ANALYSIS OF TRAVELING WAVES IN A NON-LOCAL MODEL OF CELL SURFACE MECHANICS*

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Abstract. This is an example SIAM LaTeX article. This can be used as a template for new articles. Abstracts must be able to stand alone and so cannot contain citations to the paper's references, equations, etc. An abstract must consist of a single paragraph and be concise. Because of online formatting, abstracts must appear as plain as possible. Any equations should be inline.

Key words. example, LaTeX

AMS subject classifications. 68Q25, 68R10, 68U05

1. Introduction.

The diffusion equation is used to described many scientific phenomena for decades and is very important to systems biology, in particular with respect to pattern development and the emergence of periodic structures from non-periodic sources during embryogenesis [37]. Because of it's long history and extensive applications, mathematical studies have revealed the conditions for various patterns to arise. The inclusion of biomechanics to chemical kinetic frameworks naturally leads to non-diffusion like PDEs. Here we will show that a model previosuly developed to study cellular blebbing behavior (CITE MANAKOVA ET AL) falls into this category. We believe a broad class of cellular behaviors obey similar mechanical constraints in conjunction with chemical dynamics, and therefore a study of the properties of these types of equations is a promising endeavor, and we plan to do a thorough literature review as part of our future work to identify such systems. In particular, we have chosen to investigate the conditions allowing for travelling wave solutions of a particular class of equations arising in cellular biophysics, a property already established in reaction-diffusion systems and sometimes called the Maxwell condition [8, 44]. We seek an analog of the Maxwell condition for the bleb model, and similar non-local PDEs. We will use our previously described cellular blebbing model as a test case.

2. Statement of model.

The eukaryotic cell membrane acts as the main barrier between the cell and the surrounding environment. Inside the cell, the membrane is supported by a dense networks of actin filaments called the cortex which is attached to the cell membrane via adhesion molecules. The cortex maintains the cell shape and contracts inward generating a internal pressure in the cell. Local disruptions to the cortex result in dynamic, transient protrusions of the cell membrane termed blebs. Blebs are implicated in many cellular activities including apoptosis, mitosis and motility, yet little is known about the mechanism underlying bleb formation.

Our minimal model, summarized schematically in Fig. **??**, consists of four fundamental dynamic variables, as functions of time t and location on the two-dimensional cell surface, parametrized by (x_1, x_2). The actin cortex, has local height described by $Y_C(x_1, x_2, t)$ measured normal to the mean cell surface from its steady-state configu-

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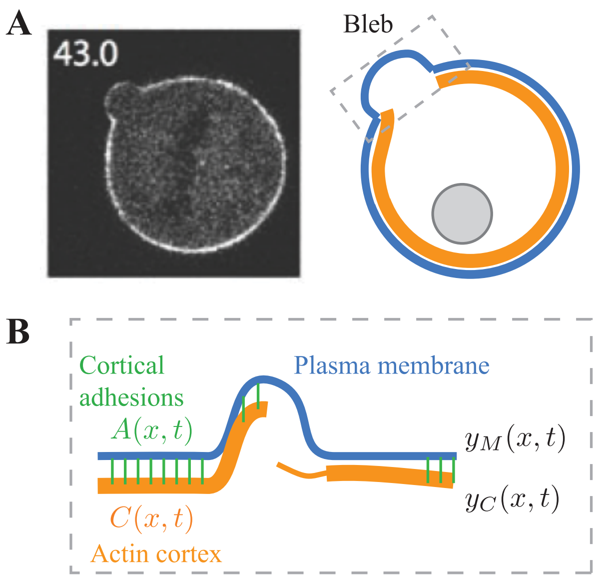

Fig. 1. *(A) Micrograph of a single bleb, induced by laser ablation on the surface of a HeLa cell, 43 seconds after initial formation. Taken from [?]. (B) Model components. At each location on the surface of the cell x, four quantities are represented: The height of the membrane $y_M(x,t)$, the height and thickness of the actin cortex $y_C(x,t)$ and $C(x,t)$ respectively, and the local density of membrane-cortex anchoring proteins, $A(x,t)$. Note that the schematic shows the range of possible model states (e.g., thick or thin cortex, protruding or proximal membrane), while specific predicted dynamics will be determined by simulation.*

ration $Y_C = 0$, and thickness $C(x_1, x_2, t)$. The cortical-cytoplasmic actin cytoskeleton can in principle have complicated morphologies that cannot be accounted for by a single location Y_C, so we think of Y_C as the weighted average position of maximal cortical actin. Membrane-cortex adhesions are described by density $A(x_1, x_2, t)$ in molecules nm^2. Finally, the plasma membrane has local height $Y_M(x_1, x_2, t)$.

2.1. Derivation, reduction to one dimensions, and non-dimensionalization. The dynamics of the actin cortex and density of adhesions attaching cortex and membrane are governed by

$$\dot{C} = \omega A - \gamma C \tag{2.1}$$

$$\dot{A} = \frac{k_{\text{on}}\, C}{C_0 + C} \exp\left(-\left(\frac{y - Y_C}{\delta}\right)\right) - k_{\text{off}} A \exp\left(\frac{k_A (Y_M - Y_C)}{F}\right) \tag{2.2}$$

Balance of forces on the cortex is determined by adhesions, which pull the cortex outwards (towards the membrane), and myosin, which contracts, pulling the cortex inwards (towards the cell body):

$$0 = A k_A (Y_M - Y_C) - \sigma_M C Y_C \tag{2.3}$$

Balance of forces on membrane is determined by adhesions, which pull the cortex inwards, and hydrostatic pressure, which pushes the membrane out.

$$0 = -A k_A (Y_M - Y_C) + \hat{\Pi}(Y_M^0 - Y_M) + \gamma_M \nabla^2 Y_M \tag{2.4}$$

Since mechanical equilibration is fast, $Y_M(t)$ and $Y_C(t)$ always evolve to satisfy these equations.

The resulting dimensionless system is:

$$\frac{dc}{dt} = \Omega a - c \tag{2.5}$$

$$\epsilon \frac{da}{dt} = \frac{c}{1+c} \exp\left(-\frac{y - y_C}{D}\right) - a \exp\left(\frac{y - y_C}{F}\right) \tag{2.6}$$

$$0 = a(y - y_C) - Mcy_C \tag{2.7}$$

$$0 = -a(y - y_C) + P(1 - y) + \frac{\partial^2 y}{\partial x^2} \tag{2.8}$$

2.2. Formulation as non-local integro-PDE.

This

2.3. Connections to a larger class of models arising in cell mechanics.

3. Analysis of ODE system.

While numerical simulation of the full model reveals a range of blebbing behavior, we seek to elucidate how biophysical parameters determine the class of dynamics, specifically whether or not a bleb forms. To this end, we simplify the model by neglecting the tension term in Eq. 2.8. This transforms the force-balance equations Eq. 2.8-2.7 into a pair of algebraic equations,

$$y = \frac{(a + cM)P}{aMc + aP + McP} \tag{3.1}$$

$$y_C = \frac{aP}{aMC + aP + McP}, \tag{3.2}$$

These are then substituted into the assembly/disassembly equations, yielding

$$\frac{dc}{dt} = \Omega a - c \tag{3.3}$$

$$\begin{aligned} \epsilon \frac{da}{dt} &= \frac{c}{1+c} \exp\left(-\frac{1}{D} \frac{MPc}{aMc + aP + McP}\right) \\ &\quad - a \exp\left(+\frac{1}{F} \frac{MPc}{aMc + aP + McP}\right) \end{aligned} \tag{3.4}$$

The model is now a system of two ordinary differential equations (ODEs) amenable to phase plane analysis (Edelstein-Keshet, 1988).

3.1. Regimes of behavior at small ϵ.

Figure 2

3.2. Bifurcation analysis in ϵ and Ω.

Figure 3

The Duck in Figure 4

4. Asymptotic analysis of PDE system.

4.1. Numerical observation of traveling waves.

Figure 5

4.2. Transformation into traveling coordinate z and matched asymptotic analysis.

$$\frac{\partial a}{\partial t} = f(a, y) \tag{4.1}$$

$$0 = g\left(a, y, \frac{\partial^2 y}{\partial x^2}\right). \tag{4.2}$$

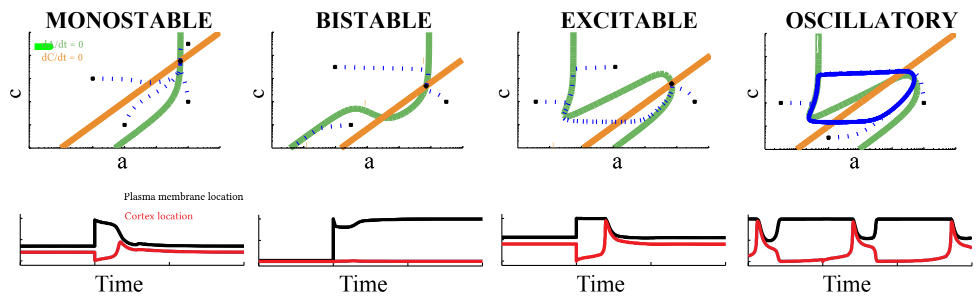

FIG. 2. *Phase plane analysis.*

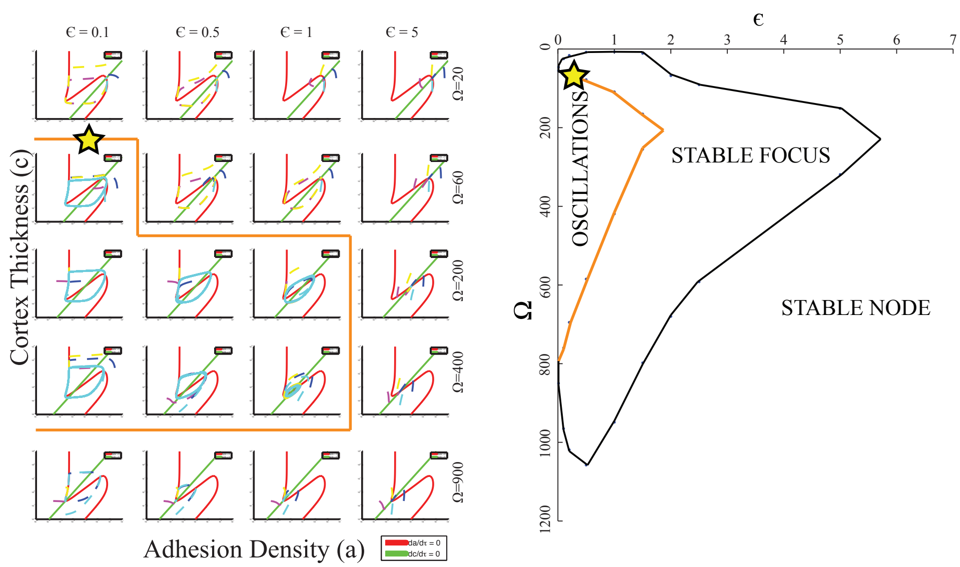

FIG. 3. *Bifurcation diagrams.*

A narrow version of the system is obtained if we assume the force balance equations are linear in a[redacted]

$$\frac{da}{dt} = f_1(y) - af_2(y) \tag{4.3}$$

$$0 = g_1(y) - ag_2(y) + \frac{\partial^2 y}{\partial x^2} \tag{4.4}$$

This can be obtained from our system given the following simplifying assumption. Assume that the cortex does not move significantly during excitation,

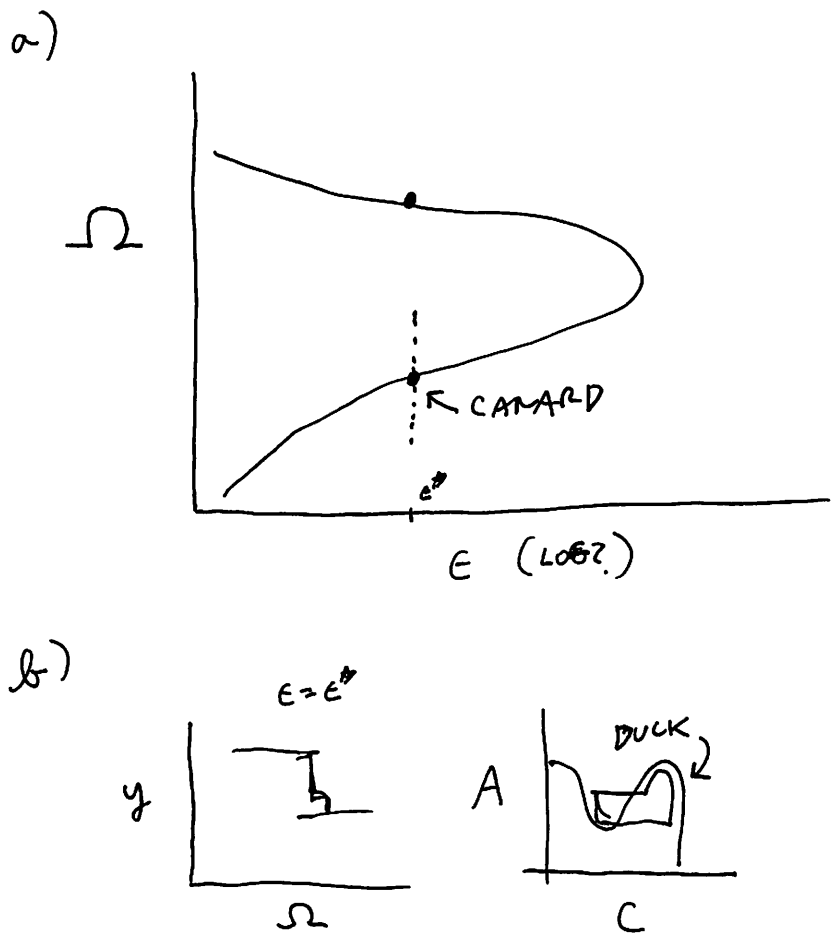

Fig. 4. *Canard explosion.*

$y_C = y_C^{ss}$, leaving us with the new system of two equations:

$$\frac{\partial a}{\partial t} = \frac{c^{ss}}{1+c^{ss}} \exp\left(-\frac{y - y_C^{ss}}{D}\right) - a \exp\left(\frac{y - y_C^{ss}}{F}\right) \tag{4.5}$$

$$0 = -a(y - y_C^{ss}) + P(1-y) + \gamma_M \frac{\partial^2 y}{\partial x^2} \tag{4.6}$$

Transform to wave coordinate $z = x - vt$ and 4.3 and 4.4 become:

$$-v\frac{da}{dz} = f_1(y) - af_2(y) \tag{4.7}$$

$$0 = g_1(y) - ag_2(y) + \frac{\partial^2 y}{\partial z^2} \tag{4.8}$$

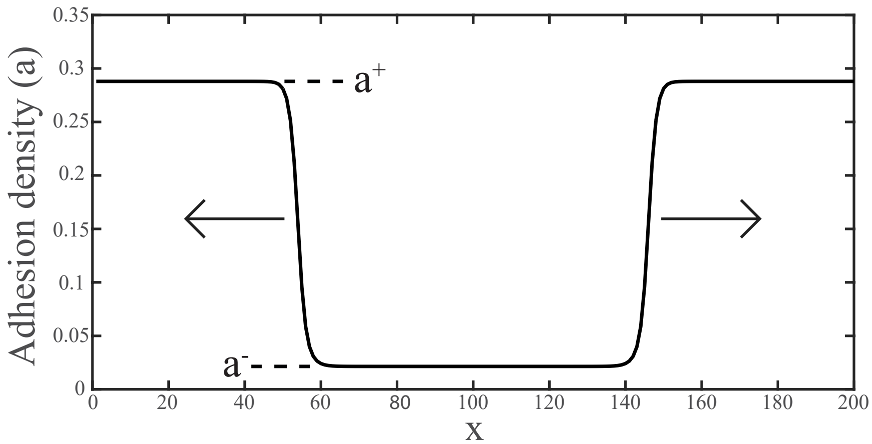

FIG. 5. *Numerical observation of traveling wave.*

We can use Eq. 4.8 to solve for a:

$$a = \frac{1}{g_2(y)} \left(g_1(y) + \frac{\partial^2 y}{\partial z^2} \right) \tag{4.9}$$

Then it follows that:

$$\Rightarrow -v\frac{\partial a}{\partial z} = f_1(y) - \frac{g_1(y)}{g_2(y)} f_2(y) - \frac{f_2(y)}{g_2(y)} \frac{\partial^2 y}{\partial z^2} \tag{4.10}$$

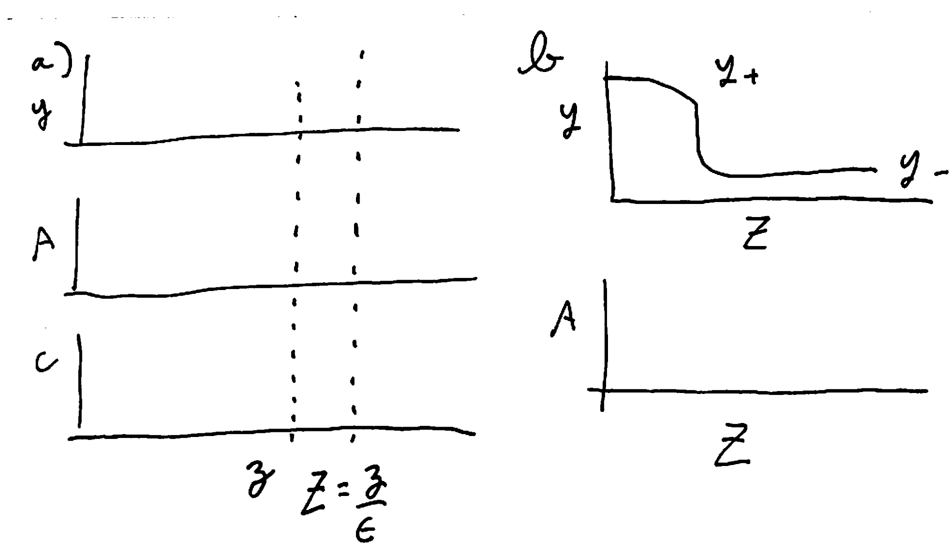

FIG. 6. *Decomposition of PDE solution into a traveling wave with regimes in different scales.*

Figure 6

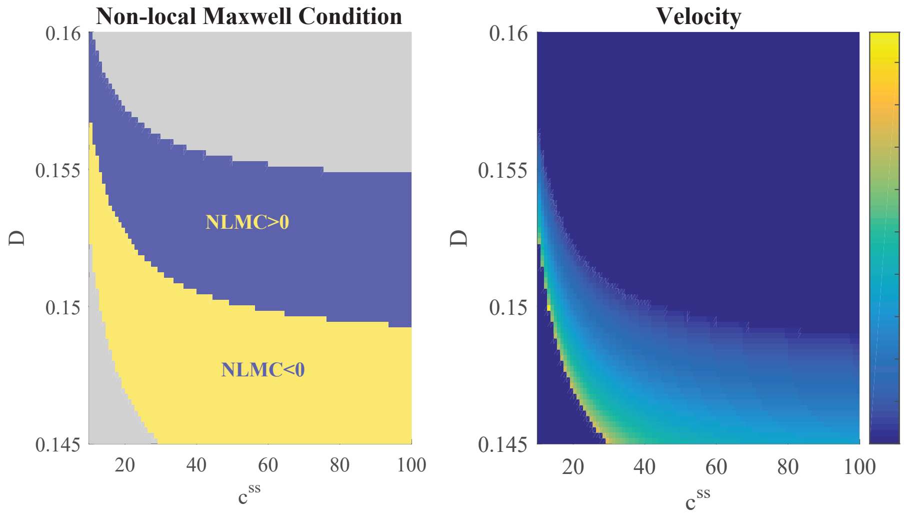

FIG. 7. *Nonlocal Maxwell condition demonstrating emergence of traveling waves.*

4.3. Non-local Maxwell Condition for traveling waves. 7

5. Conclusions.

6. Introduction. The introduction introduces the context and summarizes the manuscript. It is importantly to clearly state the contributions of this piece of work. The next two paragraphs are text filler, generated by the `lipsum` package.

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The paper is organized as follows. Our main results are in section 7, our new algorithm is in section 8, experimental results are in section 9, and the conclusions follow in section 11.

7. Main results. We interleave text filler with some example theorems and theorem-like items.

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Here we state our main result as Theorem 7.1; the proof is deferred to **??**.

THEOREM 7.1 (LDL^T Factorization [**?**]). *If $A \in \mathbb{R}^{n\times n}$ is symmetric and the principal submatrix $A(1:k,1:k)$ is nonsingular for $k = 1:n-1$, then there exists a unit lower triangular matrix L and a diagonal matrix*

$$D = \operatorname{diag}(d_1, \dots, d_n)$$

such that $A = LDL^T$. The factorization is unique.

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THEOREM 7.2 (Mean Value Theorem). *Suppose f is a function that is continuous on the closed interval $[a, b]$. and differentiable on the open interval (a, b). Then* *there exists a number c such that $a < c < b$ and*

$$f'(c) = \frac{f(b) - f(a)}{b - a}.$$

In other words,

$$f(b) - f(a) = f'(c)(b - a).$$

Observe that Theorems 7.1 and 7.2 and Corollary 7.3 correctly mix references to multiple labels.

COROLLARY 7.3. *Let $f(x)$ be continuous and differentiable everywhere. If $f(x)$ has at least two roots, then $f'(x)$ must have at least one root.*

Proof. Let a and b be two distinct roots of f. By Theorem 7.2, there exists a number c such that

$$f'(c) = \frac{f(b) - f(a)}{b - a} = \frac{0 - 0}{b - a} = 0.$$ □

Note that it may require two LaTeX compilations for the proof marks to show.

Display matrices can be rendered using environments from `amsmath`:

$$S = \begin{bmatrix} 1 & 0 \\ 0 & 0 \end{bmatrix} \quad \text{and} \quad C = \begin{pmatrix} 1 & 1 & 0 \\ 1 & 1 & 0 \\ 0 & 0 & 0 \end{pmatrix}. \tag{7.1}$$

Equation (7.1) shows some example matrices.

We calculate the Fréchet derivative of F as follows:

$$\begin{aligned} F'(U,V)(H,K) &= \langle R(U,V), H\Sigma V^T + U\Sigma K^T - P(H\Sigma V^T + U\Sigma K^T)\rangle \qquad (7.2a) \\ &= \langle R(U,V), H\Sigma V^T + U\Sigma K^T\rangle \\ &= \langle R(U,V)V\Sigma^T, H\rangle + \langle \Sigma^T U^T R(U,V), K^T\rangle. \qquad (7.2b) \end{aligned}$$

Equation (7.2a) is the first line, and (7.2b) is the last line.

8. Algorithm. Sed gravida lectus ut purus. Morbi laoreet magna. Pellentesque eu wisi. Proin turpis. Integer sollicitudin augue nec dui. Fusce lectus. Vivamus faucibus nulla nec lacus. Integer diam. Pellentesque sodales, enim feugiat cursus volutpat, sem mauris dignissim mauris, quis consequat sem est fermentum ligula. Nullam justo lectus, condimentum sit amet, posuere a, fringilla mollis, felis. Morbi nulla nibh, pellentesque at, nonummy eu, sollicitudin nec, ipsum. Cras neque. Nunc augue. Nullam vitae quam id quam pulvinar blandit. Nunc sit amet orci. Aliquam erat elit, pharetra nec, aliquet a, gravida in, mi. Quisque urna enim, viverra quis, suscipit quis, tincidunt ut, sapien. Cras placerat consequat sem. Curabitur ac diam. Curabitur diam tortor, mollis et, viverra ac, tempus vel, metus.

Our analysis leads to the algorithm in Algorithm 1.

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Algorithm 1 Build tree

Define $P := T := \{\{1\}, \ldots, \{d\}\}$
while $\#P > 1$ **do**
  Choose $C' \in \mathcal{C}_p(P)$ with $C' := \operatorname{argmin}_{C \in \mathcal{C}_p(P)} \varrho(C)$
  Find an optimal partition tree $T_{C'}$
  Update $P := (P \backslash C') \cup \{\bigcup_{t \in C'} t\}$
  Update $T := T \cup \{\bigcup_{t \in \tau} t : \tau \in T_{C'} \backslash \mathcal{L}(T_{C'})\}$
end while
return T

9. Experimental results. Quisque facilisis auctor sapien. Pellentesque gravida hendrerit lectus. Mauris rutrum sodales sapien. Fusce hendrerit sem vel lorem. Integer pellentesque massa vel augue. Integer elit tortor, feugiat quis, sagittis et, ornare non, lacus. Vestibulum posuere pellentesque eros. Quisque venenatis ipsum dictum nulla. Aliquam quis quam non metus eleifend interdum. Nam eget sapien ac mauris malesuada adipiscing. Etiam eleifend neque sed quam. Nulla facilisi. Proin a ligula. Sed id dui eu nibh egestas tincidunt. Suspendisse arcu.

Figure 8 shows some example results. Additional results are available in the supplement in **??**.

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11. Conclusions. Some conclusions here.

Appendix A. An example appendix. Aenean tincidunt laoreet dui. Vestibulum ante ipsum primis in faucibus orci luctus et ultrices posuere cubilia Curae; Integer ipsum lectus, fermentum ac, malesuada in, eleifend ut, lorem. Vivamus ipsum turpis, elementum vel, hendrerit ut, semper at, metus. Vivamus sapien tortor, eleifend id, dapibus in, egestas et, pede. Pellentesque faucibus. Praesent lorem neque, dignissim in, facilisis nec, hendrerit vel, odio. Nam at diam ac neque aliquet viverra. Morbi dapibus ligula sagittis magna. In lobortis. Donec aliquet ultricies libero. Nunc dictum vulputate purus. Morbi varius. Lorem ipsum dolor sit amet, consectetuer adipiscing

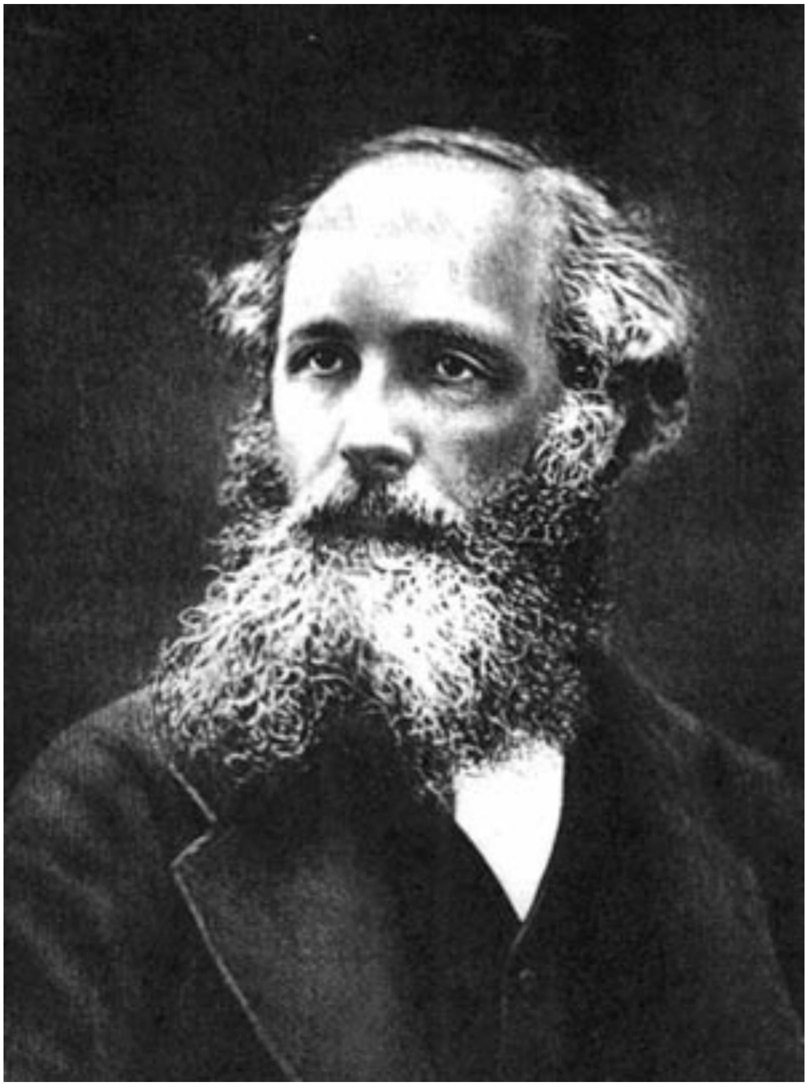

FIG. 8. *Example figure using external image files.*

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Acknowledgments. We would like to acknowledge .

REFERENCES