PhD proposal
"Modeling transport in the human placenta"

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Description

The mature placenta is a complex arborized vascular bed extending from the umbilical arteries to the chorionic surface vessels, to the fetal stem vessels and ultimately to the capillary beds of the terminal villi, the last being the anatomical site of all oxygen and carbon dioxide exchange between the mother and the fetus. From the perspective of maternal perfusion, intervillous blood flow accesses individual terminal villi at different flow rates. Oxygen dissolved in the maternal blood diffuses across the villous membrane toward and into the fetal capillaries, from where it is carried away by fetal blood. Conversely, carbon dioxide dissolved in the fetal blood diffuses into the villus and then across the villous membrane to be carried away by the maternal blood.

At this point, several questions naturally arise: How does the geometry of the placental villous architecture determine the oxygen and carbon dioxide transport efficiency? In particular, does abnormal packing density of villi affect their function? In the case of abnormally dense packing (e.g., in diabetic placentas), do some villi "shield" other villi from the maternal perfusion and limit their function? In the case of abnormally sparse packing (e.g., in preeclamptic placentas), does maternal blood transit the intervillous space without oxygen transfer? How is the oxygen flux correlated with gestational age, birth weight and other perinatal outcomes?

Based on high-resolution photographs of two-dimensional slices of the placenta, we shall model the two successive steps of the oxygen and carbon dioxide transport. The first step consists in convection-diffusion of the maternal blood flow in the intervillous space from the umbilical arteries toward terminal villi. The goal here is to determine the oxygen delivery to the villous membranes, to evaluate the impact of anatomical pathologies (e.g., overcrowding of the villi in the diabetic placentas) on the spatial distribution of partial oxygen pressure, and finally to access the role of diffusion/convection screening in normal and diseased placentas. The second step consists in studying purely diffusive transport inside individual villi, from the villous membrane to the fetal capillaries. The goal here is to determine what role plays the villus' shape and the location of fetal capillaries in it, and how these characteristics vary from normal to abnormal placentas. Combining these two steps, we shall be able to calculate the total flux of oxygen from the mother to the fetus (and similarly, the total flux of carbon dioxide from the fetus to the mother), to understand the consequences of placental diseases on the fetus, and to relate this quantity to the birthweight and other perinatal outcomes.

Understanding the efficiency of oxygen transport may have a crucial medical impact. The fetus has two functions before birth, to develop mature organs and to grow. Both these functions are dependent on adequate resources of oxygen/gas exchange. While much is known about villous structures in normal and diseased placentas, only very little is known about how changes in villous structure impact villous function. In the last two decades, increasing data support a role in lifelong disease for a poor intrauterine environment. The most commonly used proxy for the adequacy of the intrauterine environment is birthweight. Risks of death at age 50 from heart disease, risks of diabetes, certain cancers as well as neurodevelopmental and neuropsychiatric disease all have been shown to vary with birthweight. Better understanding of how fetal growth is modulated by placental function that is dependent on placental structure will help clarify how birth weight changes have such far-reaching effects, and may allow early risk prediction to improve lifelong health.

The candidate is expected to have a background in physics of diffusion/convection transport, to be skilled in numerical methods and programming, and strongly motivated to work in a cross-disciplinary project with applications in physiology and medicine.

References:

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