Computer Simulation and Applications in Life Sciences

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Part 0: Course Preliminaries
Course Preliminaries

• The course consists of 13 lectures + exercises
• Exercises will include programming tasks in MATLAB
• Overview at the end of this lecture
• Exam at the end of the lecture
• Grade based on exam, optional assignments can improve exam grade
• 6 ECTS
• Level: Master Computer Science or Bioinformatics
Course Grade

• The grade $G$ will be computed as:

\[ G = 0.1 \left( A + \left(1 - \frac{A}{100}\right) E \right) \]

• $A$ is the number of points achieved in the assignments (maximum 40 points)
• $E$ is the number of points achieved in the exam (maximum 100 points)
• Assignments should encourage active participation in the class; they are optional but can help to improve final grade.
• Assignments need to be handed in the next lecture, late submissions will not be counted.
Computation of grade

\[ G = 0.1 \left( A + \left( 1 - \frac{A}{100} \right) E \right) \]
Requirements

• Mandatory:
  – Basic Undergraduate Skills in Applied Mathematics (analysis, linear algebra)
  – Programming skills in imperative languages

• Useful but not mandatory:
  – Interest in life sciences and systems science
  – Knowledge in probability theory
  – MATLAB
Part 1: Simulation and Systems

Simulation of the fluid flow
In an chemical reactor
Systems analysis

• The **system analyst** analyses the world or parts of the world viewing it as a system

• His/Her aim can be to:
  – **Design** an artificial system
  – Change/**optimize** the system
  – **Understand** the system because of scientific curiosity, and **compare** it to other systems
  – Stabilize the system and **control** it
    or these things in combination ...

• Computer Simulation is an important tool of the system analyst
Simulation – Definition 1

1. *Simulation is a problem solving technique.*
2. *It is an experimental method.*
3. *Application of simulation is indicated in the solution of problems of (a) systems design (b) systems analysis.*
4. *Simulation is resorted to when the systems under consideration cannot be analyzed using direct or formal analytical methods.*

Another important aspect about simulation is captured in Shubik’s definition:

“A simulation of a system or an organism is the operation of a model or simulator which is the representation of the system.”

Simulation and Modelling

Input

Modeling

Output

Simulation

Optimization
In general the environment: not influenced by system but it influences system (interface: boundary), but this is often an abstraction.

**Open systems** interact with their environment (via the systems boundary), while **closed systems** do not.

However, the definition is not always used in the strict sense: In physics closed means closed w.r.t. matter exchange.

Find examples!
Black-box view of a system (model)

System-(model) (states variables, transformation laws)

Decision Variables (controllables)  
Environmental Variables (uncontrollables)  
Output Variables (observables)
System and Subsystems

• A system consists usually of several subsystems
• The subsystem models may be very different to the global model that connects them
• Multidisciplinary modeling: Coupling different subsystem-models in one system model
Example: Hydrodesalkylation plant

 Simulator: Aspen Plus™

[Emmerich et al., ECJ, Fall 2001, Vol. 9, No. 3, Pages 329-354]
Bacillus subtilis – regulatory network

System Variables

• Variables have a domain
• Variables can be stochastic or deterministic; stochastic variables
• Stochastic variables are characterized by their distribution
• Variables can be static or dynamic (functions of time)
Example 1: Simulation of an office building

- **Input variables:** Window Size, Air-Conditioning
- **Output variables:** Energy consumption, Thermal comfort
- **State variables:** Spatial Temperature distribution, Impulse of air particles in room
- **Environmental variables:** Weather conditions
Example 2: Simulation of a cell

- **Input:** Concentration of an introduced substance (e.g. a drug) outside the cell-membrane
- **Output:** Cell volume, emitted substances of cell
- **Transformation laws:** chemical reactions, material transport inside the cell
- **Inner state variables:** Concentration and spatial distribution of substances
- **Environmental variables:** Concentrations of substances outside the cell that cannot be controlled
Computer Simulation and System Analysis

- Mathematics
- Modeling Languages
- System Science
- Scientific Philosophy
- Computer Programming
- Statistics
- Application Domain
Why do we want to simulate a system?

- To understand it
- To control it
- To predict its behaviour (without risky/costly/impossible testing)
- To optimize it
- To rationalize decisions, opinions (misuse possible here!)
- To train people working with the system
- To implement realistic computer games
- To compress information
- ...
- Find examples!
Some history

- Prototypes as physical simulation models (e.g. ship design)
- Analog computers (especially in thermal simulation electric circuits were used to simulate)
- Digital Computers (.. this class)
  - SIMULA, Fortran were among the first simulation languages
  - Today wide spectrum of mainly application specific simulation languages
  - Fortran 90, C/C++, and MATLAB/SIMULINK often used to implement simulators
System and Model

• Models are never the same than the system but can show a very similar behaviour.
• In practice, models are almost always simplifications of the real world system.
• Models focus on aspect of the system that are needed to explain the systems behaviour.
• In scientific models Occam’s Razor principle is applied, but oversimplification is lurking. It is the art to find a good degree of complexity, as A. Einstein quotes:
  
  "Make everything as simple as possible, but not simpler."
• Explanatory models aim also for modeling the true underlying behavior of a system, while predictive models are measured solely by their ability to predict, no matter wether the underlying model has a relationship with reality or not.
Types of simulators: Iterated function systems

• A function is applied on its own output, repeatedly

• Fractals, Cellular automata are important examples

• Many examples in natural system simulation
Types of simulators: Finite automata and petri nets

- Finite automata are characterized by state transition diagrams
- The state changes based on events
- Petri nets allow for coupling of different states and simulation of concurrent systems
Types of simulators: Discrete Stochastic Process Simulation

- Stochastic distribution of the subsequent state is a function of the current state of a system
- Discrete markov chain analysis based on transition graph is predominant tool
- Applications e.g. in genetics and fault analysis
Types of simulators: Agent based simulation

- Multiple agents, each of which is based on the same simple rules
- Emergent behavior is difficult to be predicted from rules
- Applications in swarm simulation and for building evacuation and traffic planning
Types of simulators: Discrete event simulation

- Typical example: processing of queues
- Arrival times modeled by an stochastic distribution
- System behavior simulated by means of object-oriented computer program
- How to generate/couple random variables?
Types of simulators: Continuous simulation with differential equations I - examples

- Bacteria Population growth: $x =$ population size, $K =$ positive constant
  
  \[
  \frac{dx}{dt} = k \cdot x
  \]

- Predator prey dynamics in Lotka Volterra model: $x =$ predator population size, $y =$ prey population size; $A, B, C, \text{ and } E$: positive constants
  
  \[
  \frac{dx}{dt} = A \cdot x \cdot y - B \cdot x
  \]
  \[
  \frac{dy}{dt} = C \cdot x - E \cdot x \cdot y
  \]
Types of simulators: Continuous simulation with differential equations II

- Computing trajectories of systems in continuous time and space
- (Partial) differential equation solvers are main technique
- System diagrams used to visualize dependences between state variables

\[
\begin{align*}
\frac{dx}{dt} &= \sigma(y - x) \\
\frac{dy}{dt} &= x(\rho - z) - y \\
\frac{dz}{dt} &= xy - \beta z
\end{align*}
\]
Types of simulators: (Non-)linear equation systems solvers

- Often the observed state of a system is the system in an equilibrium.
- In this case the solution of a differential equation system reduces to the solution of an equation system as change rates are zero.
- Examples: chemical equilibria, molecular simulation, (hydro)statics, economical equilibra of markets.

\[
\begin{align*}
\frac{dx}{dt} &= A - C y + E x \\
\frac{dy}{dt} &= B x - D
\end{align*}
\]

\[
\begin{align*}
dx/dt &= 0, \ dy/dt = 0 \ (\text{Equilibrium}) \\
A-Cy + Ex &= 0 \\
Bx - D &= 0
\end{align*}
\]

(existence of solutions depends on constants)
Types of simulators: Stochastic continuous simulation

- Differential equations with stochastic variables
- Ito Integrals and random field simulation are techniques
- Applications in financial market, biological systems, brownian motion, neurodynamics
Simulation Examples

- growth simulation of plants, cities, etc (iterated function systems)
- Evacuation strategies for buildings, football stadiums (discrete event, cellular automata)
- analysis of pollutant dispersion using dispersion models (differential equations)
- design of complex systems such as logistics systems and queues (discrete event simulation)
- design of noise barriers to effect roadway noise mitigation (stochastic simulation)
- flight simulators to train pilots (computational geometry, differential simulation)
- weather forecasting (stochastic differential equations, cellular automata)
- behavior of structures under stress and other conditions (nonlinear equation systems)
- design of chemical processing plants (nonlinear equation systems)
- Strategic Management and Organizational Studies (discrete event simulation)
- Reservoir simulation for the petroleum engineering (data driven modeling, cellular automata)
- Traffic engineering to plan or redesign parts of the street network (multi-agent, cellular automata)
- Simulation of cells and metabolic pathways in biology (differential equations)
## Classification of simulators

<table>
<thead>
<tr>
<th>Type of state variables</th>
<th>Discrete</th>
<th>Continuous</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time</td>
<td>Discrete</td>
<td>Continuous</td>
</tr>
<tr>
<td>Stochasticity</td>
<td>Deterministic</td>
<td>Stochastic</td>
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</tbody>
</table>
Aim of the course

• Get familiar with the main types of simulation programs, and how to implement them
• Learn how to validate simulation models
• Learn how to classify behavior of dynamic systems
• Get insight into the dynamics of real world systems with application focus life sciences
Structure of CSA course

1. Discrete time, deterministic (Iterated function systems, cellular automata, …)
2. Discrete time and space, stochastic (discrete random variables, markov chains, monte-carlo)
3. Continuous time, discrete space, stochastic (cont. random variables, discrete event simulation, queues)
4. Continuous time and space, deterministic (differential equations, dynamic systems models)
5. Continuous time and space, stochastic (Ito, Random fields)
6. Validation and calibration of system models
7. Experimental design and optimization

Examples will be provided throughout the class
Assignment 1 (4/40 Points)

- Describe a complex system of your choice, answer the following questions:
  - Describe the system, its environment, and boundary
  - What are the different kinds of system variables and their domains.
  - What are typical questions the system analyst might be interested in when analysing the system
  - What type of system simulation could be used to analyse this system
- Write about 2 DIN A4 pages in het Nederlands or English
- Hand in your answer in the next lecture as a hardcopy, including student number and name
- Working in pairs is possible.