includes a parametric analysis on the effect of using different materials for the encapsulating layer and a study on the effect of the thickness of the nano-gel layer on the drug's delivery rate. Since these tasks require an in-depth analysis, they are submitted one week after the laboratory was performed and are considered as assignments in the course. A copy of the laboratory manual is available upon request from the corresponding author.

4. Assessment and Feedback

At the end of the term, a survey designed by the Faculty of Engineering of the University of Waterloo was conducted between students who were enrolled in the NE-336 course. The objective of the survey is to provide instructors with feedback as to how the teaching methods and skills were received by the students. From the responses of the survey, there was a clear consensus that the new skills learned in this course will be relevant to the future careers of the students and that the course introduced them to a new aspect of engineering: modeling and simulation. Also, the students could immediately realize how the recently acquired knowledge could be applied to their careers as engineers. A follow-up on a few of the students who were enrolled in this course indicated that some of them are currently applying the skills and subjects learned in this course to perform their fourth-year projects and in their co-operative terms (work internships).

Although students expressed appreciation of the hands-on experience provided by the computational laboratories, some of them also considered that the laboratory tasks were lengthy. This aspect coincides with the evaluation of the course where the required course

workload was unfavorably evaluated by the students, in contrast with a very positive evaluation of the assignment contribution. Some students also expressed that more time could be spent in class explaining the systems to be simulated in the computational laboratories. These valuable comments from the students have been taken into consideration to improve the design and the learning experience for nanotechnology students that will take this course in the coming future. Some relevant comments expressed by the students in the survey are the following:

Student 1: *"I think the best aspect of the course content was the numerical PDE/ODE section, because it provides the mathematical foundation for doing any computational mathematics".*

Student 2: *"I think this was a vital course to have in undergraduate education, especially in engineering or applied science. Most of the mathematics tackled by us are not analytical, but numerical. This course provides the toolkit to approach such applied math problems".*

5. Concluding Remarks

A general overview on the modeling and simulation course offered in the Nanotechnology Engineering undergraduate program at the University of Waterloo was presented. The aim of this course is to make nanotechnology engineering students familiar with the modeling and simulation of physical systems that involve the multiphysics nature of most of the processes relevant in engineering. To achieve this task, students must complete a series of computational laboratories that cover the implementation of multiphysics models in a suitable educational software package such as COMSOL. A computational laboratory that addresses the implementation of a

relatively simple drug release model was presented. The goal of this laboratory is to train the students in the implementation of extended multiphysics systems and to show that the microscopic behavior of a process has a direct effect on the macroscopic measurable properties of the system. Many of the students who took this course in the Fall 2008 are currently applying the tools learned in the course in their fourth year projects and in their work term internships. This confirms that the learning goals specified for this course were accomplished and that the modeling and simulation of multiphysics systems is an essential component in the curriculum of the nanotechnology engineering students.

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Table I. Model parameter values.

Parameter	Value
D_r	8 x10^{-19} m^2/s
D_p	1 x10^{-19} m^2/s
Np	1 x10^{10}
δ	10 nm
R	50 nm
V	1 x10^{-4} m^3
kc	0.5 m/s
C_{A0}	20 mol/m^3

Figure Captions

Figure 1.- Physical System.

Figure 2.- Coupling of the macro and the nano systems.

Figure 3.- Concentration profile in the nano-particle, C_A, for different times from 600 – 1000 s.

Figure 4.- Time dependent profile of the drug concentration in the tank, C_A^{∞}.

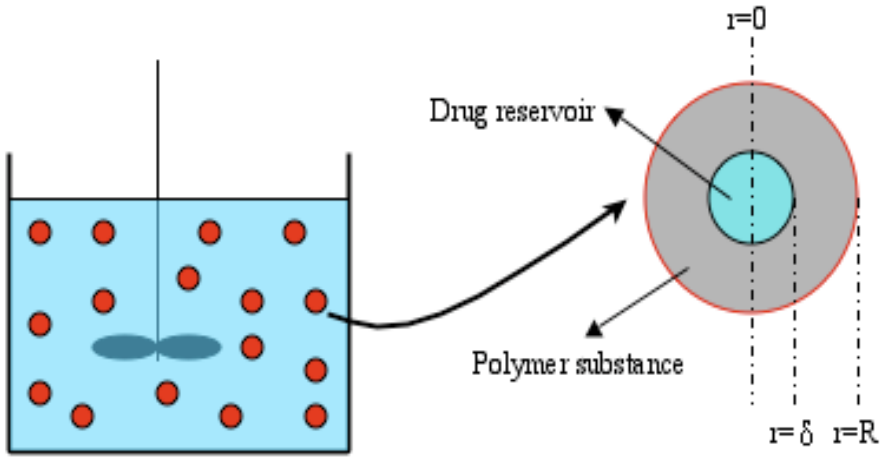

Figure 1

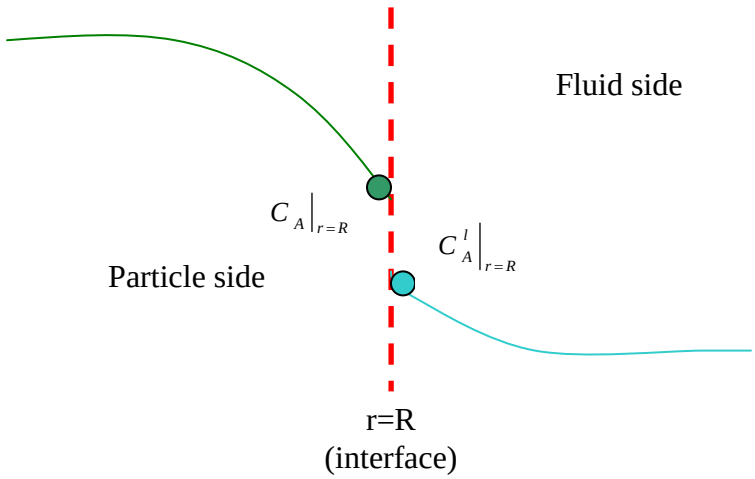

Figure 2

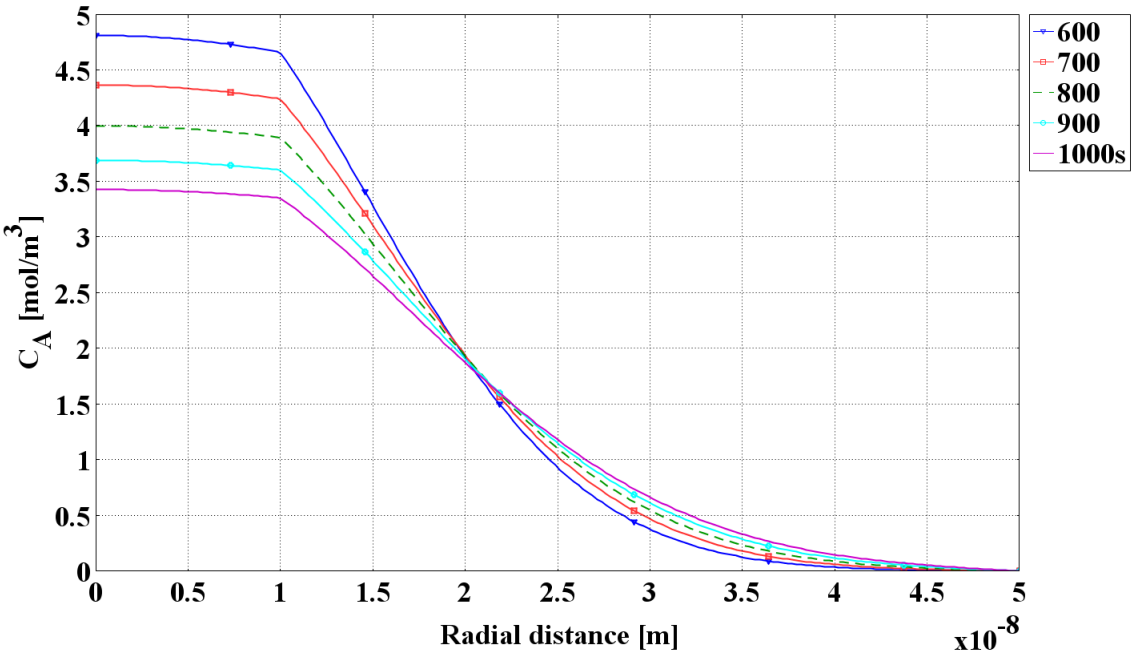
600
700
800
900
1000s
C_A [mol/m^3]
Radial distance [m]
x10^{-8}
0
0.5
1
1.5
2
2.5
3
3.5
4
4.5
5

Figure 3

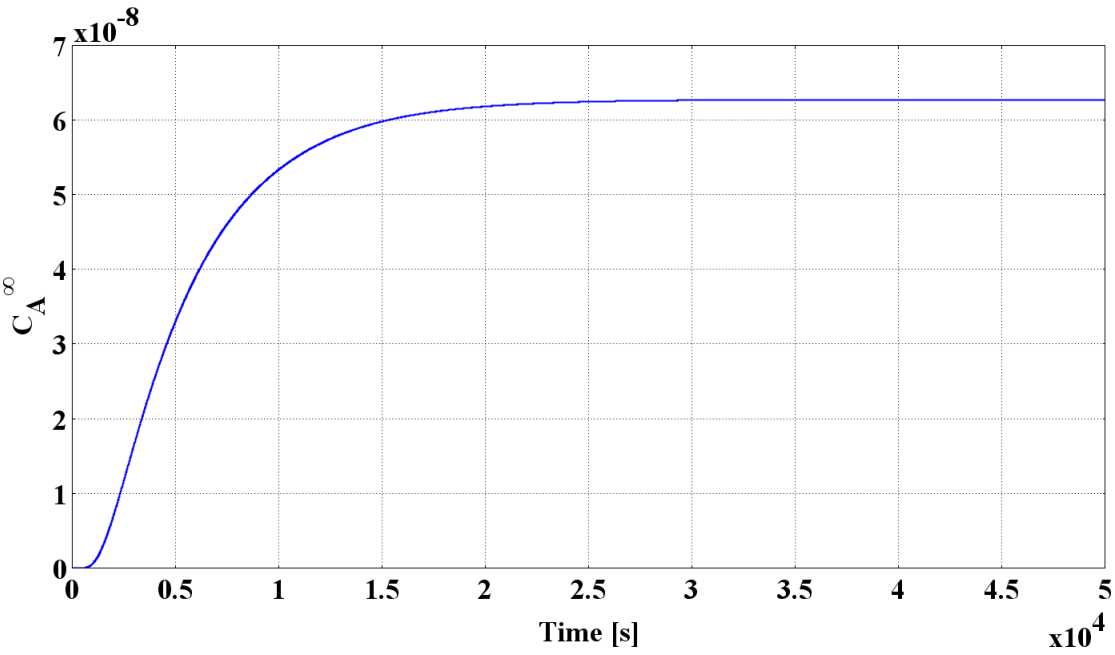

Figure 4