LA-UR- 10-00739

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Intended for: Visual Communications and Image Processing Sponsored by IEEE Huang Shan, An Hui, China, 11-14 July, 2010.

Los Alamos NATIONAL LABORATORY EST. 1943

OPTIMAL TRANSPORT AND THE PLACENTA

QINGLAN XIA, CAROLYN SALAFIA, AND SIMON MORGAN

ABSTRACT. The goal of this paper is to investigate the expected effects of (i) placental size, (ii) placental shape and (iii) the position of insertion of the umbilical cord on the work done by the foetus' heart in pumping blood across the placenta. We use optimal transport theory and modeling to quantify the expected effects of these factors. Total transport cost and the shape factor contribution to cost are given by the optimal transport model. Total placental transport cost is highly correlated with birth weight, placenta weight, FPR and the metabolic scaling factor beta. The shape factor is also highly correlated with birth weight, and after adjustment for placental weight, is highly correlated with the metabolic scaling factor beta.

1. INTRODUCTION

1.1. **Brief Introduction.** The goal of this paper is to investigate the expected effects of (i) placental size, (ii) placental shape and (iii) the position of insertion of the umbilical cord on the work done by the foetus' heart in pumping blood across the placenta. We use optimal transport theory and modeling to quantify the expected effects of these factors. This size, shape and position data is readily available from measurements from photographs of {1000 placentas from the UNC data set?} and is the only available data that is ready for use in modeling. If more data becomes available, such as placental thickness and cross sectional measurements, then the modeling method is ready to incorporate these factors.

In general, the less distance the blood has to travel the less energy needs to be expended. So one may expect the optimum shape for the chorionic plate to minimize transportation energy to be a circle with a centrally inserted umbilical cord. If the umbilical cord insertion point is eccentric within a circular chorionic plate then overall the blood will have farther to travel to get to the umbilical cord. Also if the chorionic plate is not circular, but elliptical or lobate then again, overall, the blood will have farther to travel and so more energy will be needed. Therefore one may expect that placental shape and location of umbilical cord are important factors in determining the energy needed to pump blood across the placenta. Also for a larger placenta, the more blood needs to be transported over a greater distance. Thus the more energy is required to pump it.

In this article, we model the vascular tree structure of each placenta, in a simplified form, by an idealized optimal transport network. The total transport cost given by this model represents the total work done by the heart of fetus to pump blood across the placenta. This total transport cost, calculated from the model, is highly correlated with birth weight, placenta weight, FPR and the metabolic

Q. Xia is supported by the NSF grant DMS-0710714. The work by Simon Morgan was funded by the Department of Energy through the LANL/LDRD office #X1LJ, LA-UR#XXXX. Thanks to IPAM at UCLA for additional support.

scaling factor beta. Total transport cost decomposes into a size factor and a shape factor incorporating both placental shape and umbilical cord insertion position. We are able to separate these two factors out from total transport cost, and consider contributions of each factor separately. It turns out that the shape factor is also highly correlated with birth weight, and after adjustment for placental weight, is highly correlated with the metabolic scaling factor beta.

1.2. **Background on placental research.** The human newborn is entirely composed of nutrients transferred from the maternal to the fetal circulation across the placenta. By extension, birth weight depends on placental function. Physiologic determinants of total placental supply capacity include "driving forces" such as nutrient concentration, charge and oncotic gradients, blood flow (via uterine and umbilical arteries), the physical aspects of the placental villous barrier related to passive permeability (e.g., villous surface area, thickness of the maternal-fetal blood partition, pore size), and transporter function at the microvillous surface. The "net" (or "effective") placental functional capacity - the nutrients available to the fetus for use in metabolism and, importantly, growth– would equal the amount of nutrients provided in each fetal-placental cardiac cycle minus the fetal energy costs of placental perfusion and the energy consumed by placental metabolism. [1] Recent results demonstrate that, at least in populations predominantly delivered at term, placental weight scales to birth weight to the $\frac{3}{4}$ power. From this we suggested that the allometric relationship between placental and birth weight is consistent with the hypothesis that the fetal-placental unit functions as a fractal supply limited system. Furthermore, we have recently demonstrated that deviations from spatially filling symmetric fractal vascular growth are associated with reduced placental vascular efficiency, that is, a smaller birth weight than predicted by the allometric scaling for the given placental weight (REF).

1.3. **Background on optimal transportation.** The optimal transportation problem aims at finding an optimal way to transport the source into the target. It has been used to analyze a number of biological relationships over the years, from feeding strategies to locomotor gaits (recently reviewed by [24]). An optimal transport path is a mathematical concept used to model tree-shaped branching transport networks. Transport networks with branching structures are observable not only in nature as in trees, blood vessels, river channel networks, lightning, etc. but also in efficiently designed transport systems such as used in railway configurations and postage delivery networks. Recently, mathematicians (e.g. [5],[4],[3],[2],[1]) have shown great interests in modeling these transport networks with branching structures. In this article, we will model the blood vessel structure of a placenta via an optimal transport path which was introduced in [5].

Applications of optimal transport path may be found in [9],[12] and [8]. For instance, we have used the idea of the theory to understand the dynamic formation of a plant leaf [9] (see figure 1). We elected this model because the model does not predetermine the shapes of tree leaves. And the path developed depends on the relative transportation cost from the more distal branches to the root, both assumptions that are appropriate to the human placenta that assumes a random shape based on outgrowth from the original vasculogenic site at the base of the cord insertion.

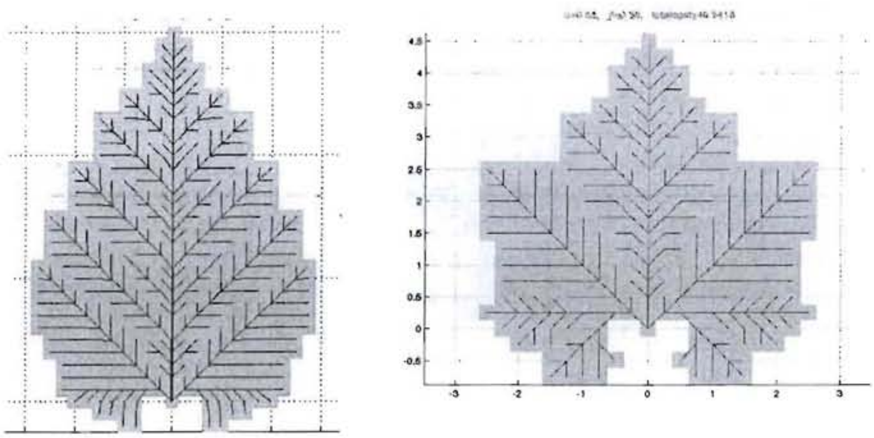

FIGURE 1. Examples of computer visualization of tree leaves ([9]), which resemble many known leaves including the maple and mulberry leaf.

2. MODELING METHOD

For each placenta, we apply the modeling method of ramified optimal transportation [5] leading to the computation of an idealized transport network based on the data for that placenta. The idealized transport network provides a means of transporting blood from the whole of the chorionic plate surface to the umbilical cord. In the absence of more detailed information about blood supply, we assume a uniform supply of blood per unit area over the whole surface of the placenta. We also model the placenta by a region in the plane because the data is from photographs of the placenta flat on a table, rather than in the curved inside surface of the uterus. The umbilical cord insertion position is represented as the central point recorded from the photograph.

The idealized transport network is a branched network of straight segments e_i each with a capacity weighting w_i and a direction of flow. For each branch point, the sum of flows in must equal the flow out. Since there are many ways to construct a transport network we need to find an optimal network which minimizes the amount of work done in pumping blood through the network. In the model of ramified optimal transportation, we use the cost function $(w_i)^\alpha l_i$ for each edge e_i of length l_i where α is a branching parameter ($0 \leq a < 1$). Technically, as x^α is strictly concave for this range of α, this ensures that branched structures will emerge and corresponds to the general principle of favoring transportation in groups and branched vessel structures. The total cost for each transport network, which reflects the work done to pump the blood, is the sum of the costs for each edge. The computer algorithm finds a nearly optimal transport network for the data provided for each placenta. A typical one is similar to the left one of the figure 2.

The actual value of $\alpha = 0.85$ used in the calculations was picked so that for a round placenta with a centrally inserted umbilical cord, 6 branches will emerge from the umbilical cord. This is consistent with the typical observation that 4 to

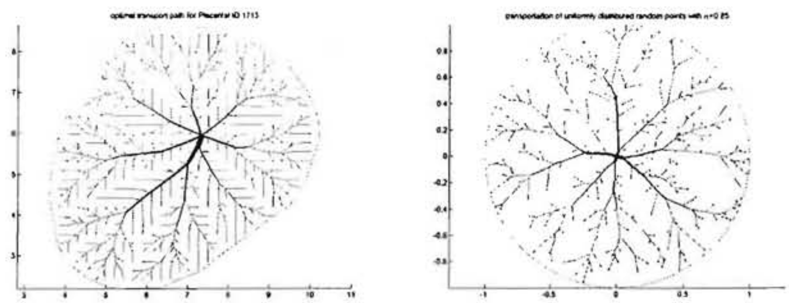

FIGURE 2. Examples of modeling blood vessels of a placenta by a nearly optimal transport network; The left one is uniformly distributed, while the right one is randomly dsituributed

6 branches emerge from the umbilical cords in normal round placentas. It is not chosen in accordance with any metabolic scaling law.

Now, we take $\alpha = 0.85$. Using algorithms stated in [11], we build an approximating optimal transport path for each placentas in the data. As a result, we calculate the total transport cost C for each placenta in the data.

3. Analysis of output from model

After getting the output of the total transport cost C for each placenta in the data, we want to investigate the role of the shape played in contributing total transport cost. To do so, we express the total cost as

$$C = S * A^{0.5+\alpha}$$

the product of two independent variable, where

$$S = \frac{C}{A^{0.5+\alpha}}$$

is called the shape factor. As shown in the Appendix, S is a function of shape and cord position only, but independent of the size, while $A^{0.5+\alpha}$ is solely determined by the placenta size.

Thus we can separate out the contribution to foetal energy required to pump blood in this ideal hypothetical situation into a contribution from area and a contribution from shape that can be calculated separately.

3.1. Some remarks on the model computation.

We do not model blood vessel structures exactly we just look at the best possible simplified mathematical branched distribution system, for the given shape and position of the umbilical cord. This is exactly the same calculation as could be done for a road network, electricity supply network or canal network. We do not model arteries and veins separately. Thus the network created is idealized with no biological features, but it does give a minimum cost to transporting blood across the surface with any branched network. Thus it shows that a biological system can do no better than a certain effectiveness.

This does not use any geometric criterion of symmetry or fractal dimension based on any scaling laws. Any apparent symmetry or fractal like geometric appearance is an emergent structure

The computation is initially based on a square grid, but this has no influence on the shape of the branched network, in that if different sizes of squares, different shapes other than squares or squares were oriented in a different direction, the network would be the same.

The model is a directed transport system that can be viewed equally as a vein system transporting blood to the umbilical cord or as an artery system transporting blood away from the umbilical cord. The only difference is the direction of flow of the blood.

In this article, we use a two dimensional optimal transport model. In this model the contribution of placental area has an effect that can be separated out from the combined effects of placental shape and umbilical cord insertion position. The variable total optimal transport cost is calculated by the model. We can remove the effect of area A from the cost by dividing by a power of A. The result is a contribution to cost by placental shape and umbilical cord insertion position. These variables from the optimal transport modeling correlate highly with measured biological variables such as birth weight and FPR. This indicates that using our highly simplified mathematical modeling captures some biologically meaningful information about placental function. We can separate out contributions from area and combined contributions from shape and eccentricity of umbilical cord insertion point.

4. Materials and Methods Clinical cohort

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5. RESULTS

Transport efficiency and total transport cost (variables suggested by XIA) are highly correlated with birth weight (both) and placental weight, FPR and beta (total transport cost only).

Correlations

	birth weight	placental weight	FPR	beta	
transport efficiency	Pearson Correlation	-.080	-.020	-.056	.039
	Sig. (2-tailed)	.008	.508	.062	.192
total transport cost	Pearson Correlation	.421	.489	-.154	.272
	Sig. (2-tailed)	.000	.000	.000	.000

After adjustment for placental weight in regression analysis, the significant relationships of both total transport cost and transport efficiency remained.

Both variables were also highly correlated with the metabolic scaling factor beta after adjustment for placental weight.

Coefficients(a)

Model		Unstandardized Coefficients		t	Sig.
		B	Std. Error		
1	(Constant)	2483.951	54.964	45.193	.000
	total transport cost	.590	.038	15.400	.000
2	(Constant)	1546.922	64.502	23.983	.000
	total transport cost	.210	.037	5.639	.000
	placental weight	3.307	.158	20.958	.000

a Dependent Variable: birth weight

Coefficients[a]

Model		Unstandardized Coefficients		t	Sig.
		B	Std. Error		
1	(Constant)	3693.731	152.020	24.298	.000
	transport efficiency	-594.053	222.689	-2.668	.008
2	(Constant)	1985.163	134.301	14.781	.000
	transport efficiency	-501.411	173.258	-2.894	.004
	placental weight	3.734	.139	26.837	.000

a. Dependent Variable: birth weight

Coefficients[a]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	.743	.006		130.033	.000
	transport efficiency	.011	.008	.039	1.306	.192
2	(Constant)	.667	.004		152.921	.000
	transport efficiency	.015	.006	.054	2.670	.008
	placental weight	.000	.000	.740	36.544	.000

a. Dependent Variable: beta

6. DISCUSSION

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Coefficients[a]

Model		Unstandardized Coefficients B	Unstandardized Coefficients Std. Error	Standardized Coefficients Beta	t	Sig.
1	(Constant)	.731	.002		334.290	.000
	total transport cost	1.43E-005	.000	.272	9.374	.000
2	(Constant)	.680	.002		324.002	.000
	total transport cost	-6.2E-006	.000	-.117	-5.104	.000
	placental weight	.000	.000	.796	34.606	.000

a. Dependent Variable: beta

References

[1] A. Brancolini, G. Buttazzo, F. Santambrogio, Path functions over Wasserstein spaces. J. Eur. Math. Soc. Vol. 8, No.3 (2006),415–434.

[2] M. Bernot; V. Caselles; J. Morel, Traffic plans. Optimal Transportation Networks: Models and Theory. Series: Lecture Notes in Mathematics , Vol. 1955 , (2009).

[3] E.N. Gilbert, Minimum cost communication networks, Bell System Tech. J. 46, (1967), pp. 2209-2227.

[4] F. Maddalena, S. Solimini and J.M. Morel. A variational model of irrigation patterns, Interfaces and Free Boundaries, Volume 5, Issue 4, (2003), pp. 391-416.

[5] Q. Xia, Optimal paths related to transport problems. Communications in Contemporary Mathematics. Vol. 5, No. 2 (2003) 251-279.

[6] Q. Xia. Interior regularity of optimal transport paths. Calculus of Variations and Partial Differential Equations. 20 (2004), no. 3, 283–299.

[7] Q. Xia. Boundary regularity of optimal transport paths. Preprint.

[8] Q. Xia, An application of optimal transport paths to urban trasnport networks. Discrete and Continuous Dynmical Systems, Supp. 2005, pp 904-910.

[9] Q. Xia. The formation of tree leaf. ESAIM Control Optim. Calc. Var. 13 (2007), no. 2, 359–377.

[10] Q. Xia. The geodesic problem in quasimetric spaces. Journal of Geometric Analysis: Volume 19, Issue2 (2009), 452–479.

[11] Q. Xia and A. Vershynina. On the transport dimension of measures. arXiv:0905.3837, Accepted by the SIAM Journal on Mathematical Analysis (2009)

[12] Q. Xia and D. Unger, Diffusion-limited aggregation driven by optimal transportation. Accepted by the Fractals journal (2009)

[13] Qinglan Xia. Numerical simulations of optimal transport paths. To appear on the Proceedings of the 2nd International Conference on Computer Modeling and Simulation (ICCMS 2010)

7. APPENDIX

For a placenta, we set C to be total transport cost (corresponding to $\alpha = 0.85$), and A to be the area of its plate. We now prove that

$$S = \frac{C}{A^{\alpha+0.5}}$$

is independent of the size of a placenta.

Indeed, suppose D_1 and D_2 are two placentas of the same shape. Then D_1 can be viewed as a rescale of D_2 with a length scaling factor $\lambda > 0$. Thus,

$$Area\,(D_1) = \lambda^2 Area\,(D_2)\,.$$

Let G_1 and G_2 be the corresponding optimal transport network for D_1 and D_2. One may also show that the total cost for D_1 is the total cost for D_2 multiplied by

$\lambda^{2\alpha+1}$. As a result,

$$S_1 = \frac{C_1}{A_1^{0.5+\alpha}} = \frac{\lambda^{2\alpha+1} C_2}{(\lambda^2 A_2)^{0.5+\alpha}} = \frac{C_2}{A_2^{0.5+\alpha}} = S_2.$$

This says that if two placentas have the same shape (with different size), then they have the same shape factor. In other words, shape factor of a placenta is independent of the size of the placenta.

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