Incorporating HDL interaction in an ODE model of Atherosclerosis

Diego Lopez

Texas A&M University

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Introduction

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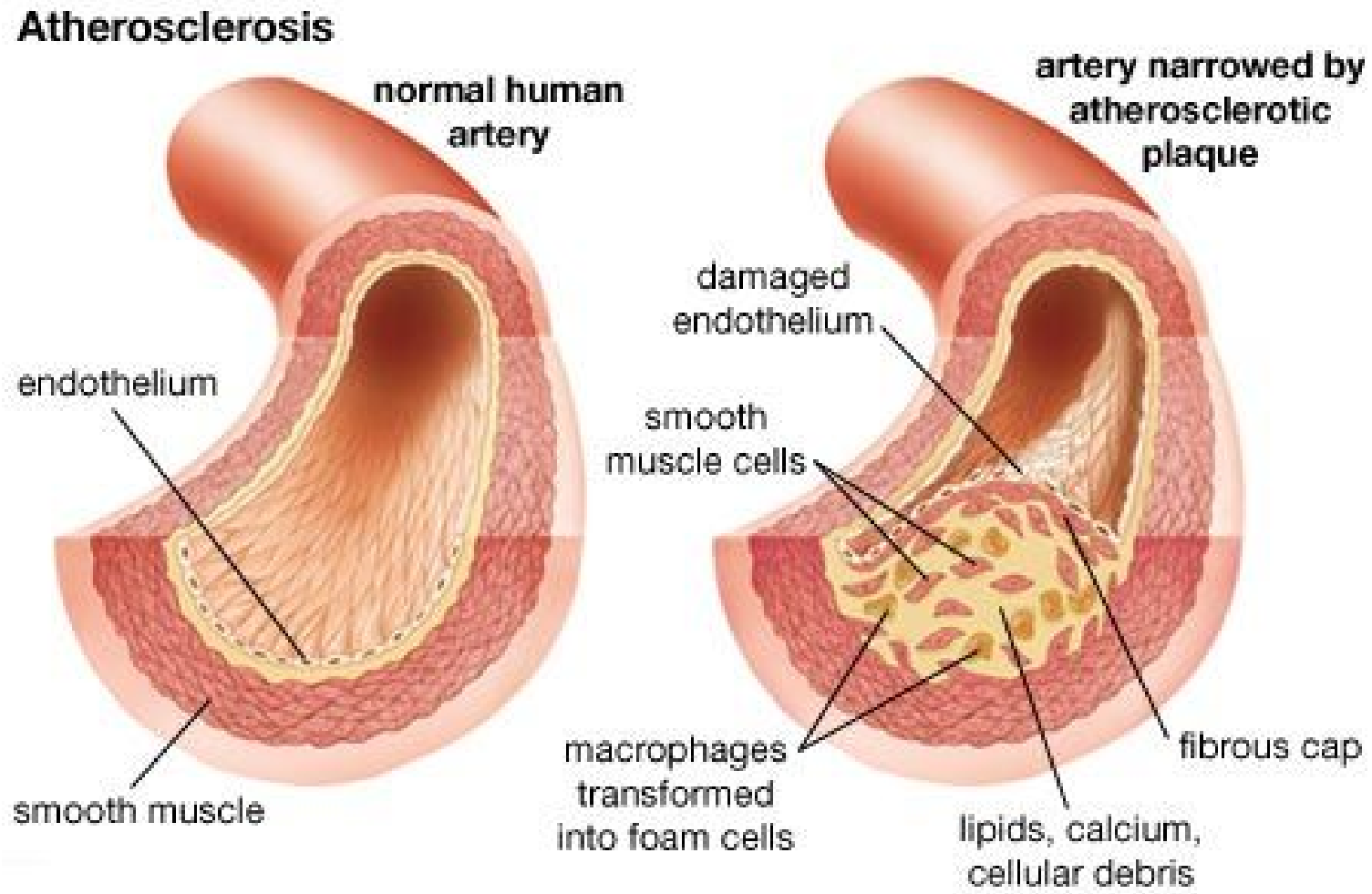
  - A disease of the arteries characterized by the inflammation of arterial walls leading to the deposition of plaques of fatty material on their inner walls.
- The medical community has long recognized the levels of different types of cholesterol in the blood plasma are directly correlated to the risk of CVDs (cardiovascular diseases) like atherosclerosis (Hao 2014). The goal of this project is to create a model that incorporates components like HDL, and to analyze the dynamics of that model to give insight into the progression of the disease.

Atherosclerotic Artery



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- **LDL**
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- **HDL**
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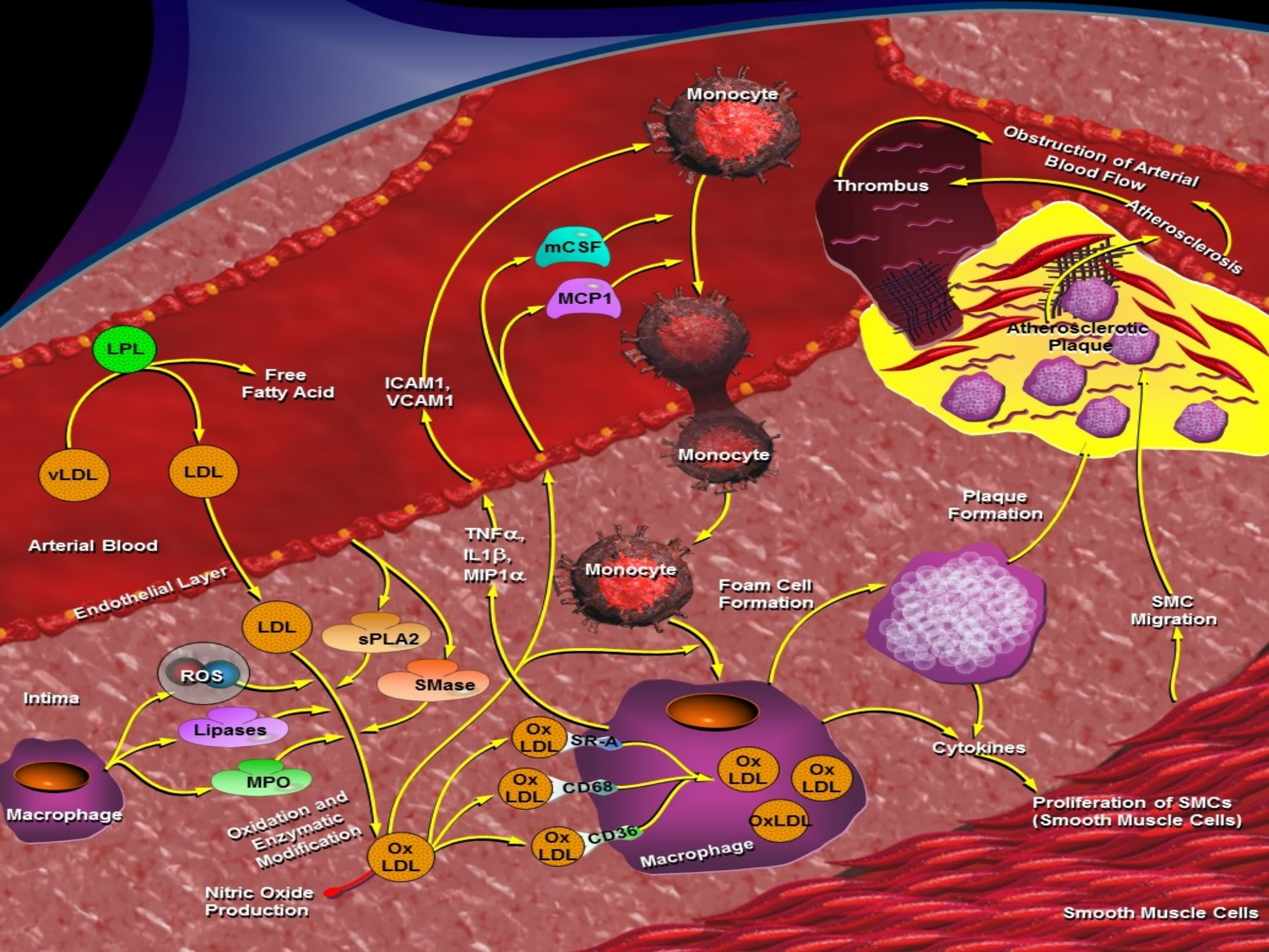
- **VLDL, IDL, Chylomicron**
  - Other lipoproteins.


Monocyte
Obstruction of Arterial Blood Flow
Thrombus
Atherosclerosis
mCSF
MCP1
Atherosclerotic Plaque
LPL
Free Fatty Acid
ICAM1, VCAM1
vLDL
LDL
Monocyte
Arterial Blood
Endothelial Layer
TNFα, IL1β, MIP1α
Monocyte
Plaque Formation
Foam Cell Formation
SMC Migration
LDL
sPLA2
ROS
SMase
Intima
Lipases
MPO
Macrophage
Oxidation and Enzymatic Modification
Ox LDL
SR-A
Ox LDL
CD68
Ox LDL
CD36
Ox LDL
Ox LDL
Ox LDL
OxLDL
Macrophage
Cytokines
Proliferation of SMCs (Smooth Muscle Cells)
Nitric Oxide Production
Smooth Muscle Cells

New Model Development

Reverse Cholesterol Transport

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- HDL plays a crucial role in RCT (Reverse Cholesterol Trasnport) (McAuley 2012).
- Studies by Annema (2012) have suggested that HDL picks up free cholesterol from foam cells and debris from inside the intima.

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3. All coefficients are positive, constant rate coefficients.

HDL Model

System of ODEs

$$\dot{L} = I(L_B - L) - r_4 LM - d_L L \tag{1}$$

$$\dot{I} = r_{20} F - r_{18} I L_{ox} \tag{2}$$

$$\dot{F} = r_{18} I L_{ox} - r_{10} F H - d_F F \tag{3}$$

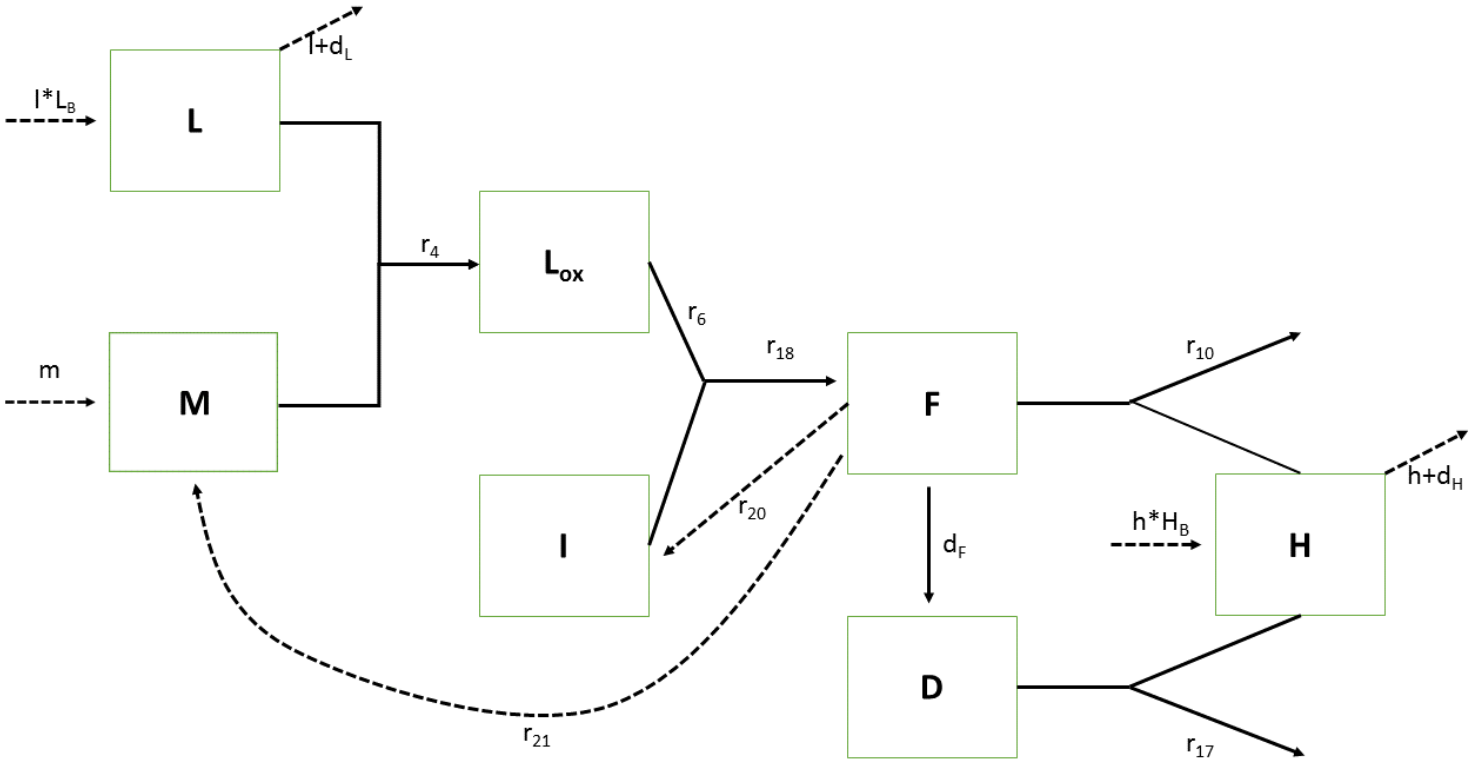
$$\dot{D} = d_F F - r_{17} D H \tag{4}$$

$$\dot{L_{ox}} = r_4 LM - r_6 I L_{ox} \tag{5}$$

$$\dot{M} = mM + r_{21} F - r_4 LM \tag{6}$$

$$\dot{H} = h(H_B - H) - r_{10} HF - r_{17} HD - d_H H \tag{7}$$

Compartment Model



Future Directions

- Using the system of ODEs and setting the concentration of the groups I, D, and F to zero, we can reduce the system of equations to two rational functions in terms of LDL concentration and HDL concentration.
- Plotting these functions and finding their intersection will prove that a healthy state equilibrium exists in terms of LDL and HDL concentration.
- If the healthy state equilibrium (if it exists) is linearly stable, then it proves that, for this model, the ratio of LDL and HDL in the blood is a controlling factor for the development of atherosclerosis.