

# Optimization Based Vascular Growth and Remodeling Using Dual Splitting: The Collaboration Between Local and Regional Regulations

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**Introduction:** Vascular growth & remodeling (G&R) is closely related to the functional adaptations of arteries to biomechanical stimuli. Previous works have been focused on characterizing local response to mechanical stress. However, physiological regulation is by nature a combination of local response and higher-level regional response. In this work, vascular G&R is modeled as an optimization process. Via dual splitting approach, the optimization problem is decomposed into a sequence of local optimization and a high-level regional optimization, providing a potential way to mathematically describe the connection between local and regional response of vascular G&R.

**Methods:** G&R is modeled here as an optimization process to (a) minimize the deviation of local vessel wall tension with homeostatic stress and (b) optimize the regional hemodynamics in the vessel, which is described by the optimization problem below

$$\min_{m(x,k+1)} \lambda \int_{\Omega_{solid}(k)} \|\sigma(x, k+1) - \sigma_h\|^2 dV + \left| \int_{\partial\Omega_{fluid}} E(x)\phi(\tau_w(x, k+1))dA - \psi(\tau_w^h) \right|^2.$$

where  $\lambda$  is the weight coefficient, the mass production rate  $m(x, k+1)$  is the decision variable and the governing equations for hemodynamics and vessel wall mechanics will be the constraints. After applying dual splitting approach, the optimization can be equivalently represented as

$$\max_{\Lambda} \left\{ -\frac{1}{4}\Lambda^2 + \Lambda\psi(\tau_w^h) + \sum_{i=1}^N \min_{m(x_i)} (\lambda\|\sigma(x_i, t) - \sigma_h\|^2 \Delta V_i - \Lambda \mathbf{1}_{\partial\Omega}(x_i) E(x_i)\phi(\tau_w(x_i, t))\Delta A_i) \right\}$$

which consists of a sequence of mutually independent local optimization problems w.r.t  $m(x_i)$  and a higher-level optimization problem w.r.t the dual variable  $\Lambda$ . Here the cost functions for local minimization problems are defined as  $f(m(x_i); \Lambda)$ .

**Results and Discussion: (Local optimization):** The local optimization problem describes the local vascular response to mechanical stress. We assume that physiologically the local optimization is solved in a gradient descent manner, then based on the negative gradient  $-\nabla_{m(x_i)} f(m(x_i))$  the mass production rate takes the following form

$$m(x_i) = K_{\sigma} (\sigma(x_i, k) - \sigma_h) + \Lambda K_{\tau} \phi'(\tau_w(x_i))$$

which is consistent with the local response propose in previous G&R model by Humphrey.

**(Regional optimization):** The regional regulation is given by the following higher-level optimization problem with respect to dual variable  $\Lambda$ , with  $f_{\min}(x_i; \Lambda)$  being the optimum for local minimization problem

$$\max_{\Lambda} -\frac{1}{4}\Lambda^2 + \Lambda\psi(\tau_w^h) - \sum_{i=1}^N f_{\min}(x_i; \Lambda).$$

**Conclusions:** A mathematical framework for vascular G&R is created in terms of optimization. Using dual splitting approach, the overall optimization problem is decomposed into a sequence of independent local optimization problems describing local vascular response to stress and a higher-level optimization problem corresponding to the regional regulation. The connection between local response and regional response is modeled via the dual variable. The resulted mathematical form of the local response matches the previous model for vascular G&R, and the higher-level optimization proposed here may provide a promising model for mathematical incorporating regional regulation into G&R framework.