Conservation Laws in Biology

Two new examples.
(Quarterly Applied Mathematics, 2021)

M. Slemrod (Univ. of Wisconsin, Madison) and M. Mussel (NIH)

1. Action Potentials via Continuum Mechanics

2. Biological form via differential geometry

1. Action Potentials via Continuum Mechanics

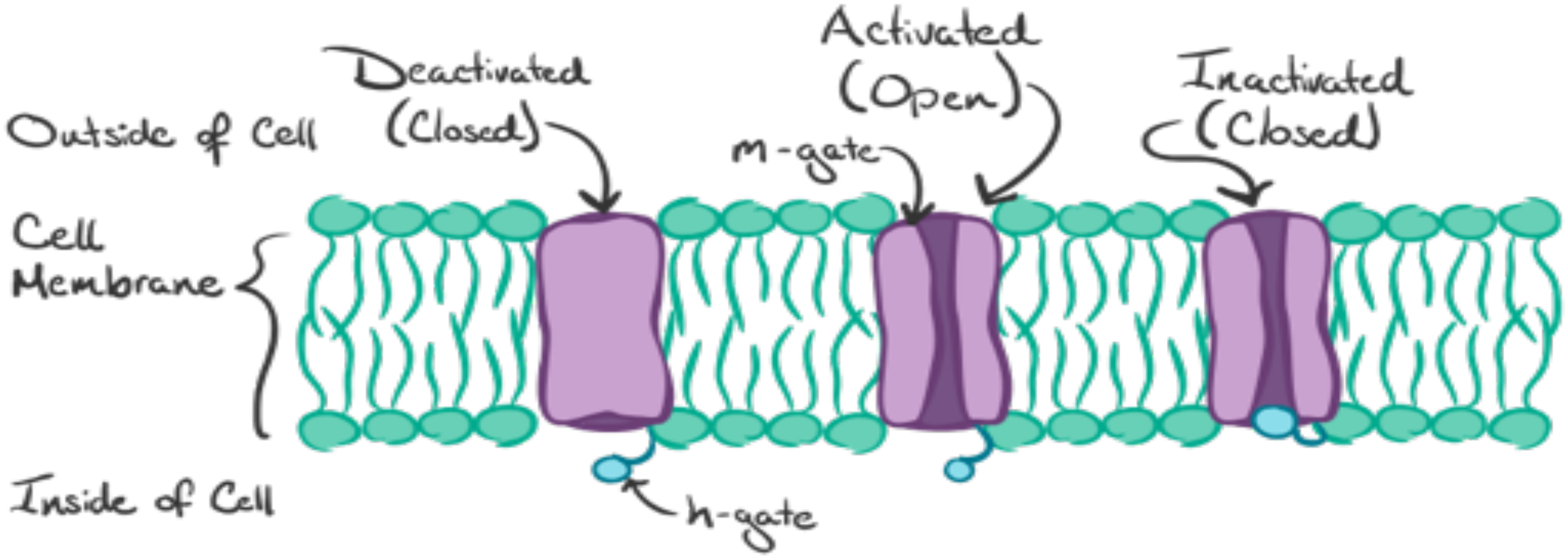
Scientific Reports nature.com, Feb. 2019

Matan Mussel and Matthias F. Schneider,

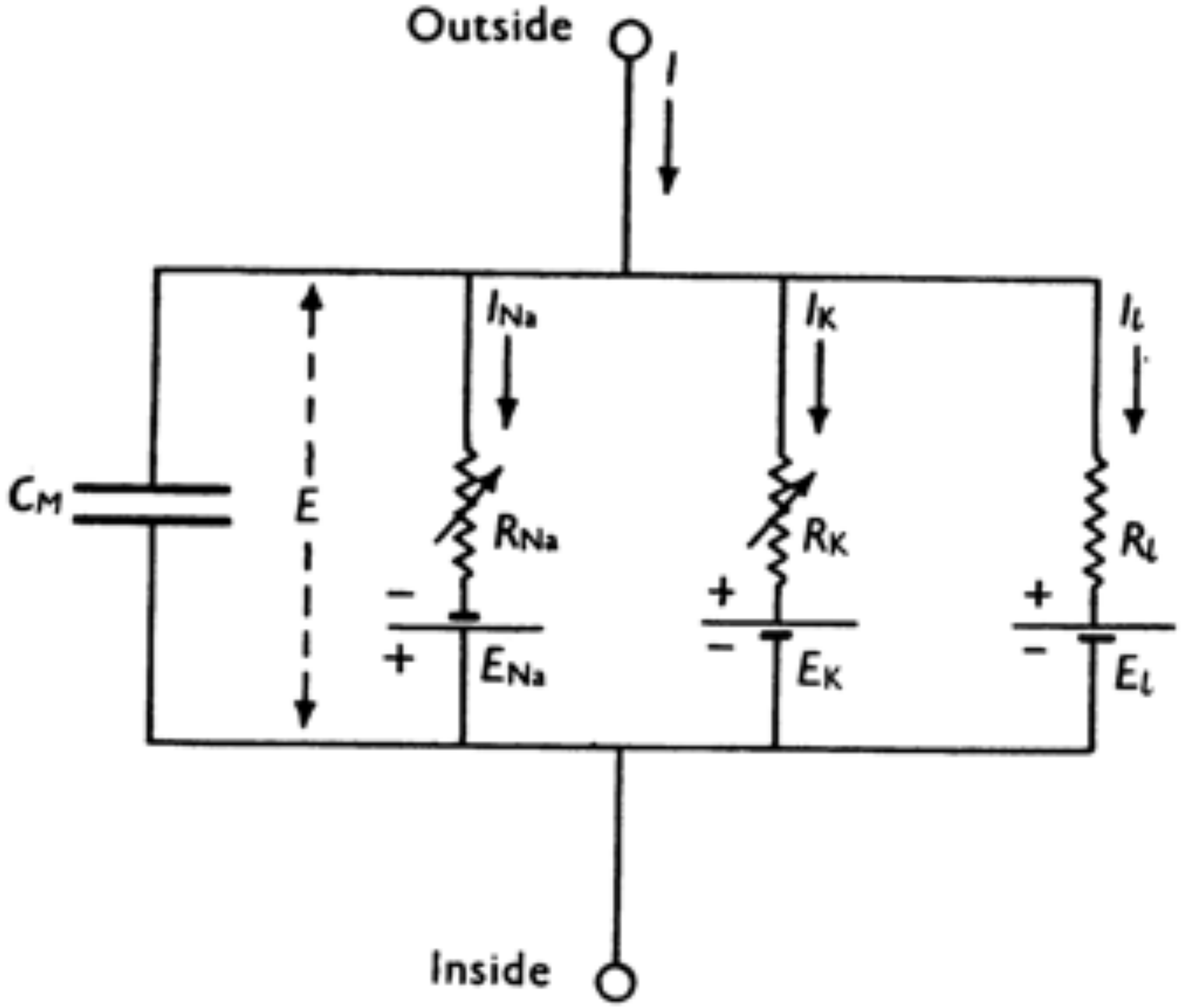
Similarities between action potentials and acoustic pulses in a van der Waals fluid.

An action potential is typically described as a purely electrical change that propagates along the membrane of excitable cells. However, recent experiments have demonstrated that non-linear acoustic pulses that propagate along lipid interfaces and traverse the melting transition, share many similar properties with action potentials.

Classically, action potentials are explained by an analogy to an electric circuit

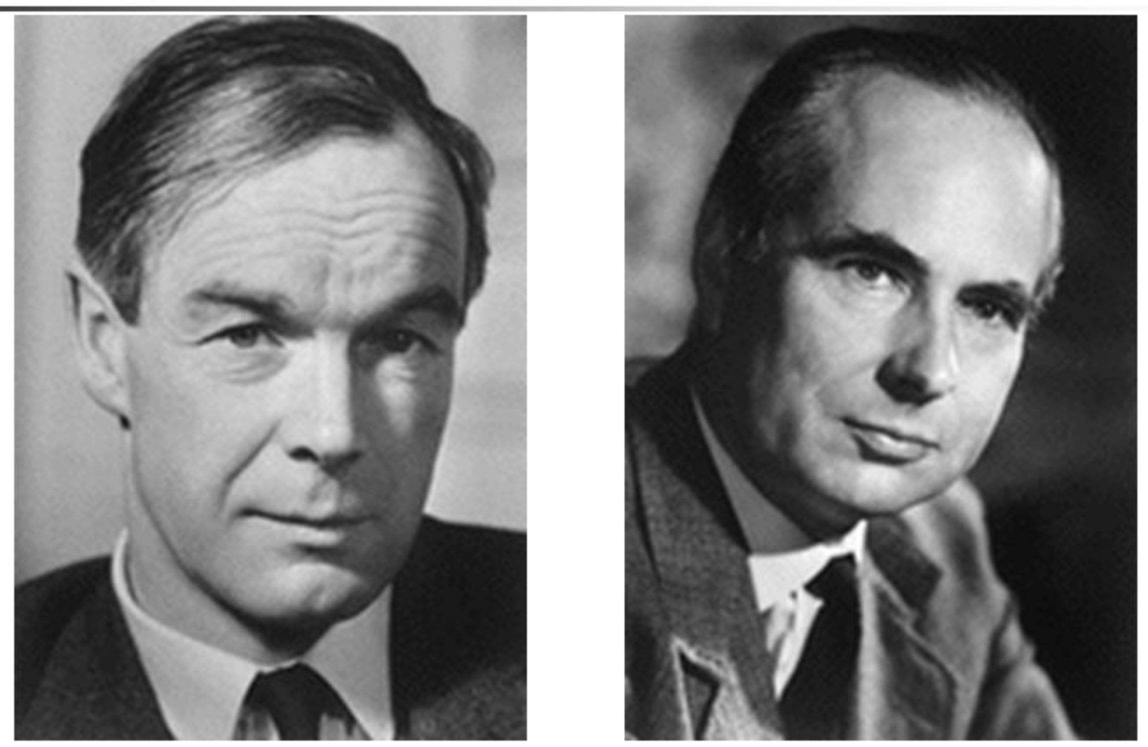


https://www.khanacademy.org



Hodgkin and Huxley, J Physiol, 1952

A.L. HODGKIN and A. F. HUXLEY



1963

Classically, action potentials are explained by an analogy to an electric circuit

$$\frac{1}{(r_i + r_o)} \frac{\partial^2 V}{\partial x^2} = c_m \frac{\partial V}{\partial t} + I_{ion}$$

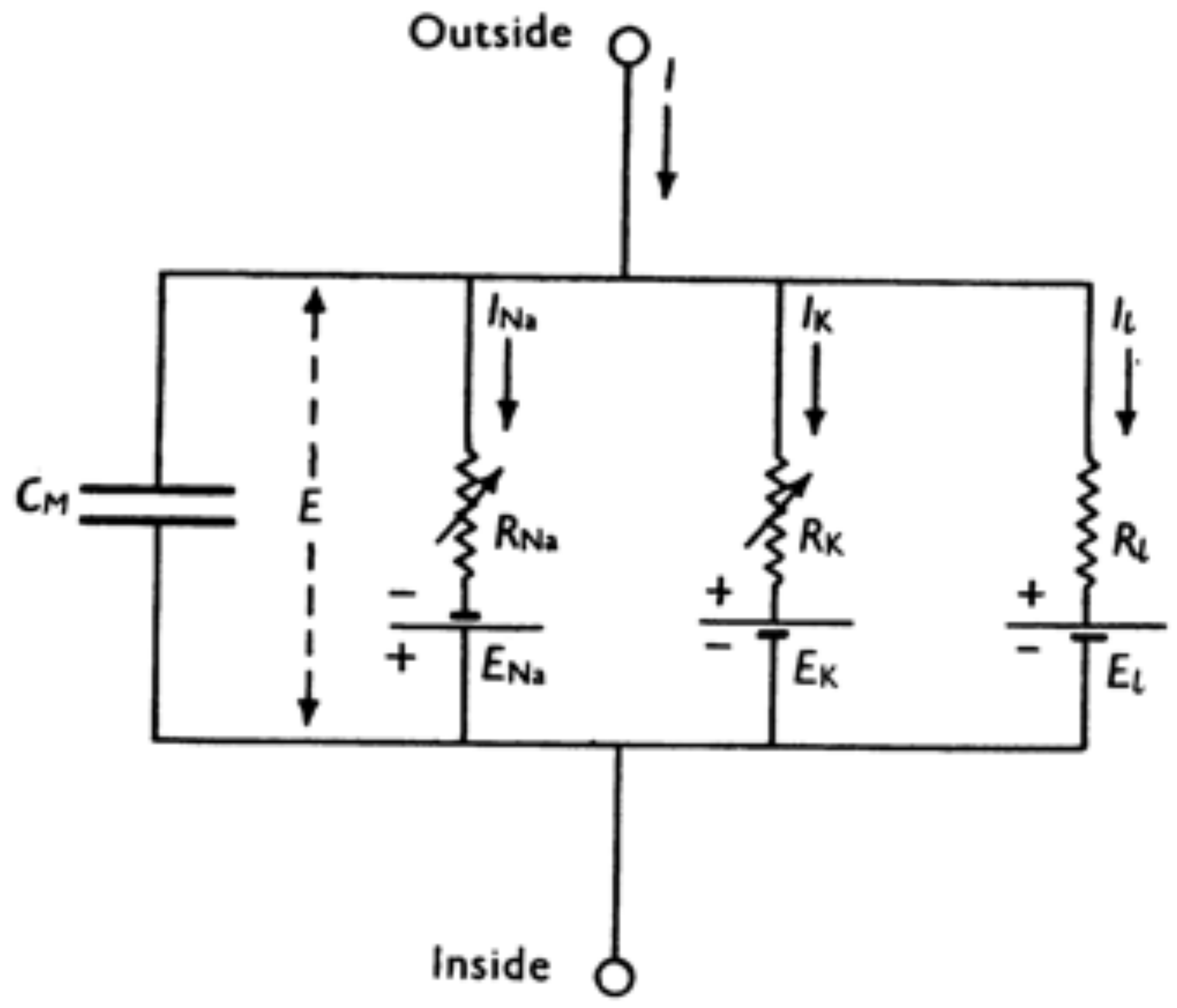
$$I_{ion} = \bar{g}_{Na} m^3 h (V - V_{Na}) + \bar{g}_K n^4 (V - V_K) + \bar{g}_L (V - V_L)$$

$$\frac{dm}{dt} = \frac{0.1(V + 25)}{\exp\left(\frac{V + 25}{10}\right) - 1}(1 - m) - 4 \exp\left(\frac{V}{18}\right) m$$

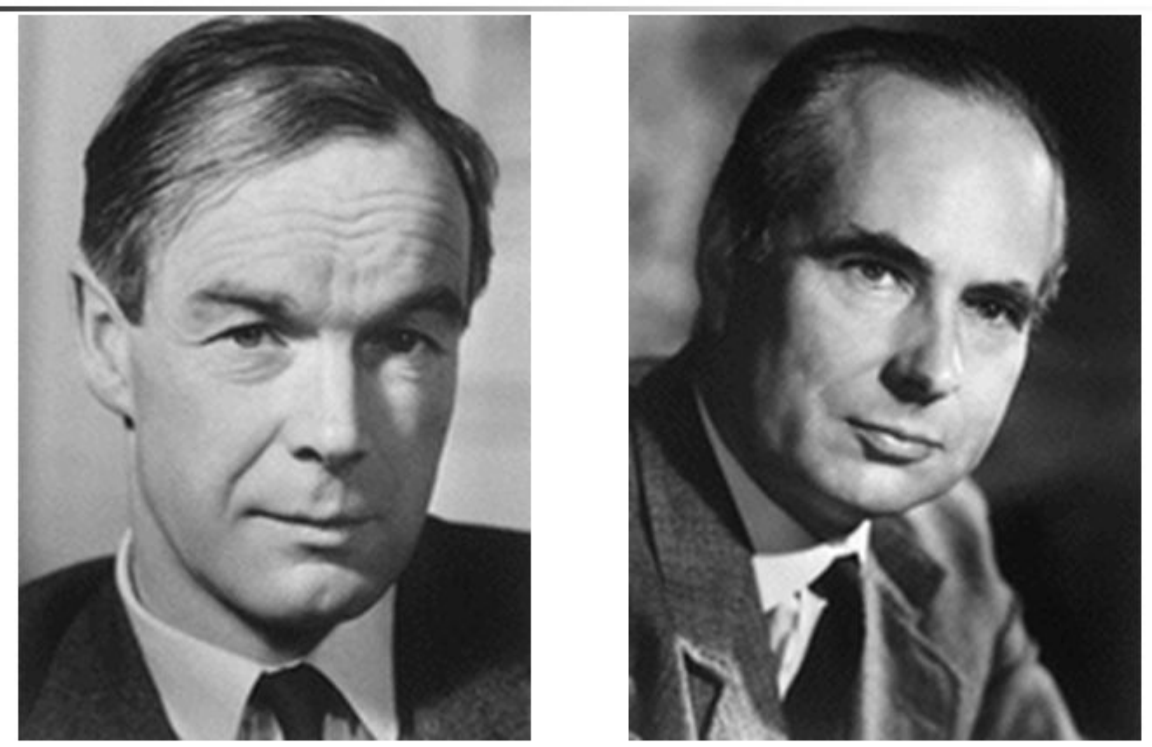
$$\frac{dh}{dt} = 0.07 \exp\left(\frac{V}{20}\right)(1 - h) - \frac{1}{\exp\left(\frac{V + 30}{10}\right) + 1} h$$

$$\frac{dn}{dt} = \frac{0.01(V + 10)}{\exp\left(\frac{V + 10}{10}\right) - 1}(1 - n) - 0.125 \exp\left(\frac{V}{80}\right) n$$

Hodgkin and Huxley, J Physiol, 1952



A.L. HODGKIN and A. F. HUXLEY



1963

G.B. Ermentrout and D.H. Terman,
Mathematical Foundations of Neuroscience, 1
Interdisciplinary Applied Mathematics 35,
DOI 10.1007/978-0-387-87708-2 1,
SpringerScience+BusinessMedia,
LLC2010

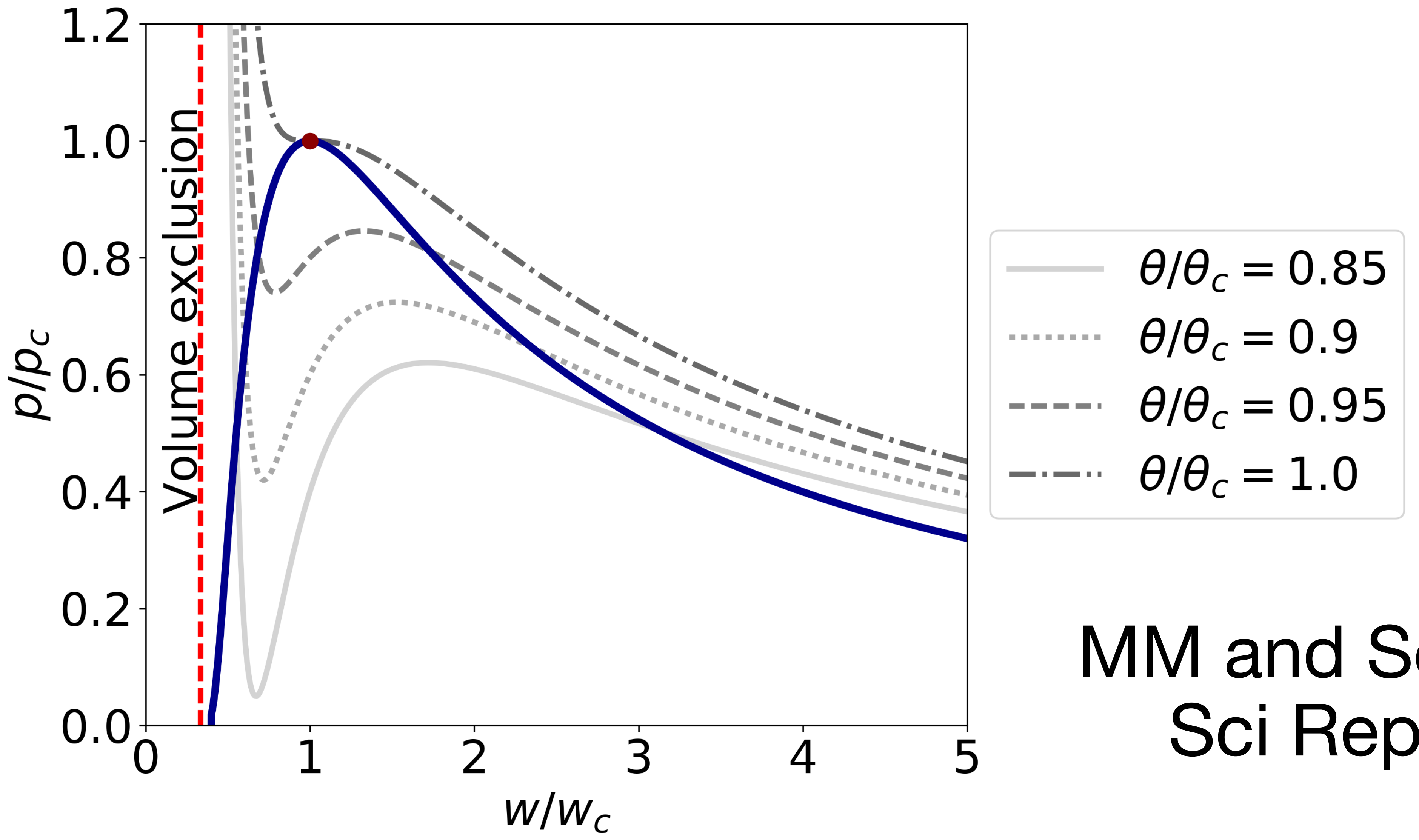
Chap.1 , The Hodgkin-Huxley Equations

Model of sound waves in lipid membrane near phase transition

Model assumptions: Conservation laws

- Mass (continuity equation)
- Momentum (Newton's 2nd law)
- Energy (1st law of thermodynamics)

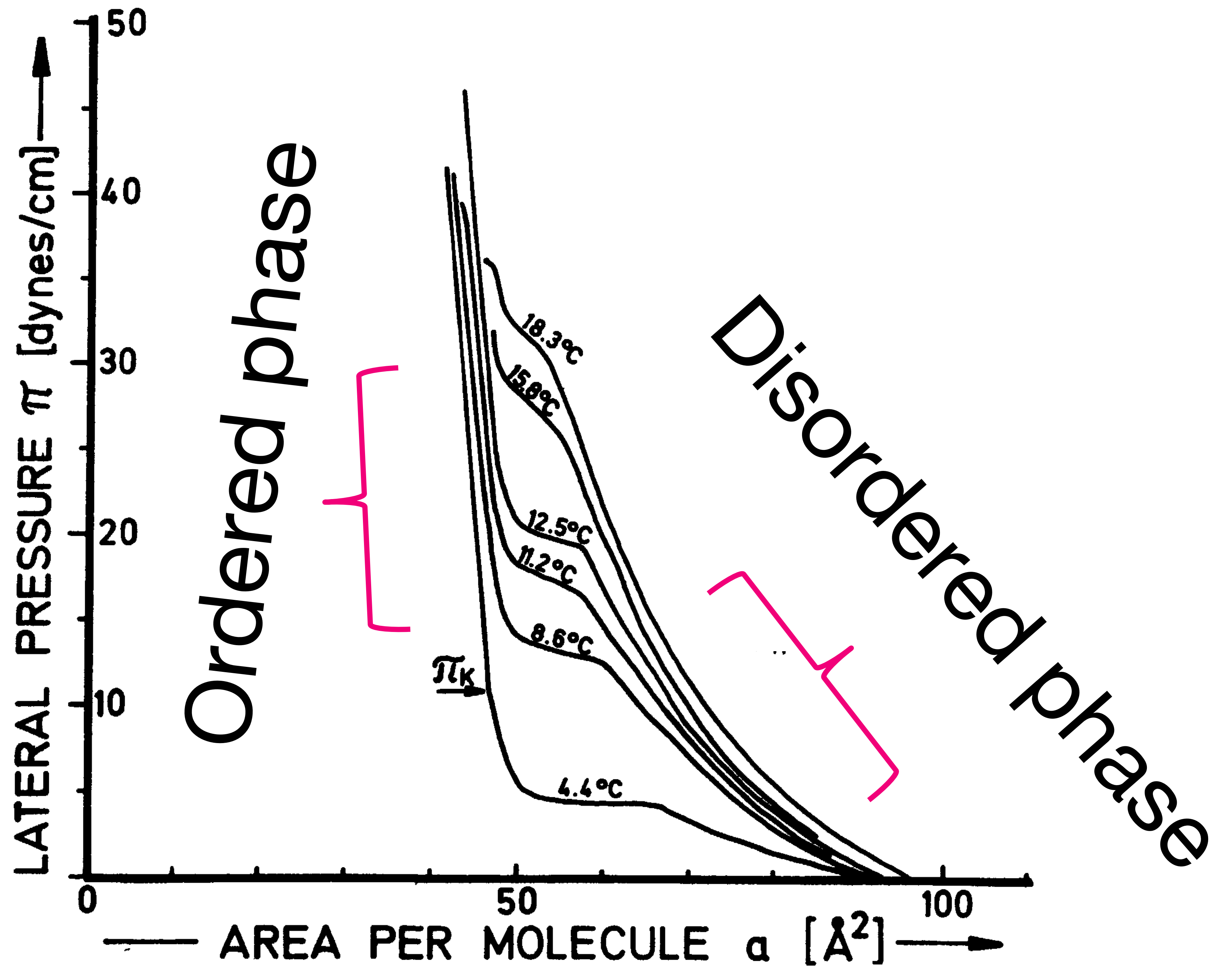
van der Waals constitutive relations



MM and Schneider, Sci Rep, 2019

Surface pressure—area isotherms in a lipid monolayer

Albrecht, Gruler, and Sackmann, J Phys, 1978



Model of sound waves in lipid membrane near phase transition

$\rightarrow x$

$+\ell$

Lipid membrane: ρ, p, θ, E, v

$-\ell$

$w = \rho^{-1}$

Model assumptions: Conservation laws

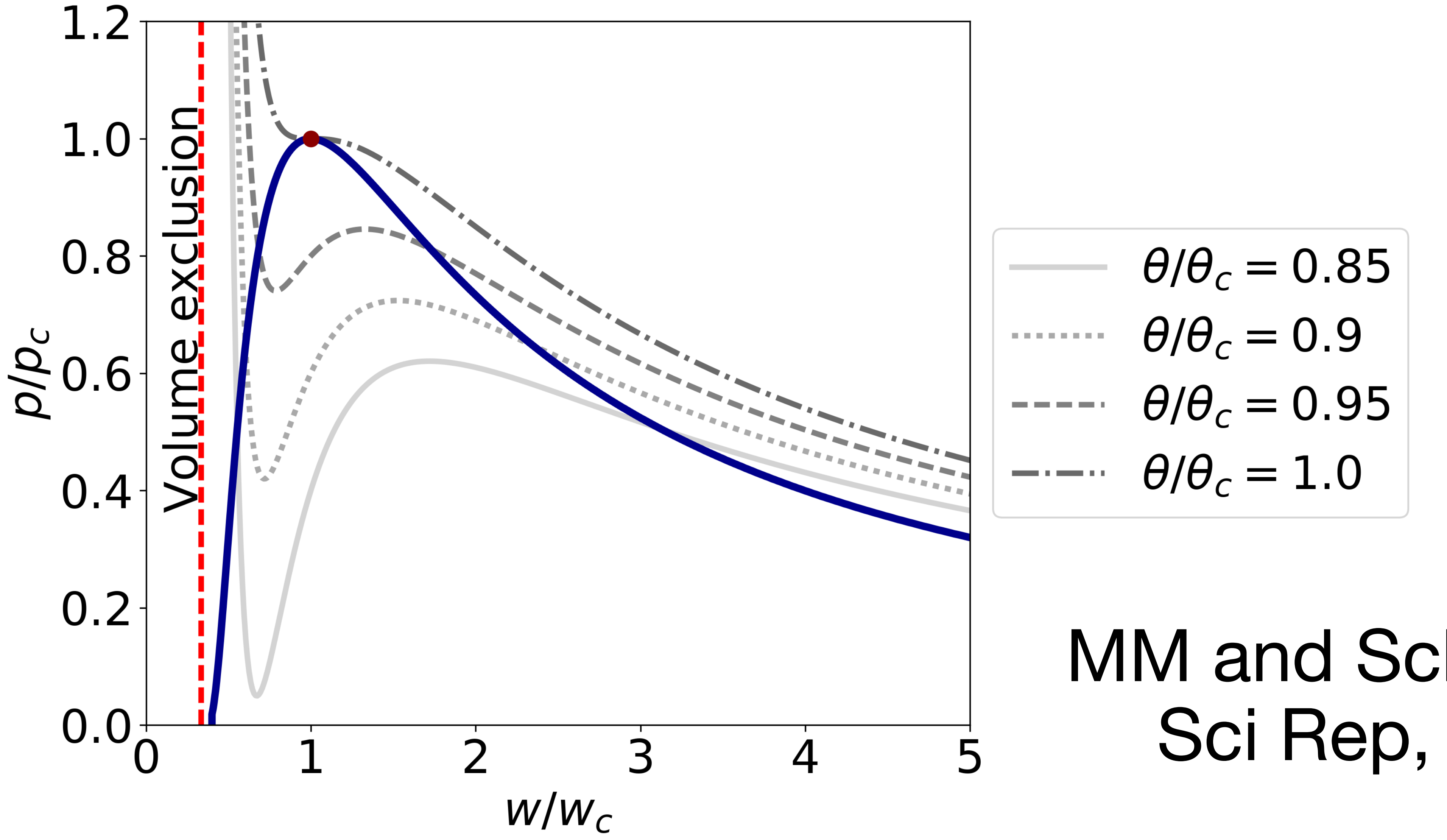
- Mass (continuity equation)
- Momentum (Newton's 2nd law)
- Energy (1st law of thermodynamics)

$$\partial_t w = \bar{w} \partial_h v$$
$$\partial_t v = \bar{w} \partial_h \tau$$
$$\partial_t E = \bar{w}\left[\partial_h(\tau v) + \partial_h(C \partial_h v \partial_h w) + k \partial_h^2 \theta\right]$$

van der Waals constitutive relations

$$\tau = -p + \zeta \partial_h v - C \partial_h^2 w$$

Slemrod, J Diff Eq, 1984



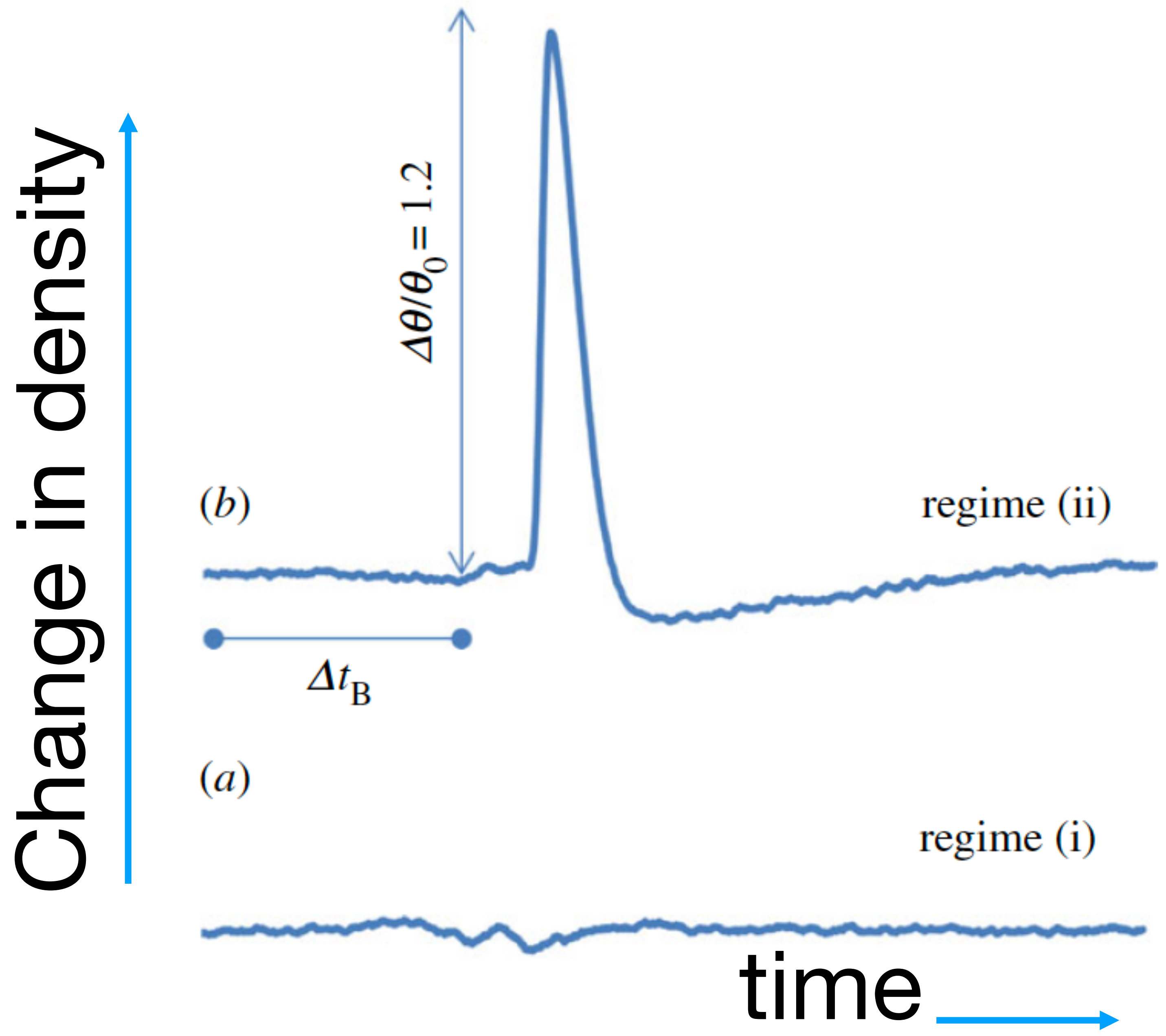
MM and Schneider, Sci Rep, 2019

$$p = \frac{k_B \theta}{mw - b} - \frac{a}{m^2 w^2}$$

$$E = c_v \theta - \frac{a}{m^2 w} + \frac{v^2}{2} + \frac{C}{2}(\partial_h w)^2$$

Density and pressure aspects vary nonlinearly near phase transition

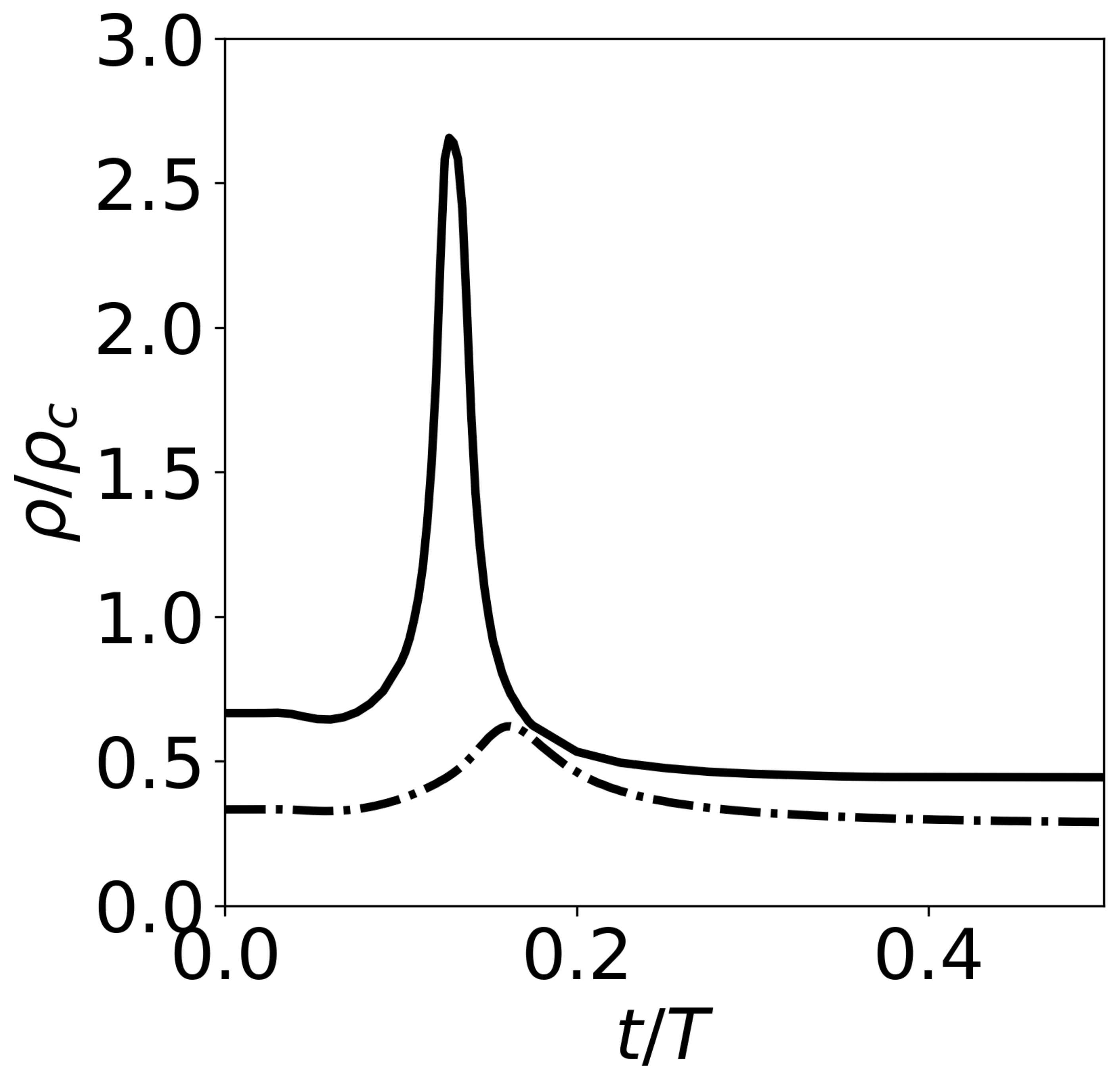
Lipid monolayer experiment



$$T \sim 10^{-3} - 10^{-2}\ s$$
$$U \sim 0.1 - 100\ m/s$$

Shrivastava and Schneider,
J Royal Soc Interface, 2014

Theory

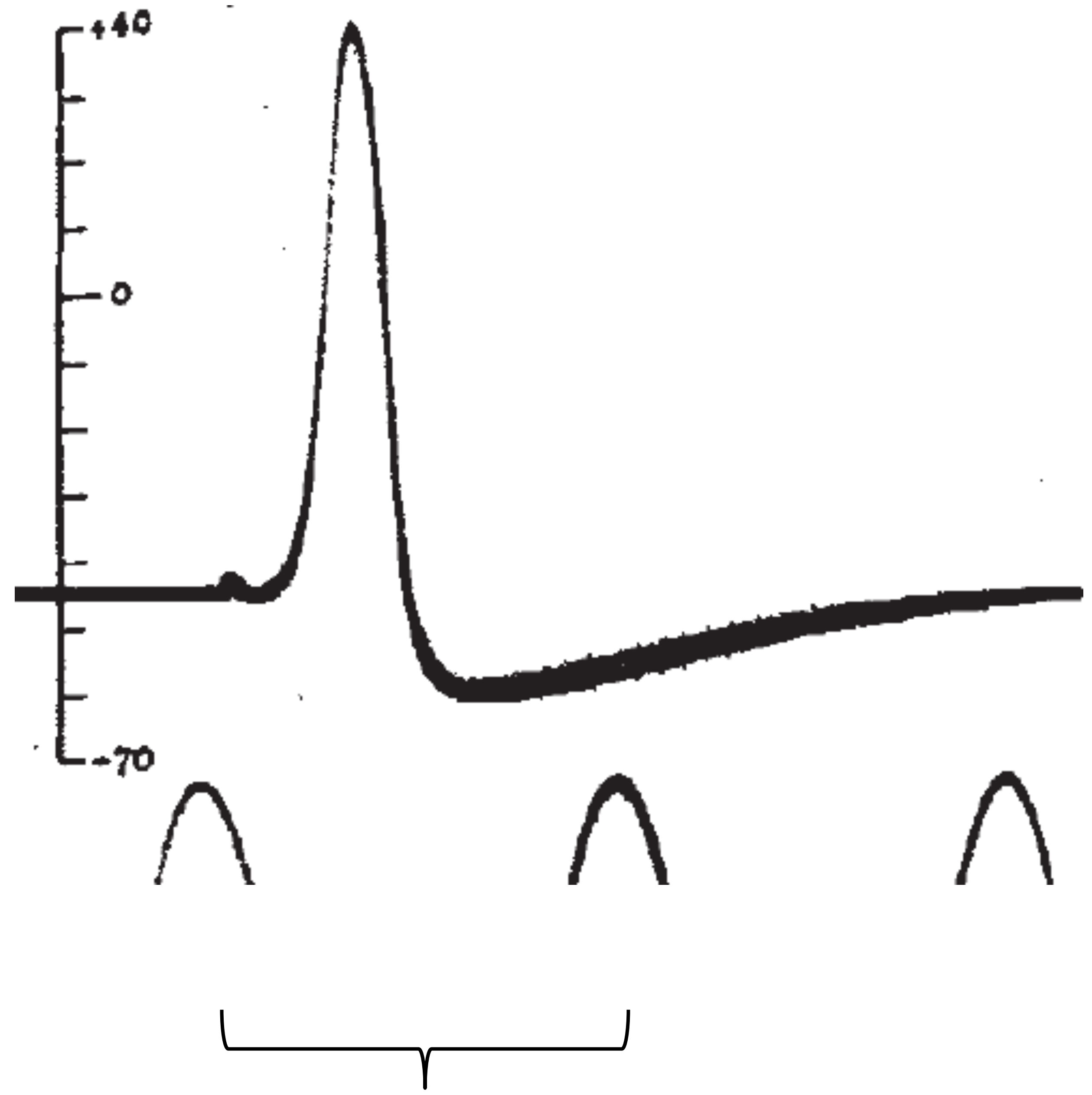


$$\boxed{T = \frac{\zeta}{p_c} \sim 10^{-2} s}$$

$$\boxed{U = \sqrt{\frac{p_c}{\rho_c}} \sim 100\ m/s}$$

MM and Schneider, Sci Rep, 2019

Action potential



$$T = 2 \cdot 10^{-3} s$$
$$U = 21\ m/s$$

Hodgkin and Huxley, Nature, 1939

vdW fluid equations are similar to the generalized Fitzhugh-Nagumo equations

JOURNAL OF DIFFERENTIAL EQUATIONS 52, 1–23 (1984)

Dynamic Phase Transitions in a Van Der Waals Fluid*

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The main tool of the analysis is the Conley–Easton theory of isolating blocks [2]. This theory has been applied by Carpenter [3] to prove the existence of traveling wave solutions to a generalization of the Fitzhugh–Nagumo equations modeling nerve impulse transmission. Surprisingly, the equations governing traveling wave solutions in the phase transition problem given here and the generalized Fitzhugh–Nagumo equations are similar. In fact, I show a modification of Carpenter's approach to the wave impulse equations that yields the desired traveling wave solution to the phase transition problem.

To capture the phase transition between liquid disordered states and liquid ordered states we seek a traveling wave solution, $w(\xi)$, $v(\xi)$, $\theta(\xi)$; $\xi = \frac{h-Ut}{\bar{w}}$ satisfying the system:

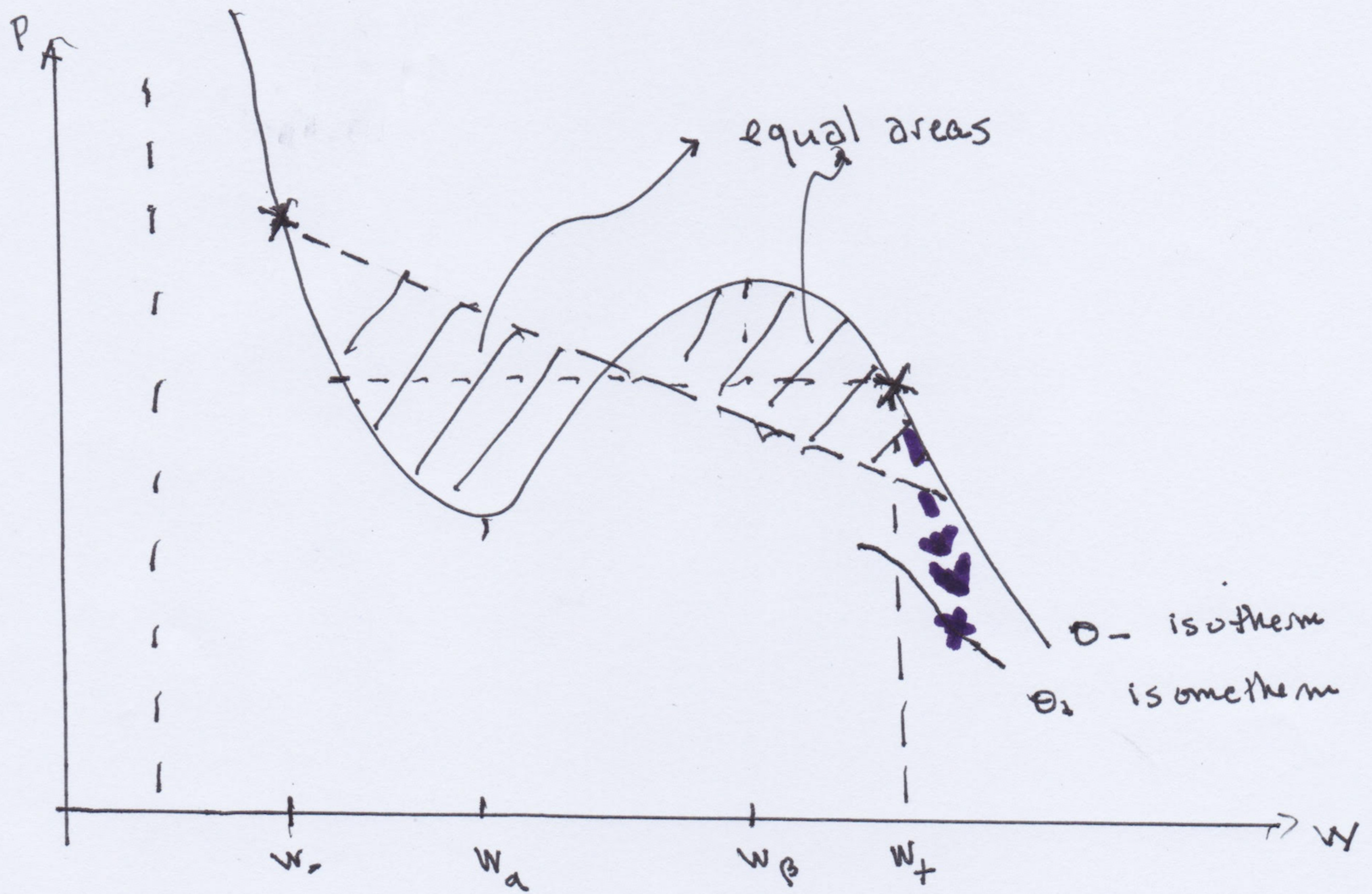
$$\begin{aligned} -Uw' &= v' \\ -Uv' &= (-p + \zeta v' - Cw'')' \\ -UE' &= [v(-p + \zeta v' - Cw'')]' + k\theta'' + C(v'w')' \end{aligned}$$

Set $w(-\infty) = w_-$, $v(-\infty) = v_-$, $\theta(-\infty) = \theta_-$,

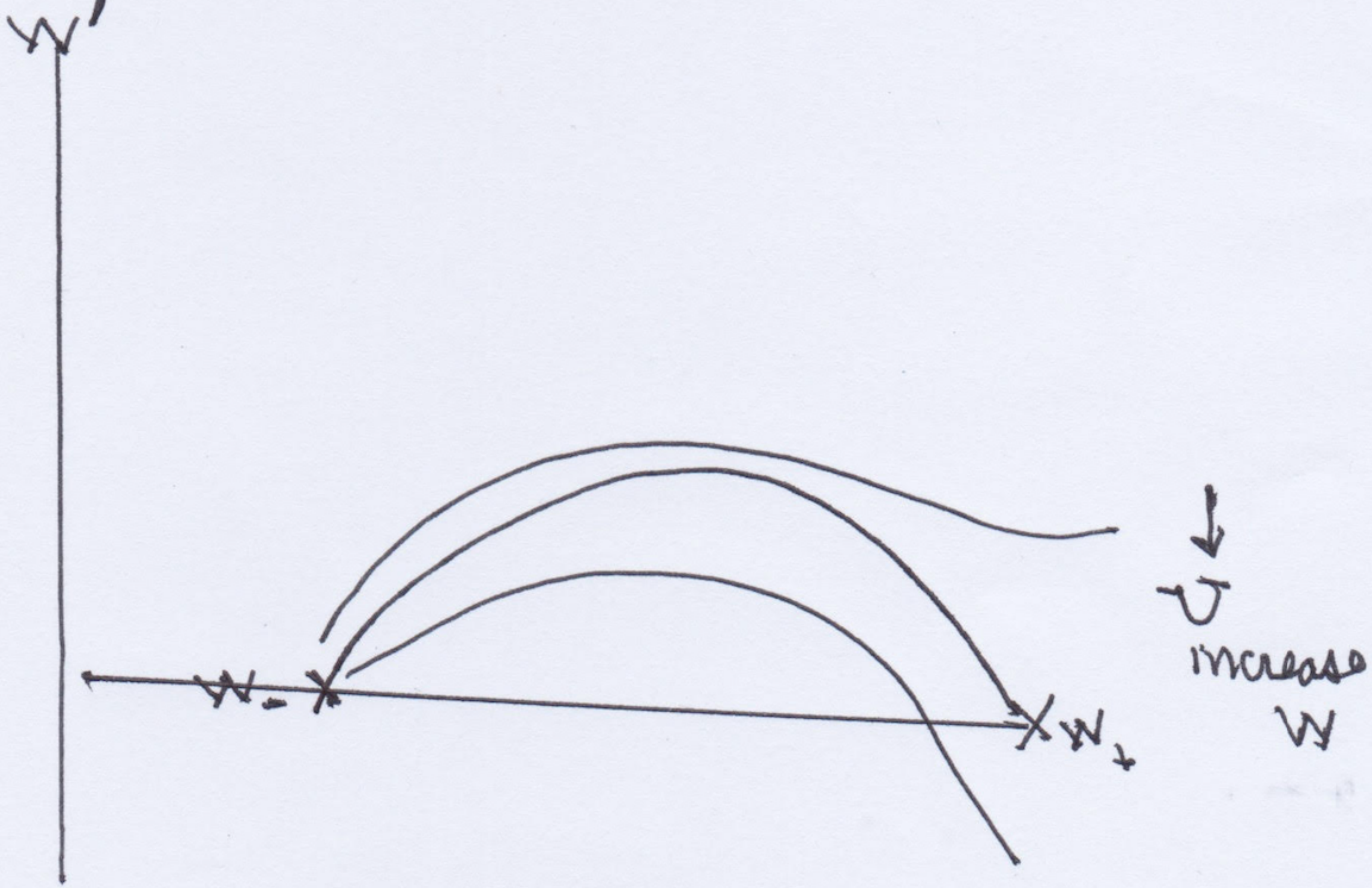
$$p_- = \frac{k_B \theta_-}{mw_- - b} - \frac{a}{m^2 w_-^2}, \quad E_- = \frac{v_-^2}{2} + c_v \theta_- - \frac{a}{m^2 w_-}$$

and integrateto find

$$\begin{aligned} -U(w - w_-) &= v - v_- \\ -U(v - v_-) &= -p + p_- + \zeta v' - Cw'' \\ -U(E - E_-) &= v(-p + \zeta v' - Cw'') + v_- p_- + k\theta' - CUw'^2 \end{aligned}$$



P
equal areas
θ - isotherm
θ_1 isometherm
w
w_-
w_α
w_β
w_+



saddle - saddle

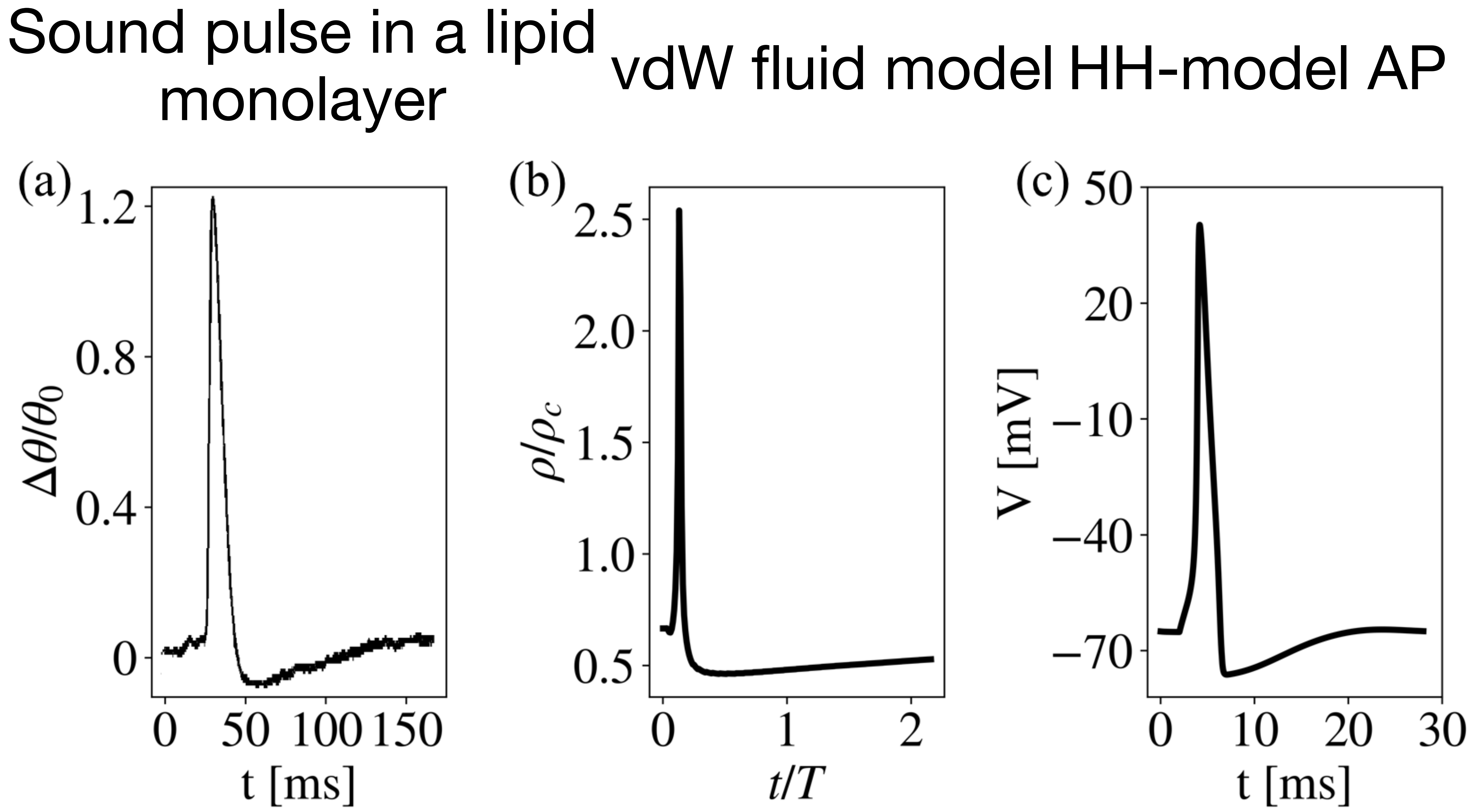
connection

Density-voltage relation

By calculating the charge density of the lipid membrane and its interaction with ions accumulating on both sides of the membrane, an electric potential difference arises

$$V \propto \rho$$

when the symmetry across the lipid membrane is broken.



MM and Slemrod, Q Appl Math, 2021

JOURNAL OF MATHEMATICAL ANALYSIS AND APPLICATIONS 36, 22-40 (1971)

Nonexistence of OscillationsIn a Nonlinear Distributed Network,

M. Slemrod,
Center for Dynamical Systems,
Division of Applied Mathematics, Brown University.

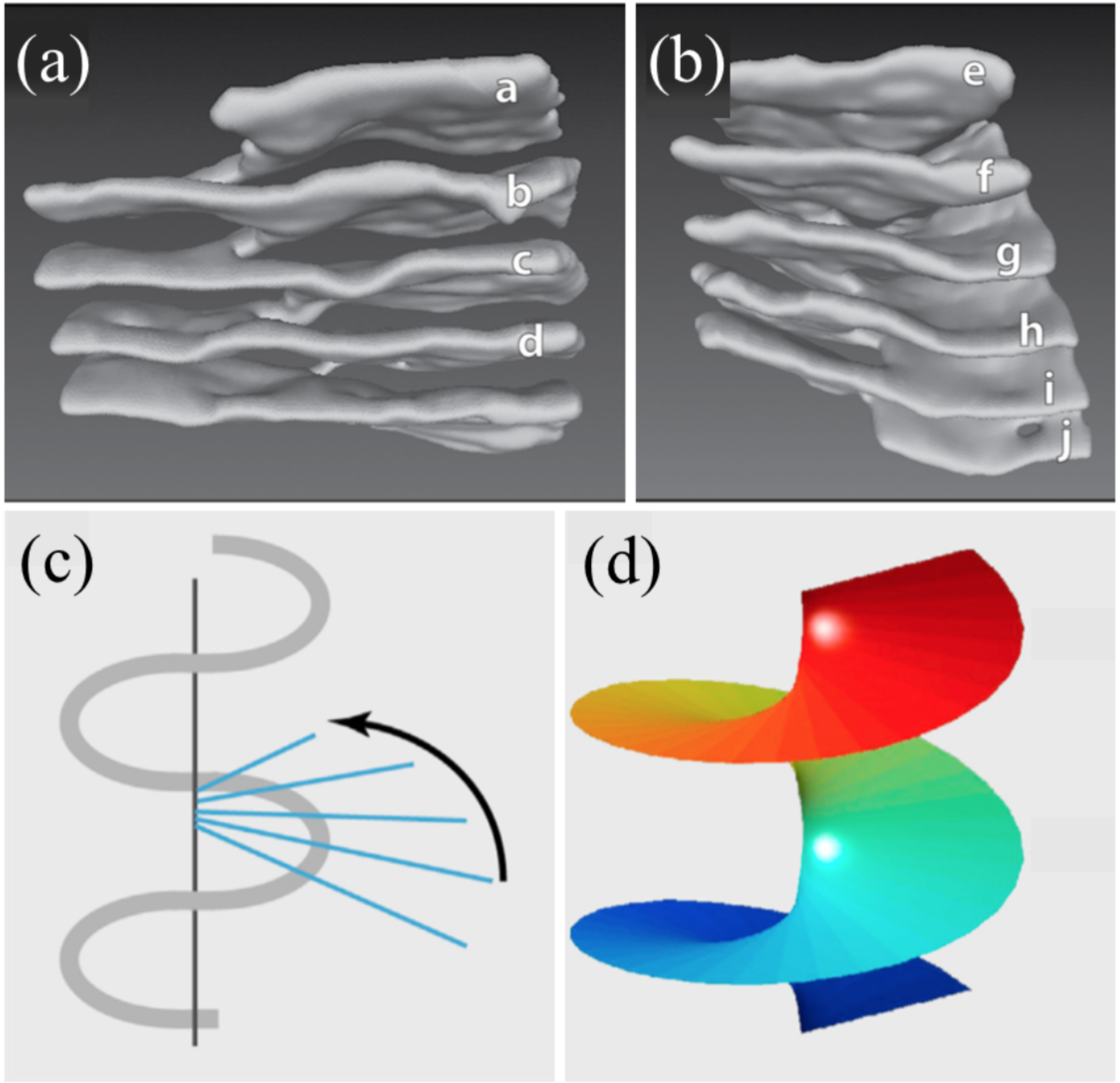
2. Biological form via differential geometry

Cell structure

Wallace F Marshall. Differential geometry meets the cell. Cell, 154(2):265–266, 2013.

``a century ago D`Arcy Wentworth Thompson proposed that physical principles such as surface tension would dictate biological form.’’

``The evidence of...proteins goes against the concept of D`Arcy Thompson and appeared to be the final nail in the coffin of his Pythagorean approach to cell biology. But a paper by Terasaki et al. ...breathes new life into the old dream of mathematical biology by describing that connections between endoplasmic reticulum (ER) sheets mimics a well-known class of mathematical surfaces, and this shape is in fact predictable
from simple physical rules governing membrane energetics.''

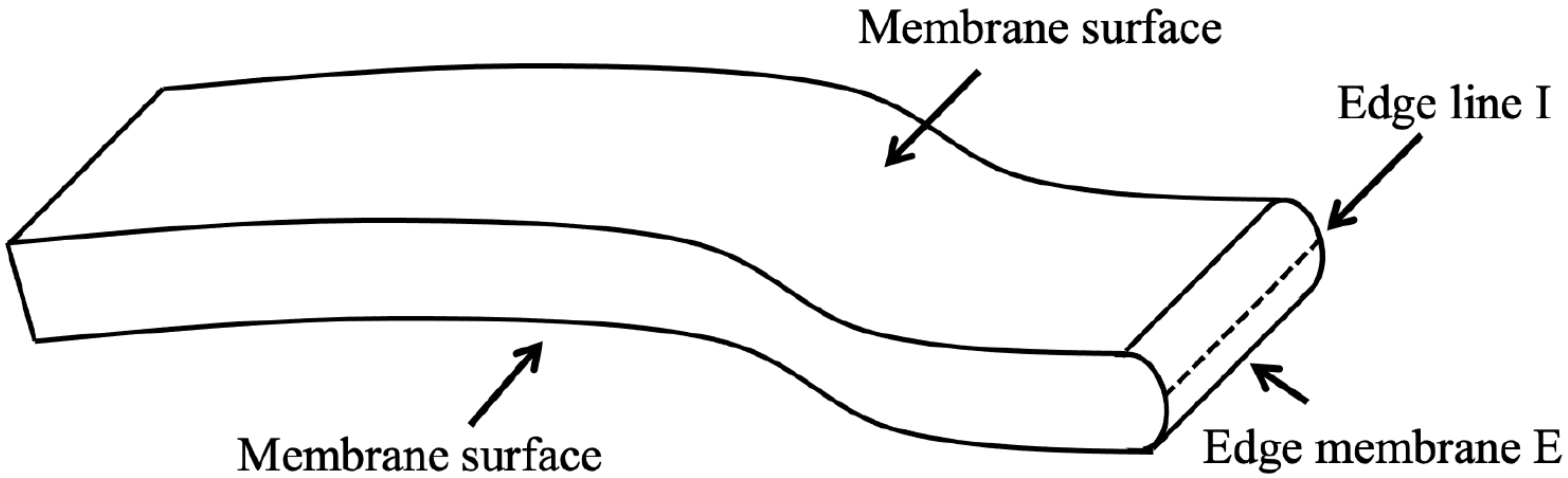


(a) and (b) show two different view angles of a 3D reconstructions of stacked ER sheets.

(c) Construction process of a helicoid from a helix by drawing lines (blue lines) perpendicular to the axis (black line) through the helix (grey curve).

(d) a 3D helicoid shape.

The ER model of Terasaki et al.



Sketch of an ER membrane

The model has three contributions to the energy:

(i) Elastic bending energy of the sheet edges. This is modeled by

$$F_e = \frac{1}{2}\kappa_e \int_I (\zeta + |\zeta_s|^2) ds$$

where ζ is the edge line curvature, and ζ_s and $\kappa_e > 0$ are constant "target" curvature and edge line bending modulus, respectively. Integration is done over the edge line I.

(ii) Elastic bending of the edge line surface. This is modeled by

$$F_s = \frac{1}{2}\kappa \int_S J^2 dA \qquad \text{(Willmore energy)}$$

where J is the mean curvature of the edge line surface and $\kappa > 0$ is the membrane bending modulus. Integration is performed over the area of the sheet surface S.

(iii) Restriction of sheet expansion is taken account by a lateral pressure acting along the sheet edge E with corresponding energy

$$F_P = \int_E P dA$$

The pressure P is assumed to be independent of the membrane edge line I and surface S.

Consider for simplicity only one connection between the sheets, consisting of an internal edge E surrounded by a sheet surface. Thus, the total energy is given by $F_e + F_S + F_P$ and minimized when

$$\begin{aligned} \zeta &= -|\zeta_S| < 0 \\ J &= 0 \end{aligned}$$

Hence, ζ becomes the signed curvature with negative sign indicating that the edge is interior to the sheet surface.

Since we have taken ζ_S a constant, the desired surface is one of mean curvature $= 0$ and edge curvature a negative constant; i.e., helicoid[4]. This helicoid assumption of ER was derived by Terasaki et al. and is remarkably consistent with their experimental observations. But examination of their experimental photograph shows that not surprisingly the experimental results are rough approximations to helicoids. This suggests the following albeit mathematical conjecture that geometric information from the helicoid is encoded in the ER surface that allows nature to produce approximate helicoidal surfaces.

Recall a helicoid has the parametric representation

$$(r_1(x,y), r_2(x,y), r_3(x,y)) = (y\sin(x), y\cos(x), cx)$$

Where $-\infty < y < \infty$, $-\infty < x < \infty$, and c is a constant. In our case we want a helicoid with an internal edge and hence if we take $-\infty < y \leq y_0 < 0$, the edge line is internal to the helicoid with

$$\frac{|y_0|}{y_0^2 + c^2} = |\zeta_S|$$

Distances on the helicoid are given by the incremental relation (first fundamental form)

$$ds^2 = Edx^2 + 2Fdxdy + Gdy^2$$

with

$$E(y) = c^2 + y^2, \quad F \equiv 0, \quad G \equiv 1$$

with associated Gaussian curvature

$$K(y) = -\frac{c^2}{(c^2 + y^2)^2} < 0.$$

Alternatively,

$$ds^2 = g_{ij} dx^i dx^j, \quad 1 \leq i, j \leq 2$$

with $g_{11} = E$, $g_{12} = F$, $g_{22} = G$, $x^1 = x$, $x^2 = y$.

To find such a surface denoted again by $(r_1(x,y), r_2(x,y), r_3(x,y)) = \boldsymbol{r}(x,y)$ will have to satisfy the incremental relation

$$\partial_i \boldsymbol{r} \cdot \partial_j \boldsymbol{r} = g_{ij}$$

for $-\infty < x = x^1 < \infty$, $y_1 < y = x^2 < y_0 < 0$ where $\boldsymbol{r}(x, y_1)$ is a prescribed non-helical external edge.

This is the equation for isometric embedding of a two dimensional Riemannian manifold (M, g) into $\mathbb{R}^3$ (three dimensional Euclidean space). Thus, we have placed our non-helicoidal surface in the framework of a two-dimensional Riemannian manifold.

For a two-dimensional surface $\boldsymbol{r}$ embedded in $\mathbb{R}^3$, we have tangent vectors $\partial_1 \boldsymbol{r}$, $\partial_2 \boldsymbol{r}$ which in turn define the unit normal $\boldsymbol{n}$ to the surface.

$$\boldsymbol{n} = \frac{\partial_1 \boldsymbol{r} \times \partial_2 \boldsymbol{r}}{|\partial_1 \boldsymbol{r} \times \partial_2 \boldsymbol{r}|}$$

Define second fundamental form h_{ij} by

$$h_{ij} = \partial_{ij} \boldsymbol{r} \cdot \boldsymbol{n}$$

where clearly $h_{ij} = h_{ji}$.

The fundamental theorem of surface theory asserts a necessary condition for a smooth embedding of a two-dimensional Riemannian manifold (M, g) in $\mathbb{R}^3$ is that the second fundamental form satisfies the Gauss equation

$$h_{11}h_{22} - h_{12}h_{21} = (\det g)K$$

and the Codazzi equations

$$\begin{aligned}
\partial_2 h_{11} - \partial_1 h_{12} &= h_{11}\Gamma^1_{12} + h_{12}(\Gamma^2_{12} - \Gamma^2_{11}) - h_{22}\Gamma^2_{11} \\
\partial_2 h_{12} - \partial_1 h_{22} &= h_{11}\Gamma^1_{22} + h_{12}(\Gamma^2_{22} - \Gamma^2_{21}) - h_{22}\Gamma^2_{21}
\end{aligned}$$

Here Γ^i_{jk} are the Christoffel symbols given by

$$\Gamma^i_{jk} = \frac{1}{2}g^{i\ell}\{\partial_j g_{k\ell} + \partial_k g_{\ell j} - \partial_\ell g_{jk}\}$$

$g^{-1} = \{g^{ij}\}$. Here again the Einstein summation convention is used.

Our interest lies in the fact the Gauss–Codazzi system when satisfied is also a sufficient condition for isometric embedding of (M, g) into $\mathbb{R}^3$. In particular, the following generalization of the classical smooth embedding theory to "rough" embeddings will be the key.

Theorem (Mardare, 2003) For (x^1, x^2) in a connected and simply-connected open subset Ω of $\mathbb{R}^2$. Assume first and second fundamental forms g_{ij}, k_{ij} with $g_{ij} \in W^{1,\infty}_{loc}(\Omega)$, $h_{ij} \in L^{\infty}_{loc}(\Omega)$ satisfy the Gauss–Codazzi system in the sense of distributions. Here $W^{p,q}$ denotes the usual Sobolev spaces. Then, there exists an embedding $\boldsymbol{r} \in W^{2,\infty}_{loc}(\Omega) \subset C^{1,1}_{loc}(\Omega)$ such that the Gauss–Codazzi equations are satisfied almost everywhere in Ω.

Set $K(y) = -\gamma^2(y) < 0$, $u = -\frac{h_{12}}{h_{11}}$, $v = \frac{\gamma}{h_{11}}$.

Theorem (Cao, Huang, Wang, ARMA 2015). For any given $y_1 < 0$ let the initial data $u(x, y_1)$,$v(x, y_1)$ satisfy

$$u(x, y_1) + v(x, y_1) \quad \textit{bounded}, \quad u(x, y_1) - v(x, y_1) \quad \textit{bounded},$$

and

$$\inf_{x\in\mathbb{R}} (u(x, y_1) + v(x, y_1)) > 0, \quad \sup_{x\in\mathbb{R}} (u(x, y_1) - v(x, y_1)) < 0,$$

or

$$\sup_{x\in\mathbb{R}} (u(x, y_1) + v(x, y_1)) < 0, \quad \inf_{x\in\mathbb{R}} (u(x, y_1) - v(x, y_1)) > 0.$$

Then, for $\Omega = \{(x, y); -\infty < x < \infty, y_1 < y < y_0 < 0\}$ there is distributional (weak) solution of the Gauss–Codazzi system where g is the helicoidal metric. Furthermore, Mardare's theorem yields an isometric embedding $\boldsymbol{r} \in W^{2,\infty}_{loc}(\Omega) \subset C^{1,1}_{loc}(\Omega)$.

References

- Wentao Cao, Feimin Huang, and Dehua Wang. Isometric immersions of surfaces with two classes of metrics and negative Gauss curvature. Archive for Rational Mechanics and Analysis, 218(3):1431–1457, 2015.

- A. L. Hodgkin and A. F. Huxley. A Quantitative Description of Membrane Current and Its Application to Conduction and Excitation in Nerve. Journal of Physiology, 117:500–544, 1952.

- Wallace F Marshall. Differential geometry meets the cell. Cell, 154(2):265–266, 2013.

- Matan Mussel and Matthias F. Schneider. It sounds like an action potential : on the electrical and pH aspects of acoustic pulses in lipids. Journal of The Royal Society Interface, 16:20180743, 2019.

- Matan Mussel and Matthias F. Schneider. Similarities between action potentials and acoustic pulses in a van der Waals fluid. Scientific Reports, 9(1):2467, 2019.

- Matan Mussel and Matthias F. Schneider. Sound pulses in lipid membranes and their potential function in biology. Progress in Biophysics and Molecular Biology, in press, 2020.
- Shamit Shrivastava and Matthias F. Schneider. Evidence for two-dimensional solitary sound waves in a lipid controlled interface and its implications for biological signalling. Journal of The Royal Society Interface 11(97):20140098, 2014.
- Mark Terasaki, Tom Shemesh, Narayanan Kasthuri, Robin W Klemm, Richard Schalek, Kenneth J Hayworth, Arthur R Hand, Maya Yankova, Greg Huber, Jeff W Lichtman, and Others. Stacked endoplasmic reticulum sheets are connected by helicoidal membrane motifs. Cell, 154(2):285–296, 2013.
- Toda, M., Athukoralage, B. (2013), Geometry of biological membranes and Willmore energy,*AIP Conf. Proc. of American Institute of Physics*, 1558 (2013), no.1, 887, pp 5; http://scitation.aip.org/content/aip/proceeding/aipcp/10.1063/1.4825638
- Toda, M., Athukoralage, B. , Geometry of biological membranes and Willmore energy. Preprint