Modular modeling of the human cardiovascular system

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Implemented models

1. Overall Circulation model by Guyton et al., 1972, (ODE).


Integrated modular models

Complex model 1:
• pulsating heart,
• kidney regulation.

Complex model 2:
• pulsating heart,
• kidney regulation,
• blood flow through arterial tree vessels.
Overall Circulation Model

Guyton A.C., Coleman T.G., Grander H.J.  
Circulation: Overall Regulation.  
Ann Rev Physiol. 1972. 41:13-41
Ann Rev Physiol. 1972. 41:13-41
Modular Overall Circulation model

18 modules
234 parameters
39 ordinary differential equations
172 assignments
Experiment with salt intake

Salt intake increased 5-fold.
Kidney functioning decreased 2-fold.
Total simulation time ~ 2 weeks.
Human CVS model with pulsating heart

Solodyannikov Y.V.
Elements of mathematical modeling and identification of cardiovascular system.
Samara. The university of Samara, 1994.
Model with pulsating heart

- 59 parameter
- 6 differential equations
- 14 assignments
- 2 events

Q – blood flow, P – pressure
R – resistance, V – volume
DO₂ – oxygen debt
H – neurohumoral factor
Simulation results

ml/s

mm Hg

Blood flow from ventricle to arteries

Blood flow through capillaries

Mean arterial pressure
Human CVS model with kidney regulation

Karaaslan F. et al.
Long-term mathematical model involving renal sympathetic nerve activity, arterial pressure, and sodium excretion.
Karaaslan F. et al.  
Long-term mathematical model involving renal sympathetic nerve activity, arterial pressure, and sodium excretion.  
Model with kidney regulation

- 86 parameter
- 11 differential equations
- 62 assignments
Model with kidney regulation

- 86 parameter
- 11 differential equations
- 62 assignments
Model with kidney regulation

- 86 parameters
- 11 differential equations
- 62 assignments
Experiment with sodium intake

Mean arterial pressure, mmHg

Total experiment time – 14 days.
Sodium intake increased from 0.126 to 0.26 mEq/l after 1 day and decreased to 0.02 mEq/l after 6 days.
Comparison with the original model

BioUML results

From original paper

Renin concentration, Ratio to normal

Aldosterone concentration, Ratio to normal

Aldosterone concentration, Ratio to normal
Complex modular model of the Human CVS:

pulsating heart
and
kidney regulation

• Same formalisms: ODE with discrete events
• Different time scales: minutes and seconds
Models integration

Pulsating heart

Kidney regulation
Models integration

Pulsating heart

Kidney regulation
Similar functional modules

Pulsating heart

Kidney regulation

Arterial System

Heart

Arteries
## Model parameters

<table>
<thead>
<tr>
<th>Pulsating heart</th>
<th>Kidney regulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial pressure (systole-diastole)</td>
<td>Mean arterial pressure</td>
</tr>
<tr>
<td>Arterial resistance</td>
<td>Arterial resistance</td>
</tr>
<tr>
<td>Cardiac output (during systole)</td>
<td>Cardiac output (per minute)</td>
</tr>
<tr>
<td>Blood volume (constant)</td>
<td>Blood volume (changing)</td>
</tr>
<tr>
<td>-</td>
<td>Right atrium pressure</td>
</tr>
<tr>
<td>Neuro-humoral regulation</td>
<td>-</td>
</tr>
<tr>
<td>-</td>
<td>Vascularity</td>
</tr>
<tr>
<td>-</td>
<td>Autonomous nerve system effect on arteries</td>
</tr>
<tr>
<td>-</td>
<td>Meanfilling pressure concept</td>
</tr>
</tbody>
</table>
Models integration
Models integration step 1
$P_{ra}$ – average right atrial pressure

$P_{ma}$ – average arterial pressure

$V$ – total blood volume
Models integration step 3

Average cardiac output

Average arterial pressure

Total blood volume
Models integration step 4

Cardiac output
Arterial pressure
Total blood volume
Complex modular model
Complex modular model

Venous System

Heart

Hormonal System

Kidney

Capillary System

Arterial System

Nervous System

Liquid Control System

Tissue Metabolism System

Sodium Intake
Complex modular model of the Human CVS:

pulsating heart, kidney regulation and arterial tree

• Different formalisms: ODE with discrete events and PDE (partial differential equations),
• Different time scales: minutes and seconds.
Arterial tree model

Possible boundary conditions at the heart exit and on the loose ends of last vessels:

1. Pressure,
2. Area,
3. Blood flow,
4. Filtration through porous medium.
Model simulation example

Pressure profile on the entrance to aorta

On the arterial tree output – constant pressure 70 mm Hg.
Models integration
Models integration
Models integration
Boundary conditions for arterial tree model

Aorta entrance:

Blood flow from heart

Loose ends of “last” arteries, Filtration law:

Capillaries resistance

Capillaries pressure
Integrated parameters of arterial tree:

- $V_A$ – total blood volume
- $R_A$ – integrated resistance
- $P_A$ – mean arterial pressure
- $Q_{AC}$ – total output blood flow
Models integration
Models integration
Complex modular model
Model can be extended further!

- Right ventricle
- Pulmonary circulation
- Lungs
- Liver
- Pancreas
- ...

...
Thank you for your attention
Experiment with sodium load

Total experiment time – 14 days.
Sodium intake increased from 0.126 to 0.26 mEq/l after 24 hours and decreased to 0.02 mEq/l after 144 hours.
Experiment with sodium load

- Sodium intake, mEq/l
- Renal symp. Nerve activity, ratio to normal
- Total blood volume, mEq/l
- Aldosterone concentration, ng/l
- Mean arterial pressure, Mm Hg
- Renin concentration, ratio to normal

Time, min
Experiment with sodium load

Mean arterial pressure

Oscillating arterial pressure

18.200 minutes

Time, minutes

Time, seconds

2 seconds

2 seconds

2 seconds
## Model with kidney regulation

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>$e_{aum}$</td>
<td>Autonomous nerve system activity.</td>
</tr>
<tr>
<td>$C_{adh}$</td>
<td>Antidiuretic hormone concentration.</td>
</tr>
<tr>
<td>$C_{anp}$</td>
<td>Natriuretic peptide concentration.</td>
</tr>
<tr>
<td>$C_{al}$</td>
<td>Aldosterone concentration.</td>
</tr>
<tr>
<td>$C_{at}$</td>
<td>Angiotensin concentration.</td>
</tr>
<tr>
<td>$C_{r}$</td>
<td>Renin concentration.</td>
</tr>
<tr>
<td>$C_{sod}$</td>
<td>Sodium concentration.</td>
</tr>
<tr>
<td>$\Phi_{co}$</td>
<td>Cardiac output.</td>
</tr>
<tr>
<td>$\Phi_{u}$</td>
<td>Urine flow rate.</td>
</tr>
<tr>
<td>$P_{ma}$</td>
<td>Mean arterial pressure.</td>
</tr>
<tr>
<td>$P_{mf}$</td>
<td>Meanfilling pressure.</td>
</tr>
<tr>
<td>$P_{ra}$</td>
<td>Pressure in the right atrium.</td>
</tr>
<tr>
<td>$R_{a}$</td>
<td>Arterial resistance.</td>
</tr>
<tr>
<td>rsna</td>
<td>Kidney sympathetic nerve activity.</td>
</tr>
<tr>
<td>vas</td>
<td>Vascularity.</td>
</tr>
<tr>
<td>$V_{ecf}$</td>
<td>Extracellular liquid volume.</td>
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</tbody>
</table>