PatientEvoPhysio

October 2023

Free open source Model Library designed to evaluate human physiological evolution in adulthood, childhood, neonatal and fetal life in the face of the occurrence of cardiovascular and respiratory anomalies or different clinical practices.

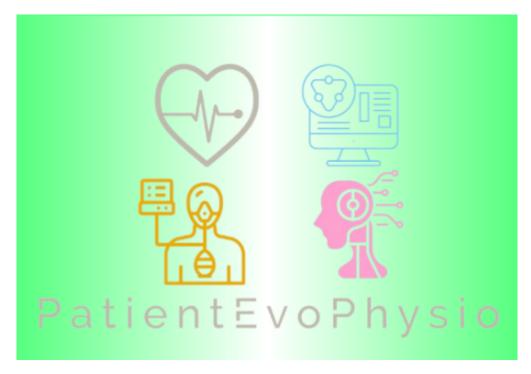


Figure 1

1 Development and contribution

1.1 Autores

- Edgar Hernando Sepúlveda-Oviedo (1)
- Leonardo Enrique Bermeo Clavijo (2)
- Luis Carlos Méndez-Córdoba (3)

1.2 Affiliations

- 1. LAAS-CNRS, Universite Federale de Toulouse, INSA, Toulouse, France.
- 2. Universidad Nacional de Colombia, "Facultad de Ingeniería, Departamento de ingeniería eléctrica y electrónica, Bogotá, Colombia.
- 3. Universidad Nacional de Colombia, "Instituto Materno Infantil Hospital La Victoria Sede, Bogotá, Colombia.

1.3 Programming language

1. Modelica

1.4 Versions:

1. Version 1.0

2 General description of the library

The internal structure of the library is shown in Figure 2:



Figure 2: Contents of the PatientEvoPhysio library

As can be seen in the Figure 2, the library is made up of 8 packages. The content of each package is explained below:

- 1. Icons: This package contains The icons of all the components that make up the physiological models of the library.
- 2. Components: This package contains all the components that are used to assemble the different physiological scenarios for evaluating the evolution of patients.
- 3. Types: Contains particular data types. All of this data is modifications of Modelica's primitive data.
- 4. Scenarios: They contain multiple models divided into 4 large categories: Adults, children, neonates and fetuses.
- 5. Connectors: This package contains different connectors that allow interaction between the internal variables of the components.
- 6. Function: This package contains mathematical functions such as the Hill function, the inverse Hill function, pulmonary or placental respiratory functions that determine changes in time-varying oxygen saturation.
- 7. Signals: This package contains the components that determine the time-varying behavior of aspects such as the variable elastance of certain vascular components, pulmonary respiration, placental respiration, the foramen ovale, among others.
- 8. UsersGuide: Contains contact information, acknowledgments of scientific articles related to the development of this library.

3 Description of the Components package

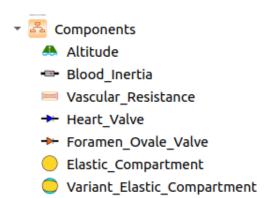


Figure 3: Components of the PatientEvoPhysio library

3.1 Altitude

The transition from fetus to neonate is governed by the availability of oxygen in the environment, leading to variations in birth outcomes between high-altitude and sea-level births. Studies have demonstrated that a decrease in the partial pressure of oxygen (P_{O_2}) in alveolar air is linked to an increase in pulmonary vascular resistance. Furthermore, chronic hypoxia resulting from living at high altitudes can not only delay fetal growth but also elevate perinatal mortality. This component represents the altitude-related phenomenon. The icon for this component is presented in Figure 4.



Figure 4: Icon of Altitude

3.2 Blood_Inertia

This component represents the inertial behavior of the blood. This inertia produces a reduction in pressure when the velocity of the flow increases. Furthermore, with this element, it is simulated that the flow velocity in the aorta increases to its maximum during systole, while the flow is reduced during diastole. The icon for this component is presented in Figure 5.



Figure 5: Icon of Blood_Inertia

3.3 Vascular_Resistance

This component represents the vascular resistances that emulate the arterial or venous ducts. This element has no accumulation of blood in the tissue and allows the entry of oxygen concentration from the outside. In this element, the blood flow of the elements connected at their ends in the direction of the flow of the element j to the element i is computed. The icon for this component is presented in Figure 6.



Figure 6: Icon of Vascular_Resistance

3.4 Heart_Valve

This component represents the valves that allow a blood flow in one direction in case the pressure gradient be greater. This element does not store blood in its tissue and simulates the mitral, aortic, tricuspid and pulmonary valves. The icon for this component is presented in Figure 7.



Figure 7: Icon of Heart_Valve

3.5 Foramen_Ovale_Valve

This component represents the existence of the foramen ovale. This existence is represented by the path that connects the right and left atria through a valve. The icon for this component is presented in Figure 8.



Figure 8: Icon of Foramen_Ovale_Valve

3.6 Constante_Elastance

This component represents cavities or compartments that accumulate blood and whose elastance allows the structure to recover its initial shape once the stress deformation has been suppressed. The icon for this component is presented in Figure 9.



Figure 9: Icon of Constante_Elastance

3.7 Time_Variant_Elastance

This component represents the elastic compartments with pulsatile flow and an elastance variant in time. These elements reflect the diastole and systole of the atria and ventricles, emulating the cardiac behavior of muscular distension and contraction. Variable elastances in time inherit the hemodynamic and respiratory behavior of elastances constant over time. The icon for this component is presented in Figure 10.



Figure 10: Icon of Time_Variant_Elastance

4 Description of the Types package

This package contains all the data types used in the components of the physiological models.

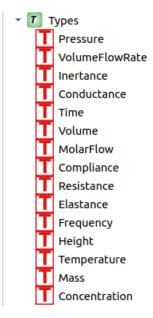


Figure 11: Types of data of the PatientEvoPhysio library

The following data types are unit modifications of native Modelica data:

- Pressure
- VolumeFlowRate
- Time
- Volume

- Frequency
- Height
- Temperature
- Mass
- Concentration

For more information on these data types, please refer to the Modelica documentation. In addition, we have declared the following types of data:

- Inertance: Inertance refers to the tendency of blood to resist changing its speed or flow. It is like the resistance of a moving object to stopping or changing its speed. In the cardiovascular system, it is related to the inertia of blood as it moves through blood vessels.
- Conductance: Conductance is the ease with which blood flow can pass through a vessel or artery. The higher the conductance, the easier the blood flow. It is related to the width of blood vessels and their ability to accommodate blood flow.
- MolarFlow: Molar flow refers to the amount of substance that flows through a point in a
 system in a given period of time. In the cardiovascular and respiratory context, it is used
 to measure the amount of oxygen that flows in the blood through a vessel or valve in a
 certain time.
- Compliance: Compliance is the ability of blood vessels and arteries to expand and contract in response to blood pressure. The greater the compliance, the easier it is for the vessels to expand to accommodate blood flow.
- Resistance: Resistance is the opposition to the flow of blood in the blood vessels. The greater the resistance, the more difficult it is for blood to flow through the vessels. It is similar to electrical resistance in a circuit, but in this case, it is applied to blood circulation.
- Elastance: Elastance refers to the ability of a blood vessel or cardiovascular structure to recover its original shape after being stretched or contracted. The higher the elastance, the stiffer the structure, and the less it expands with blood pressure.

5 Description of the Scenarios package

This package contains all the physiological scenarios tested in the library.



Figure 12: Scenarios of the PatientEvoPhysio library

A brief description of the models contained in this package by category is presented below.

5.1 Adult

In this version this package only contains a single adult model.

5.1.1 Healthy

Contains a cardiovascular model of a healthy adult.

5.2 Child

It contains two scenarios.

5.2.1 Healthy

Model of a child of six months of extrauterine life and weighing 8 kilograms with non-congenital aortic stenosis.

5.2.2 Stenosis

Model of a child of six months of extrauterine life and weighing 8 kilograms with non-congenital aortic stenosis.

5.3 Neonate

Physiological models of the Neonate. This package contains models of a healthy neonate with stenosis and four cardiac pathologies. Some heart diseases affect only the values of the components such as Stenosis. While other heart diseases not only affect the values but also the structure of the cardiovascular system. Congenital heart diseases occur due to malformations in fetal life of the heart or the vessels associated with it. These heart diseases commonly cause the greatest pediatric mortality and morbidity and are classified into 4 basic categories: left-to-right shunts, right-to-left shunts, obstructive lesions, and complex shunts. This package explores some of the most well-known heart diseases.

5.3.1 Healthy

Model of a healthy neonate

5.3.2 Stenosis

This disease increases cardiac muscle mass and reduces flow from the left ventricle to the aorta.

5.3.3 Coarctation of the Aorta

This is a vascular obstruction that decreases blood perfusion, generating an overload in pressure of the left ventricle and a dilatation of the right ventricle.

5.3.4 Tetralogy of Fallot

This cardiac anomaly refers to a combination of four related heart defects that commonly occur together. These defects are: pulmonary stenosis, ventricular septal defect, dominant aorta and hypertrophy of the right ventricle.

5.3.5 Transposition of the Great Arteries

In this congenital defect the pulmonary artery and the aorta are transposed. As a result, deoxygenated blood does not pass through the lungs and recirculates throughout the body. Transposition of the great arteries is the most frequent congenital defect in newborns and frequently causes death in patients who have not had surgery. It is only compatible with extrauterine life in case of a timely surgery or when there exists a defect of the ventricular septum (or a similar compensating defect) that allow the mixture of oxygenated and deoxygenated blood. Because of the high incoming flow caused by this defect, the right ventricle becomes hypertrophied.

5.3.6 Persistence of Ductus Arteriosus

The Ductus arteriosus is a large vessel that connects the pulmonary bed with the descending aorta. It usually closes after birth. Therefore, if it remains open, its persistence becomes a cardiac pathology. The PDA decreases the pulmonary vascular resistance, converting the foetal bypass from right to left in left to right derivation. This fact generates excessive pulmonary blood flow and dilatation of the left ventricle. Another important effect of PDA is that about one-half to two-thirds of the aortic blood passes through the ductus arteriosus into the pulmonary circulation.

5.4 Fetus

In this version this package only contains a single Fetus model.

5.4.1 Fetus to neonate transition

Included in this package is a unique model that analyzes the effect of adequate moment of umbilical cord clamping on the adaptation of the healthy term newborn to extrauterine life.

6 Description of the Connectors package

This package contains all the connectors used in the physiological components.

7 Description of the Functions package

This package contains all the mathematical functions used for pulmonary and placental respiration.

8 Description of the Signals package

This package contains all the time-varying signals that will modify the vascular resistance of the physiological components. It also contains signals associated with respirations and the Umbilical Cord Clamping.

9 Description of the Signals package

This packet contains contact information, the scientific articles used as a basis for the project, and acknowledgments to people whose contributions made a significant contribution to this research.

10 Related scientific articles

Articles related to the data and models presented in this library are listed below.

- Sepúlveda-Oviedo EH, Bermeo Clavijo LE, Méndez Córdoba LC. OpenModelica-based virtual simulator for the cardiovascular and respiratory physiology of a neonate. Journal of Medical Engineering & Technology. 2022;46(3):179-97.
- Sepulveda-Oviedo, EH., Bermeo, L., y Méndez, L. (2018). Desarrollo de una herramienta de simulación cardiovascular neonatal para la enseñanza y la investigación. XLVI Congresso Brasileiro de Educação em Engenharia (COBENGE) e no 1º Simpósio Internacional de Educação em Engenharia da ABENGE, Salvador bahia, Brasil.
- Sepúlveda-Oviedo EH. Estudio de la práctica del pinzamiento del cordón umbilical usando análisis computacional de la información bibliográfica, modelos de eventos discretos y modelos dinámicos [diploma thesis]. Universidad Nacional de Colombia; 2019.
- Yigit MB, Kowalski WJ, Hutchon DJR, Pekkana K. Transition from fetal to neonatal circulation: Modeling the effect of umbilical cord clamping. Journal of Biomechanics. 2015;48(9):1662-70.
- Hoppensteadt, F. y Peskin, C. (2002). Modeling and Simulation in Medicine and the Life Sciences (2nd Edition). Springer, NewYork.
- Goodwin, J., van Meurs, W., Sá-Couto, C., Beneken, J., y Graves, S. (2004). A model for educational simulation of infant cardiovascular physiology. Anesth Analg,99(6):1655-1664.
- Sá-Couto, P., Van-Meurs, W., Bernardes, J., Marques de Sá, J., y Goodwin, J. (2002).
 Mathematical model for educational simulation of the oxygen delivery to the fetus. 10(1):59-66.
- Sá-Couto, C. D., van Meurs, W. L., Goodwin, J. A., y Andriessen, P. (2006). A model for educational simulation of neonatal cardiovascular pathophysiology. 1(Inaugural):4-9.
- Serov, A., Salafia, C., Filoche, M., y Grebenkov, D. (2015). Analytical theory of oxygen transport in the human placenta. J Theor Biol., 368:133-144.
- Mateják, M. y Kofránek, J. (2015). Physiomodel an integrative physiology in modelica. En Conf Proc IEEE Eng Med Biol Soc., pp. 1464-7. Huikeshoven, F., Coleman, T., y Jongsma, H. (1980). Mathematical model of the fetal cardiovascular system: the uncontrolled case. Am J Physiol., 239(3):R317-25.
- Koch, G. (1968). Alveolar ventilation, diffusing capacity and the a-a po2, difference in the newborn infant. Respiration Physiology, 4(2):168 192.
- Guyton, A. (1991). Textbook of medical physiology (8th Edition). W.B. Saunders Company, Philadelphia.
- Graham, T. y Jarmakani, M. (1971). Evaluation of ventricular function in infants and children. Pediatric Clinics of North America, 18(4):1109 - 1132.
- Paul, A. y Das, S. (2017). Valvular heart disease and anaesthesia. Indian J Anaesth, 61(9):721–727.
- Avery, G., Fletcher, M., y MacDonald, M. (1999). Neonatology: Pathophysiology and management of the newborn (5th Edition). Lippincott Williams and Wilkins, Philadelphia.

11 Acknowledgments

This study mainly thanks researcher Marek Matejak from Charles University in Prague for the development of his Physiolibrary library which was the basis for the development of some components contained in this library.

This study also especially thanks the Instituto Materno Infantil – Hospital La Victoria in Bogotá Colombia, for allowing us a series of validations with a group of health professionals over several years.