Modeling and Simulation

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Introduction

- Modeling and simulation – usage of model (in our case) for a system in order to simulate it.
- Mathematical model – a common representation for one systems using mathematical concepts
  - Linear/nonlinear
  - Deterministic/Probabilistic (Stochastic)
  - Discrete/Continue
  - Logic (Deductive, Inductive)
- How good is an model?
  - Measure of error between experimental output and model output, for the same inputs must be smallest, that is the fitting is close to 100% (for some situations, RMSE < 1% is a very good result)
  - Model process is connected with identification process

- In many situations, a black-box (input-output pairs of data) is given. The task is to propose “something” inside box that model the systems. A good model is a model that have physical (or chemical) explanations. Without it, there are a simple or complex mathematical formula, very correct, but no connection with phenomenological aspects.

- Refine of the model to improve the performances
- Systems of Differential Equations
- Compartmental Models (e.g. epidemiological, SIR, SEIR, Swine Flu (A1H1N1), Ebola, etc.)
- Model
  - Polynomial model
  - RSM (response surface methos)
  - System of (partial) differential equations
  - Transfer functions (continuous, discrete)
  - Regression models (ARMA, ARX, NARX, etc).

$$a_n \frac{d^n y}{dt^n} + a_{n-1} \frac{d^{n-1} y}{dt^{n-1}} + .. + a_0 y = b_m \frac{d^m u}{dt^m} + b_{m-1} \frac{d^{m-1} u}{dt^{m-1}} + .. + b_0 u, \quad t \in \mathbf{R}, \quad (\text{LTI})$$

$$a_i \in \mathbf{R}, \; a_n \neq 0, \; b_i \in \mathbf{R}.$$

Initial conditions and causality

$$u(t) \equiv 0, \; y(t) \equiv 0, \; t < 0.$$

$$u^{(k)}(-0) = 0, \quad k = \overline{0, m-1},$$

$$y^{(k)}(-0) = 0, \quad k = \overline{0, n-1}.$$

Laplace $U(s) = \mathscr{L}\{u(t)\}$, $Y(s) = \mathscr{L}\{y(t)\}$

$$G(s) \triangleq \frac{Y(s)}{U(s)} = \frac{b_m s^m + b_{m-1} s^{m-1} + \ldots + b_0}{a_n s^n + a_{n-1} s^{n-1} + \ldots + a_0},$$

$$Y(s) = G(s) U(s).$$

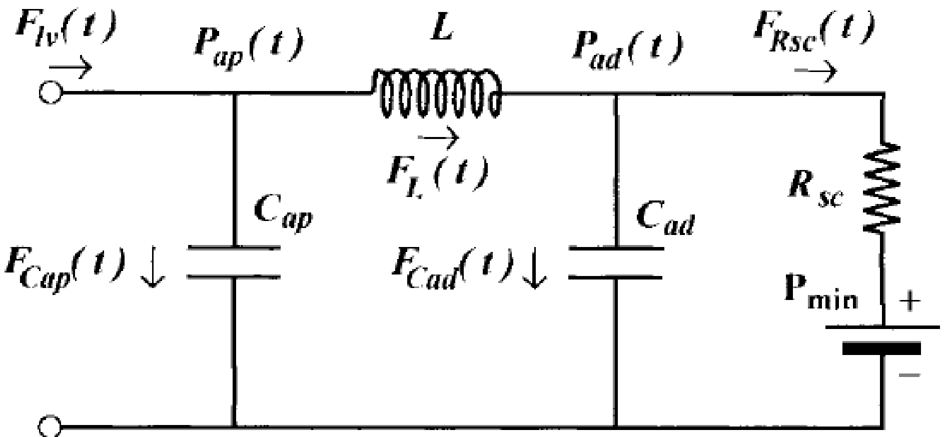
G(s) - Transfer function

$$\begin{aligned} \dot{\mathbf{x}} &= \mathbf{A}\mathbf{x} + \mathbf{B}\mathbf{u} \\ \mathbf{y} &= \mathbf{C}\mathbf{x} + \mathbf{D}\mathbf{u} \end{aligned}$$

LTI (Linear Time Invariant Systems)

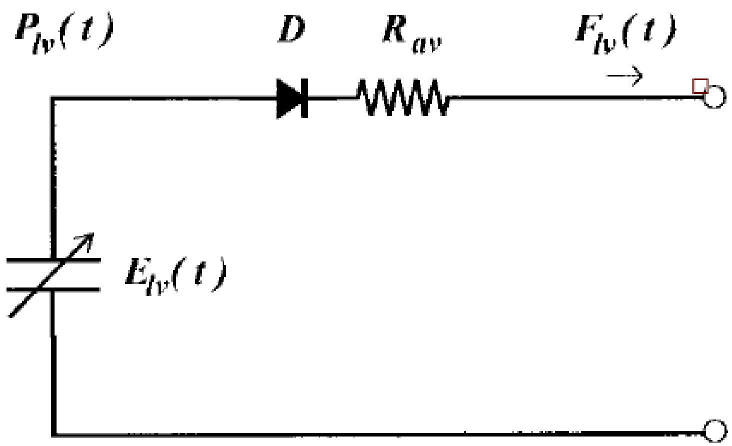
- Many systems are non-linear. The initial step is to “guess” a first model (e.g. sum of decay models). Refinements are constructed in the next steps.
- Such models require ability and experience in modeling and simulation
- Stochastic models (e.g. transition to one compartment to another with some probability.
- Stochastic differential equations (Euler–Maruyama Method, Higham's discretized Brownian paths)

- When a model that use transfer function is useful?
  - Stability analysis
  - Control engineering
  - System identification
- Matlab/Simulink has toolboxes that are used for transformation *state space* ↔ *transfer function*, *continuous* ↔ *discrete*, etc.
- Numerical solutions (stiff and non-stiff equations) for differential equations and system of partial differential equations are available using *ode* (Matlab).
- Other nonlinear models propose to other equivalent circuits in order to made a correspondence that are easily to be manipulated. Electric equivalent circuit for arterial load is an example from cardiovascular system (Guarini)



Aortic load model.

C_{ap}	aortic capacitance;
C_{ad}	distal arterial capacitance;
L	aortic blood column inertia;
R_{SC}	systemic resistance;
$P_{\min}$	pressure at zero flow.



Left-ventricular model.

Marcello Guarini, Jorge Urzua, Aldo Cipriano, Waldo Gonzalez,
Estimation of Cardiac Function from Computer
Analysis of the Arterial Pressure Waveform,
IEEE TRANSACTIONS ON BIOMEDICAL ENGINEERING,
VOL. 45, NO. 12, DECEMBER 1998

Numerical Methods

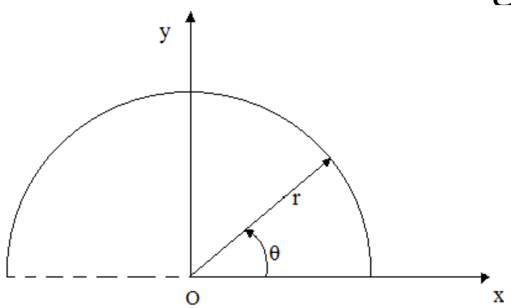
- Analytical solution for biological models are not very frequently (especially we refer to 2D or 3D models)
- Finite Difference method (FDM). The basic idea of FDM is to replace the partial derivatives by approximations obtained by Taylor expansions near the point of interests
  - Forward difference (explicit method)
  - Backward difference (implicit method)
  - Central difference approximation
  - Crank–Nicolson scheme
- Numerical accuracy
  - The problem to be solved
  - Discretization scheme (How define a set of grid points in the domain D)
  - Algorithm used
- Current issues in FDM: Numerically stability and convergence
- Other methods (Newton–Raphson method) – derivative of function, optimization

Mathematical Modeling and Simulation for Keloid Scars Formation From The Prosthetic Blunt Socket[1]

- This paper tries to simulate the formation process using data from keloide proceeds model healing of biology.
- From a medical point of view the physiological stages of wound healing the operators are: inflammation, proliferation, remodeling.
- The phase hemostasis (some authors do not consider that this is a phase)
- The common problems of wear that occur in the bone-to-muscle tissue and blunt-socket are: pain from pressure and friction, wound, sweating, elimination of water after metabolic process, impairment of immune function and skin protection, microscopic fractures in the muscle fibers, changes in temperature.
- The scar forms because of the excessive dermal collagen deposition. A keloid scar is heterogeneous in nature, with more cellular activity at the periphery than in the centre.
- central cells show a tendency to decrease under the ptosis.

[1]M. Turnea, M. Rotariu, D. Arotaritei – Mathematical Modeling and Simulation for Keloid Scars Formation From The Prosthetic Blunt Socket, ATEE, 2013, pp. 1-4.

- The Sheratt-Chaplain model is used: the cells can be in one of three states: proliferation *p(x,t)*, quiescent (static) *q(x,t)* and necrotic *n(x,t)*.
- The keloid is modeled as a spatial spheroid.
- We assume that the *p(x,t)* and *q(x,t)* populations have equal motility, the movement term is given by



Spherical coordinates

$$\frac{\partial}{\partial x}\left(\frac{p}{p+q}\frac{\partial(p+q)}{\partial x}\right)$$

$$\frac{\partial}{\partial x}\left(\frac{p}{p+q}\frac{\partial(p+q)}{\partial x}\right)$$

$$\begin{cases} \frac{dp}{dt} = \frac{\partial}{\partial x}\left(\frac{p}{p+q}\frac{\partial(p+q)}{\partial x}\right) + g(c)p(1-p-q-n) - f(c)p \\ \frac{dq}{dt} = \frac{\partial}{\partial x}\left(\frac{p}{p+q}\frac{\partial(p+q)}{\partial x}\right) + f(c)p - h(c)q \\ \frac{dn}{dt} = h(c)q \end{cases}$$

$$c = \frac{c_0\gamma}{\gamma+p}(1-\alpha(p+q+n))$$

c(x,t) – concentration of nutrients, f and h are decreasing functions, *g*(0) is set to 1 (initial conditions), *g* is an increasing function (functions of increasing/decreasing of population

$f(c)=(1-tanh(4c-2))/2$

$g(c)=\alpha e^{\alpha c}$, $\alpha=0.5$ ($\alpha \in (0, 1]$) (Gompertz)

- q(x,0) = 0, n(x,0)=0, c=1 – initial conditions
- Finite difference equations, Mx+1 segments, Δx=(xf-x0)/(Mx+1) and Δt=(tf-t0)/(Nt+1) , Mx+2 and Mt+2 discrete points.

$$p_i^{j+1} = p_i^j + \Delta t\left[u_i^j + g(c_i^j)p_i^j(1 - p_i^j - q_i^j - n_i^j) - f(c_i^j)p_i^j\right]$$

$$q_i^{j+1} = q_i^j + \Delta t\left[v_i^j + f(c_i^j)p_i^j - h(c_i^j)q_i^j\right]$$

$$n_i^{j+1} = n_i^j + \Delta t\left[h(c_i^j)q_i^j\right]$$

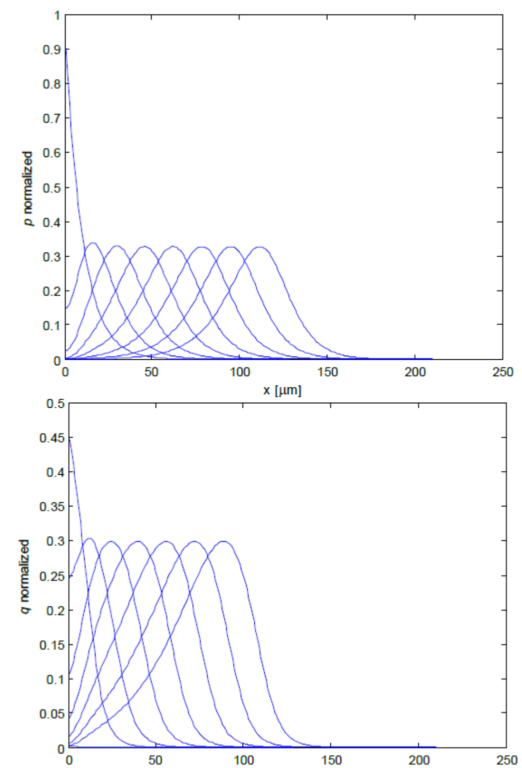
$$c_i^j = \frac{c_0\gamma}{\gamma+p_i^j}\left(1 - \alpha\left(p_i^j + q_i^j + n_i^j\right)\right)$$

where

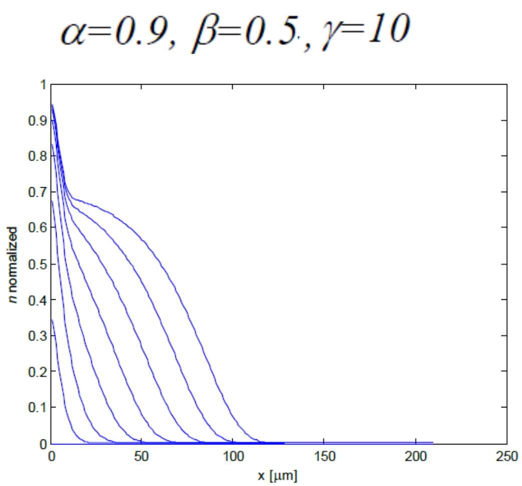
$$u_i^j = \frac{(p_{i+1}^j - p_{i-1}^j)r_i^j(r_{i+1}^j - r_{i-1}^j) + 4p_i^j r_i^j(r_{i+1}^j - 2r_i^j + r_{i-1}^j) - p_i^j(r_{i+1}^j - r_{i-1}^j)^2}{4(\Delta x)^2(r_i^j)^2}$$

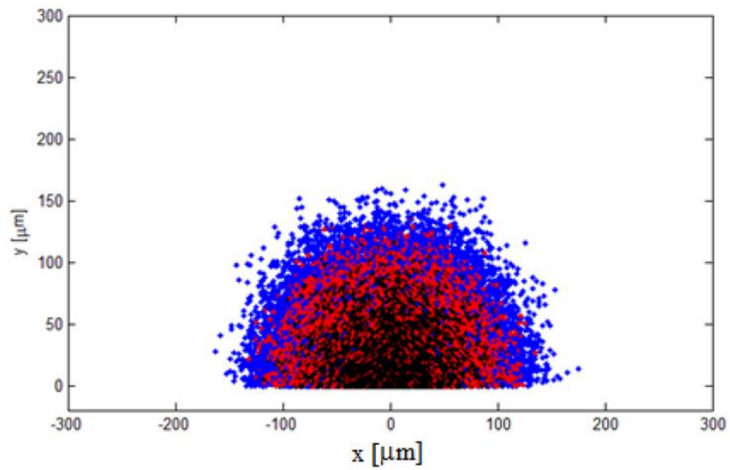
$$v_i^j = \frac{(q_{i+1}^j - q_{i-1}^j)r_i^j(r_{i+1}^j - r_{i-1}^j) + 4q_i^j r_i^j(r_{i+1}^j - 2r_i^j + r_{i-1}^j) - q_i^j(r_{i+1}^j - r_{i-1}^j)^2}{4(\Delta x)^2(r_i^j)^2}$$

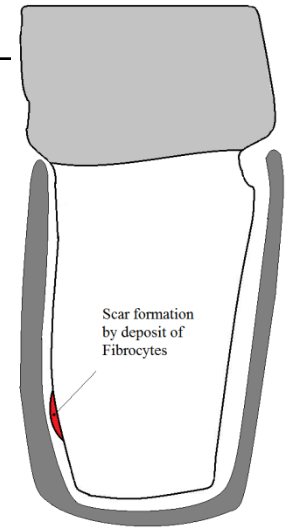
$$r_i^j = p_i^j + q_i^j$$



α=0.9, β=0.5, γ=10







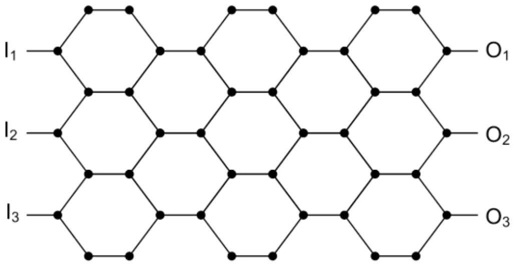
- The contact between the abutment and exo-prosthesis cup is considered a friction coupling that undergoes wear faster or slower depending on the characteristics and structure of the material components.
- The system of tribological wear is the process by which material suffer loss or gains for the surface modification of the initial state.
- The keloid scars directly influence the contact between the abutment and the prosthesis cup, increasing the pressure points.
- A study for evolution of keloid scars could provide valuable insights about the mechanisms of cell growth and the proliferation at the interface between scar blunt-level socket.
- The graphical output of the mathematical model for a keloid scars, shows interactions in the evolution of cells proliferating.
- Validating a model means essentially examining whether it is good enough in relation to its intended purpose.

Axon-inspired Communication[2]

- Communication on an axon could be modeled by an array of logic gates, where each logic gate emulates a voltage-gated ion channel.
- The probability of correct communication is estimated using such a model and an associated reliability analysis for logic gates/circuits known as probabilistic gate matrix (PGM)
- Such an approach can easily be extended to other types of (regular) arrays of logic gates, and to more complex connection patterns, including even feedbacks (that could model the time dependence of neighboring voltage-gated ion channels on any given voltage-input ion channel).
- Nanotechnology – intention to application in hardware
- Experimental data – provided by Al Ain University (UAE)
- Simon software validation (Al Ain University (UAE))

[2]D. Arotaritei, V. Beiu, M. Turnea, M. Rotariu, Probabilistic Gate Matrix for Axon-inspired Communication, The 4th IEEE International Conference on E-Health and Bioengineering - EHB 2013, November 21-23, ISBN: 978-I-4799-2.

- A hexagonal array was proposed in for emulating the signal transmission realized by voltage-gated ion channels on an axon.



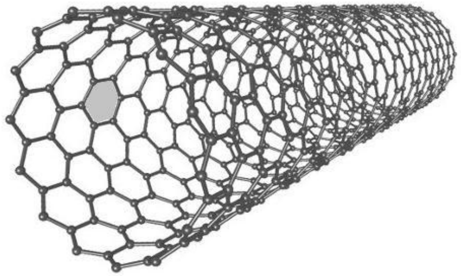
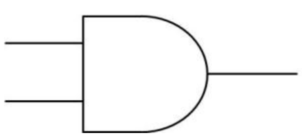


Fig. 1. 2D hexagonal array.

Fig. 2. 3D hexagonal array used to model axon communication.

- Communication takes place through the nodes of each hexagonal cell, from the inputs $I_1, I_2, \ldots, I_n$ to the outputs $O_1, O_2, \ldots, O_n$. The network has n inputs, n outputs, and m levels of nodes. The number of inputs should be equal to the number of outputs (an arbitrary condition) and, for simplifying an output voting process, n should be of the form $n = 2k+1$.
- A *probabilistic gate matrix* (PGM) is used to model "noisy" logic gates
- The error-free function of one logic gate or one combinational logic circuit (CLC) can be represented by its truth table.

- If the functionality of the gate/CLC is affected by errors, the behavior is modeled by a *probabilistic transfer matrix* (PTM)
- Let us denote by $p = PF_{\mathrm{GATE}}$ the probability that the logic gate will give an incorrect output. As an example, the PTM for an AND-2 gate is presented in Fig. 3. In the presence of errors, for input vector 00 the output of the gate will be 0 with probability *p*, while for input vector 00 the output of gate will be 1 with probability 1–*p*. The PTMs for other logic gates (OR-2, NAND-2 and NOT) are shown in Fig. 4.



inputs \ output	0	1
00	$1-PF_{gate}$	PF_{gate}
01	$1-PF_{gate}$	PF_{gate}
10	$1-PF_{gate}$	PF_{gate}
11	PF_{gate}	$1-PF_{gate}$

(a)

inputs \ outputs	0	1
00	1-p	p
01	1-p	p
10	1-p	p
11	p	1-p

(b)

inputs \ outputs	0	1
00	1-p	p
01	p	1-p
10	p	1-p
11	p	1-p

(c)

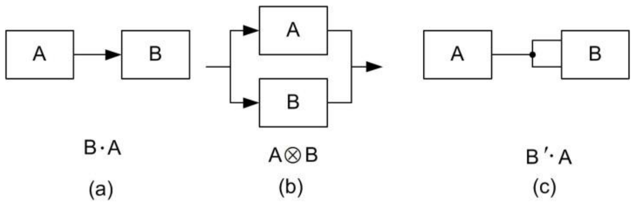
inputs \ outputs	0	1
00	p	1-p
01	p	1-p
10	p	1-p
11	1-p	p

(d)

inputs \ outputs	0	1
0	p	1-p
1	1-p	p

PTMs for: (a) AND-2; (b) OR-2; (c) NAND-2; and (d) NOT.

- It is assumed that the errors occur independently. PTM assumes that all the gates are connected into sub-circuits, and all the sub-circuits are connected together in order to produce an input/output transfer with probability represented by a PTM associated to the entire circuit
- Basic operations in PTM "algebra" applied to interconnected logic circuits: (a) serial; (b) parallel; and (c) fan-out.



$$I=\begin{bmatrix}1 & 0\\0 & 1\end{bmatrix}$$

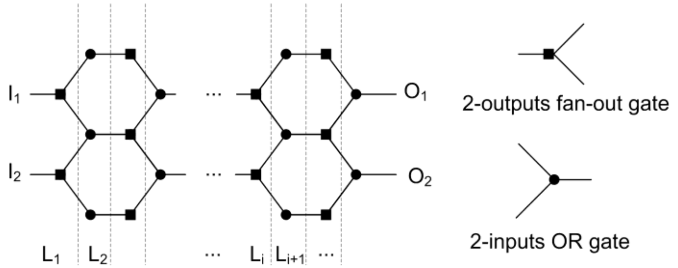
(a)

$$F_2=\begin{bmatrix}1 & 0 & 0 & 0\\0 & 0 & 0 & 1\end{bmatrix}$$

(b)

Matrices for wiring gates/circuits: (a) I_2 identity matrix.

- 2D hexagonal array: rectangles represent fan-out nodes and circles represent logic gates (OR-2).



- Parallel composition of two or more logic circuits (gates) is made using the tensor product (Kronecker) A⊗B.
- The parallel composition of two matrices of $m \times n$ and $p \times r$ elements will have $(m \times n) \times (p \times r)$ elements, and leads to a dimensionality explosion of PTM when applied to large circuits.
- In order to improve the computational efficiency of matrices, algorithms that use Algebraic Decision Diagrams (ADD) can be used.
- Another solution for correct tensor is the usage of product with zero padding
- Using PTM for the circuit having n inputs I_i, the probability of failure of the layers is given by:

$$PL_1 = PL_{junctions} = \underbrace{F_2 \otimes F_2 \otimes \ldots \otimes F_2}_{n\ times} \qquad R_{parallel} = (1-R)^{\sqrt{2n}}$$

$$PL_2 = PL_{OR\ gates} = \underbrace{OR \otimes OR \otimes \ldots \otimes OR}_{n\ times}. \qquad R_{serial} = [1-(1-R)^n]^{m/2}.$$

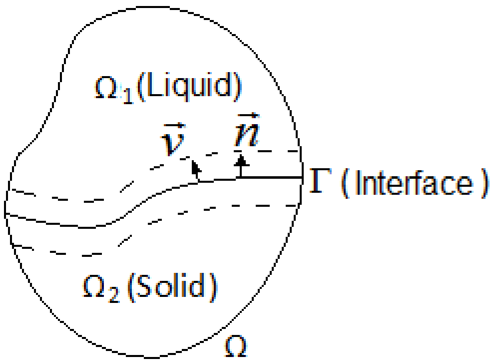
$$PL_{nm} = 1-(1-p^{\sqrt{2n}})^{m/2}$$

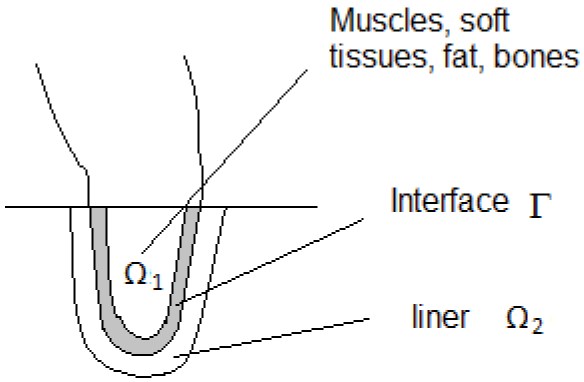
- The result we have obtained is . If we consider the extreme case when $Rel_{\mathrm{GATE}} = 1 - PF_{\mathrm{GATE}} = 0.5$ (reliability is denoted by *Rel*), for $n = 3$ and $m = 8$ we get $Rel_{3,8} \approx 0.586$, which is better than 0.5. If we suppose that $PF_{\mathrm{GATE}} = 0.1$ we get $Rel_{3,8} \approx 0.996$ which shows that an array can significantly improve the reliability of transmission at the system/circuit level
- We could use other types of array (like, e.g., triangular ones), or other types of gates (like, e.g., NAND, AND, XOR or MAJ) using the same method presented above

Modeling skin fracture in prosthetic application

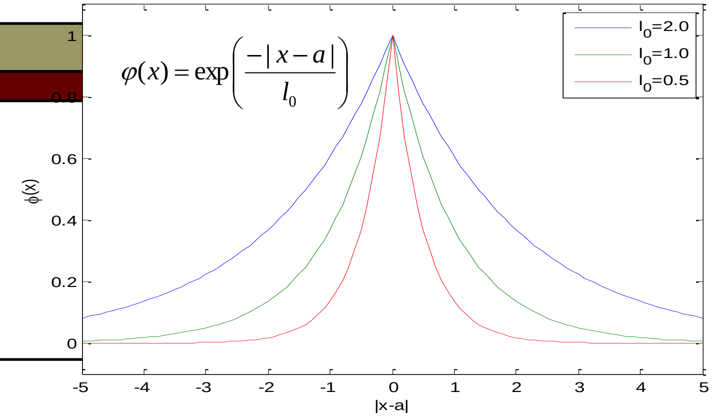
- Fracture in materials can happen in various forms in different medical applications. In recent years, the introduction of phase field model that describe the kinetic of transition between two phases (in our case two different materials was proven to be useful for crack modeling. A parameter makes distinction between two phases of the material, the solid one and the “broken” one, the crack.
- Based on Landau–Ginzburg approach, Caginalp proposed a phase-field model that incorporated surface tension, anisotropy, curvature and dynamics of the interface
- Caginalp based approach that can be used for materials with memory in conjunction with temperature evolution due to frictional caused at the phase field interface.
- ABAQUS is a suitable CAD to develop own model for fractures. UEL and UMAT subroutines can be used to develop phase field model for brittle fracture numerical approach

- Material that occupy a zone Ω can exists in two phases: Ω_1 – liquid or Ω_2 – solid. The phases are separated by an interface Γ. The dotted lines indicate a possible interface between two phases.





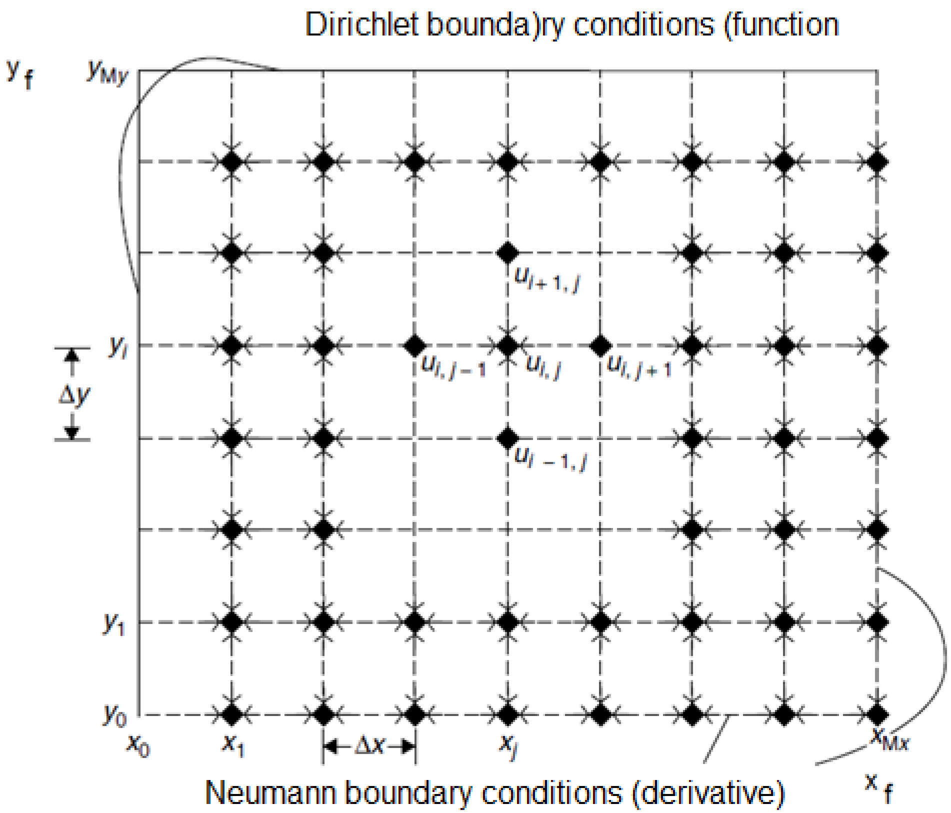
- The Caginalp model is a complex one, analytical solution is not found yet.
- Numerical methods (discretization is a challenge in 3D).



$$\begin{cases} \varphi_t(t,x) - \dfrac{\xi^2}{\tau}\Delta\varphi(t,x) + \dfrac{1}{2\tau}(\varphi^3 - \varphi)(t,x) = \dfrac{2}{\tau}u(t,x) + f(x,t),\ (t,x) \in R_+ \times \Omega \\ \left(u(t,x) + \dfrac{l}{2}\varphi(t,x)\right)_t - \displaystyle\int_{-\infty}^{t} a(t-s)\Delta u(s,x)dx = g(t,x) \end{cases}$$

$$\begin{cases} \varphi(0,x) = \varphi_0(x), \quad u(0,x) = u_0(x),\ x \in \Omega \\ u(t,0) = u^0(t,x), \quad (t,x) \in R_- \times \Omega \end{cases}$$

$$\begin{cases} \varphi(t,x) = \varphi_1(x) \\ u(t,x) + \alpha\dfrac{\partial u}{\partial \nu}(t,x) = h(x), \quad x \in R_+ \times \Omega \end{cases}$$

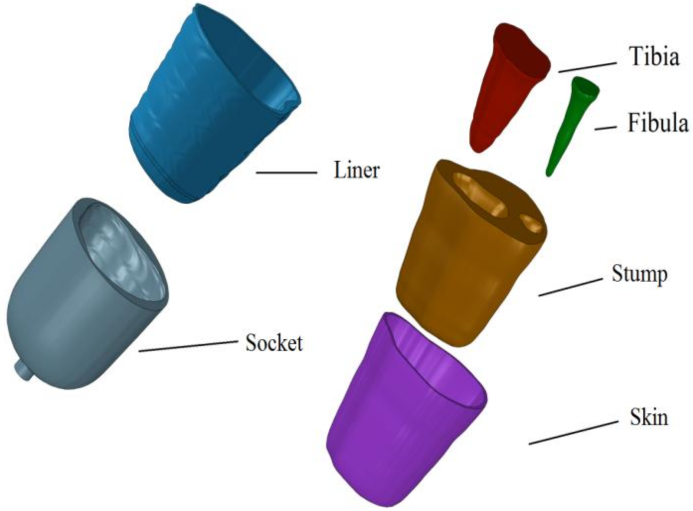


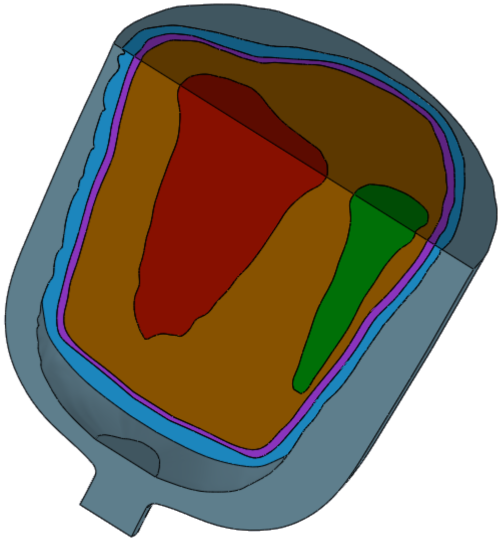
$$H\frac{u_{i+1}^k - 2u_i^k + u_{i+1}^k}{\Delta x^2} = \frac{u_i^k - u_i^{k-1}}{\Delta t}, \qquad H \text{ constant}$$

$$-ru_{i-1}^k + (1+2r)u_i^k - ru_{i+1}^k = u_i^{k-1}, \qquad r = H\frac{\Delta t}{\Delta x^2}, \quad i = 1,2,\ldots,M-1$$

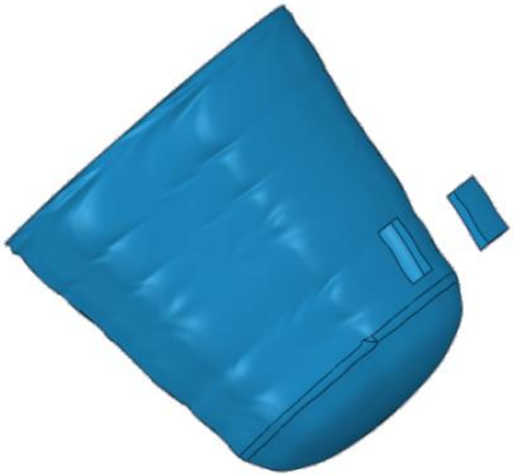
$$\begin{bmatrix} 1+2r & -r & 0 & \cdot & 0 & 0 \\ -r & 1+2r & -r & \cdot & 0 & 0 \\ 0 & -r & 1+2r & \cdot & 0 & 0 \\ \cdot & \cdot & \cdot & \cdot & \cdot & \cdot \\ 0 & 0 & 0 & \cdot & 1+2r & -r \\ 0 & 0 & 0 & \cdot & -r & 1+2r \end{bmatrix} \begin{bmatrix} u_1^k \\ u_2^k \\ u_3^k \\ \cdot \\ u_{M-2}^k \\ u_{M-1}^k \end{bmatrix} = \begin{bmatrix} u_1^{k-1} + ru_0^k \\ u_2^{k-1} \\ u_3^{k-1} \\ \cdot \\ u_{M-2}^{k-1} \\ u_{M-1}^{k-1} + ru_M^k \end{bmatrix}$$

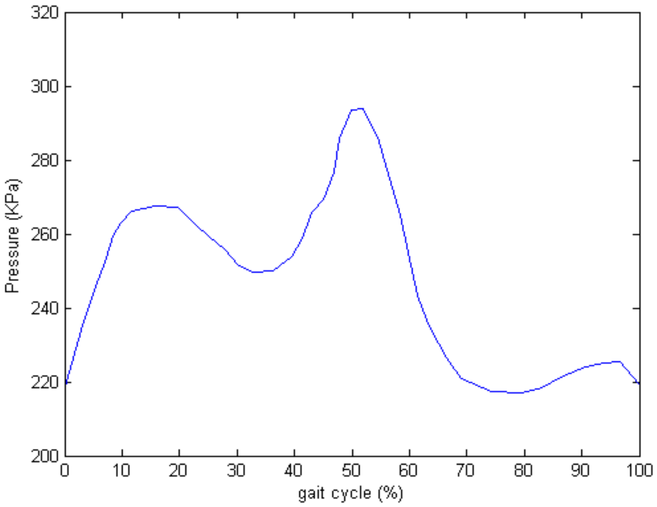
Crank-Nicholson method

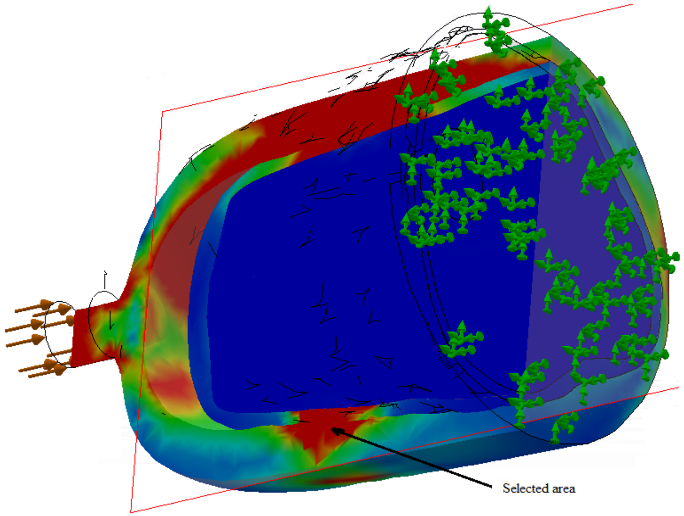




Pressure in. popliteal depression (PD).



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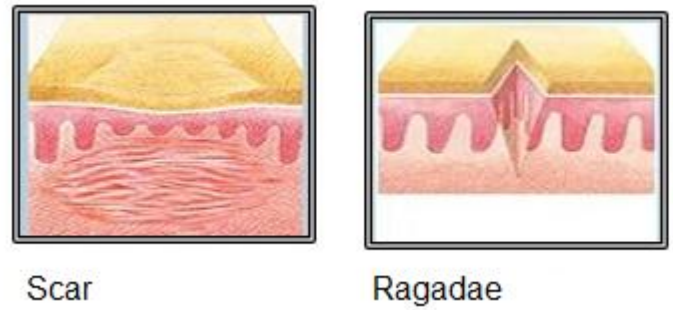
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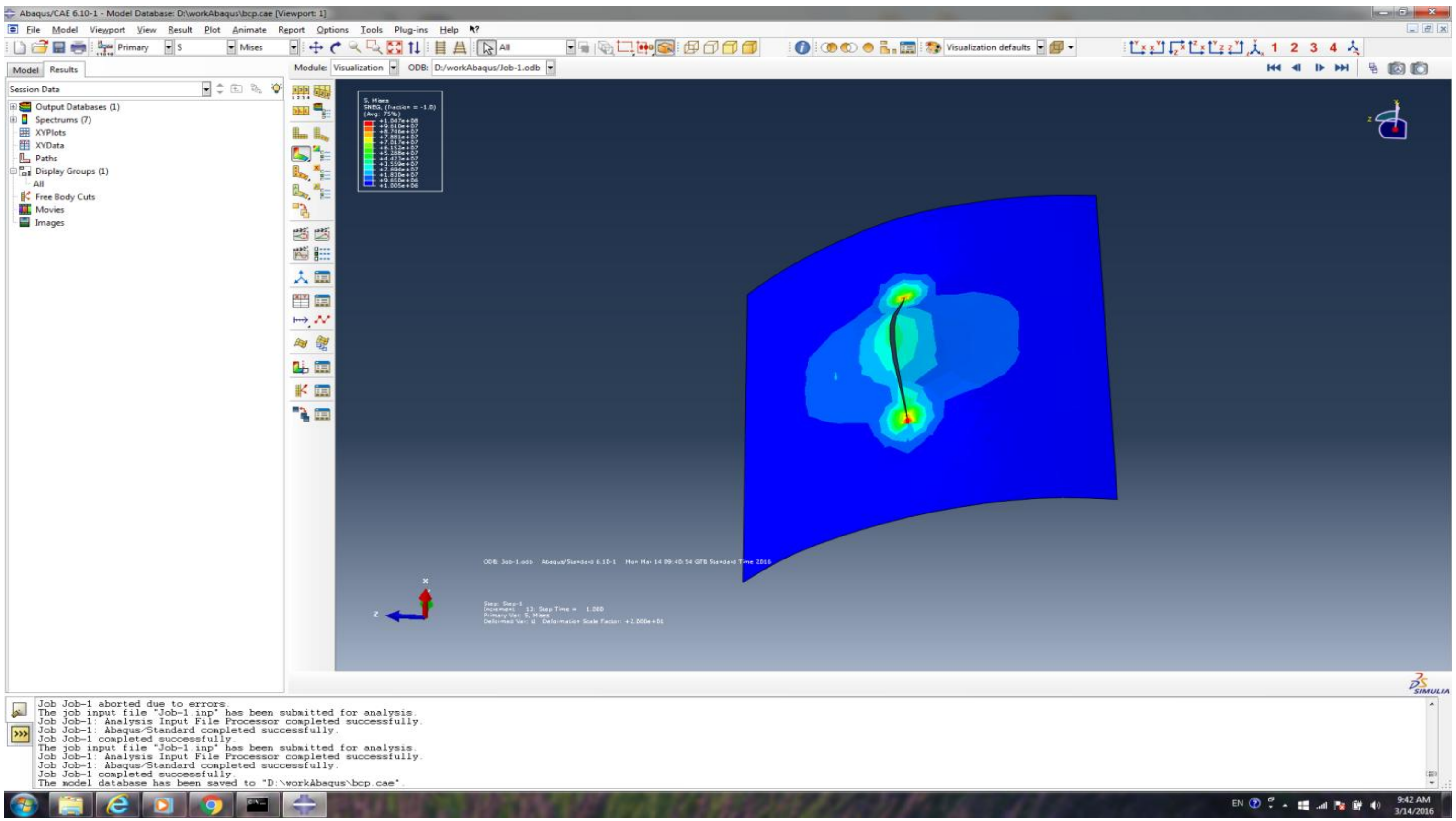
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Job Job-1: Analysis Input File Processor completed successfully.
Job Job-1: Abaqus/Standard completed successfully.
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Conclusions

- The model representation must be adequate to objective of the problem.
- State space models are used frequently in control engineering problems (e.g. control anesthesia)
- Compartmental model are used frequently in epidemiological models but also can be used also in Pharmacokinetics-Pharmacodynamic compartmental model
- System of differential Equations (SDE) or System of partial differential Equations (SPDE) can be considered the most used model for deterministic modelling.
- Applications from farmacokinetics (chemical equations) can be translated in quantitative SDE or SPDE and solved numerically (e.g. Model of epidermal wound Healing by J. Sherratt).
- Chemical Decomposition Reactions can be translated are using *Law of mass action*, e.g. Michaelis-Menten kinetics

- Bayesian models use inference model, there is a probabilistic approach. Most of usage in biomedical engineering is oriented toward expert systems and decision support system
- Stability of numerical methods are tested usually in practical application, the is the convergence of solution is tested most frequently heuristic
- The most suitable solution for modeling a biomedical phenomenon and not only depend also of experience.

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Thank you for your attention!