Modeling Adipose Tissue Hormone Regulation

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Short abstract — **Motivated by global obesity and type 2 diabetes epidemics, researchers have realized the integral role of adipocytes in energy balance. In addition to their role as lipid stores, adipocytes participate in shaping the milieu of circulating hormones in the blood. Knowledge of adipocyte biology is therefore crucial to understanding the pathophysiology of metabolic diseases. In this poster, we present a spatial model of the dynamics of fatty acid uptake by adipose tissue informed by data collected from mouse explants using a microfluidics platform combined with a recently developed fluorescent reporter of fatty acids. We demonstrate that fatty acid uptake is hormone-dependent on a short timescale. We also address whether diffusion of fatty acids through adipose tissue is mediated through gap junctions by comparing the model diffusion pattern to the data.**

Keywords — **adipocyte, hormone, insulin, glucose, microfluidics, microscopy, fluorescence, finite element method.**

I. BACKGROUND

As calorie stores, adipocytes are well suited to regulate energy balance. They play this crucial role through a number of mechanisms such as secretion of adipose-derived molecules (adipokines), initiation of neural signals via the peripheral nervous system, and breakdown of fat (lipolysis) and release of fatty acids for direct use as an energy source [1].

Although adipocyte mass represents excess energy intake relative to energy expenditure, the rate of adipogenesis is not merely proportional to ingested calories. Indeed, there are hormonal effects that complicate a strict interpretation of energy balance by the First Law of Thermodynamics. For example, insulin, which is secreted by pancreatic β-cells, is required for glucose uptake by adipose tissue and has the effect of repressing lipolysis [3]. To determine the extent to which hormones affect fatty acid uptake and release, Easley et al developed a fluorescent sensor of intracellular free fatty acid (FFA) that is used in combination with a microfluidics platform [2].

Acknowledgements: This work was supported by the NIH Intramural Research Program.

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To quantify the rate of fatty acid uptake, they pulsed square waves of fluorescent FFA to mouse adipose explants with various concentrations of insulin and glucose in the bath. Here, we show that the rate of fatty acid uptake can change rapidly with an increase in insulin. We also address whether diffusion of fatty acids through adipose tissue is mediated through gap junctions.

II. MODEL

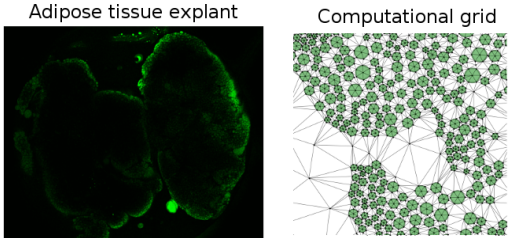
We model the concentration $u(x,t)$ of fatty acid in the microfluidic chamber containing adipocytes by

$$\begin{cases} u_t + du_{xx} = gWu & B(0,R)\times(0,T] \\ u = f(t,x) & \partial B(0,R)\times(0,T] \\ u_x\cdot\vec{n} = [u(c_i)-u(\partial C_i)]/r_i & \partial C_i\times(0,T]\ \forall i \end{cases}$$

where variables have the following meanings

- $C=\cup C_i$: collection of adipocyte cells,
- $d>0$: fatty acid diffusion coefficient,
- $g\geq 0$: gap junction fatty acid diffusion coefficient,
- W: cell coupling matrix.

To create a computational grid that mimics the geometry of the adipose explant, we segment microscopy images and triangulate the result.



III. CONCLUSION

We constructed a model of adipose tissue informed by experiments with state-of-the-art microscopy and fluorescence techniques to characterize the rate of fatty acid uptake in various metabolic conditions. This understanding should be useful for developing interventions to mitigate a global obesity epidemic.

REFERENCES

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