# Dissipation of the Excitation Wave Fronts

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An excitation wave in cardiac tissue will fail to propagate if the transmembrane voltage at its front rises too slowly and does not excite the tissue ahead of it. Then the sharp voltage profile of the front will dissipate, and the subsequent spread of voltage will be purely diffusive. This mechanism is impossible in FitzHugh-Nagumo type systems. Here a simplified mathematical model for this mechanism is suggested. The model has exact traveling front solutions, and gives conditions for the front dissipation. In particular, a front will dissipate if it is not allowed to propagate faster than a certain nonzero speed. This critical speed depends only on the properties of the fast sodium current.

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*Introduction.*—Fifty years ago, Hodgkin and Huxley proposed a mathematical model of the electric action of the giant squid axon [1]. It spawned a large family of models describing other biophysical phenomena, e.g., excitability of heart muscle. These models are rather complicated [see (4)] and are mostly treated numerically.

FitzHugh [2] and Nagumo *et al.* [3] suggested a simplified analog of the Hodgkin and Huxley (HH) equations:

$$\begin{aligned} \partial_t E &= \partial_x^2 E + \epsilon_E(E - E^3/3 - v), \\ \partial_t v &= \epsilon_v(E + \beta - \gamma v), \end{aligned} \tag{1}$$

where $E$ corresponds to the transmembrane voltage [4] and $v$ represents all other, slow variables. FitzHugh has shown that an appropriate two-dimensional projection of the "phase portrait" of the HH model looks "similar" to that of (1), and Nagumo *et al.* have demonstrated that it describes propagating pulses similar to those in HH. This model is much simpler than the HH-type systems, and allows a great deal of analytical and qualitative study.

Throughout these 40 years, the FitzHugh-Nagumo (FHN) system and its modifications served well as simple but reasonable models of excitation propagation in nerve, heart muscle, and other biological excitable media.

In this paper, we discuss a phenomenon in biophysically detailed models, which cannot be adequately reproduced in any FHN-type system. This is *dissipation of the excitation wave fronts,* a specific mechanism of propagation block when the sharp gradient of the transmembrane voltage at the wave front smears out and the spread of voltage becomes diffusive, as the main excitation current gets inactivated. This phenomenon, although seen by physiologists and researchers working with detailed models, has not been identified so far as deserving special attention and is understandable in terms of simplified models. Understanding the mechanisms of propagation blocks in heart tissue is of enormous practical importance, as it is thought to be a major factor of cardiac arrhythmias (see [5] as an example of a recent study).

*Two different mechanisms of propagation block.*—A typical scenario of propagation block in heart is that an excitation propagates where the tissue has not fully recovered after the previous wave, and a recovery wave moves before the new excitation wave. If the recovery wave is slower than the excitation wave, the latter runs into more and more unfavorable conditions and may eventually fail to propagate at all. This happens differently in realistic models and in FHN-type caricatures. Figure 1 illustrates this using an ultimate idealization of the excitability completely but temporarily suppressed in a part of the medium. The illustrations are for two models, the detailed model of human atrial tissue by Courtemanche *et al.* [7] (CRN) and for the FHN system (1). In the CRN model, when the propagation stops, the wave fronts dissipate. When the conditions for propagation are restored, the excitation wave does not resume, as the sharp increase in the voltage necessary to trigger such

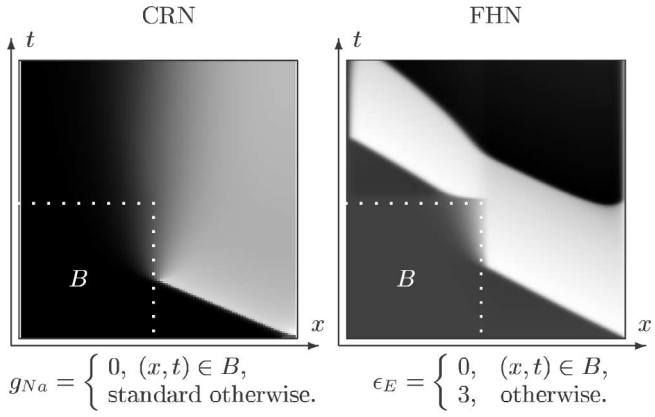


FIG. 1. Temporary local block of propagation: excitability is suppressed for $(x, t) \in B = (0, x_b) \times (0, t_b)$ (shown by the white dots) [6]. Here and below, solutions shown as density plots, where black is the smallest and white is the largest value of $E$ within the solution. In CRN, time range 80 ms, space range 50 s.u. [4], all the kinetic parameters as in [7]. In FHN, time range 50, space range 50, $\beta = 0.75$, $\gamma = 0.5$, $\epsilon_v = 0.03$.

  

a wave is not present. Subsequent spread of the voltage is purely diffusive. In the FHN system, the high voltage at the front itself is enough to excite new cells if other conditions are right again, so the excitation front can propagate with arbitrarily slow speed or even stop, without dissipation. When propagation conditions are restored, the excitation wave resumes the propagation, even though the voltage profile in the unexcitable region has been smeared out.

The FHN wave will not resume propagating only if the block lasts longer than the action potential, so the back of the wave reaches the block site. In contrast, the CRN wave loses the ability to propagate within milliseconds, long before the end of the action potential.

*Excitation fronts in FHN-type systems do not dissipate.*—If $\epsilon_v \ll \epsilon_E$, system (1) belongs to a class of systems

$$\partial_t E = \partial_x^2 E + f(E, v), \qquad \partial_t v = \epsilon g(E, v), \qquad 0 < \epsilon \ll 1, \tag{2}$$

($v \in \mathbb{R}^m$, $m \geq 1$), for which the asymptotic theory developed in the 1970s and 1980s (see, e.g., [8–11]) can be applied. In a relevant region of $v$, function $f(E, v)$ is assumed to have three simple roots in $E$, $E_-(v)$ (recovery) $< E_*(v)$ (threshold) $< E_+(v)$ (excitation), where recovery and excitation are stable, $\partial_E f(E_\pm(v), v) < 0$, and the threshold is unstable, $\partial_E f(E_*(v), v) > 0$. Propagation of fronts and backs of excitation waves in the limit $\epsilon \to +0$ is described by trigger waves in the first of the Eqs. (2) with $v = \text{const}$ between $E_-(v)$ and $E_+(v)$ with a speed which is a function of $v$, $c = c(v)$. The sign of $c(v)$ coincides with the sign of $\int_{E_-(v)}^{E_+(v)} f(E, v)dE$ and thus may change as $v$ changes, i.e., a wave front may stop and reverse to become a wave back. The motion of the wave front/wave back on the large scale is described by an ordinary differential equation

$$dX/dt = -c(v(X, t)) = -C(X, t). \tag{3}$$

In any case, as long as the excitability stays, the sharp structure of the front is preserved; i.e., it does not dissipate.

*Constructing the simplified model of the excitation front.*—The Hodgkin-Huxley–type models are fairly similar in the part that interests us; for definiteness, we refer to the original model [1],

$$\begin{aligned} \partial_t E &= \partial_x^2 E + g_{\mathrm{Na}}(E_{\mathrm{Na}} - E)m^3 h + g_{\mathrm{K}}(E_{\mathrm{K}} - E)n^4 \\ &\quad + g_l(E_l - E), \\ \partial_t m &= [\overline{m}(E) - m]/\tau_m(E), \\ \partial_t h &= [\overline{h}(E) - h]/\tau_h(E), \\ \partial_t n &= [\overline{n}(E) - n]/\tau_n(E), \end{aligned} \tag{4}$$

where $E$ is the transmembrane voltage [4], $g_{\mathrm{Na,K},l}$ are maximal conductivities per membrane capacitance of Na, K, and leakage currents, $E_{\mathrm{Na,K},l}$ are their reversal potentials, $m$, $h$ and $n$ are fractions of open channel gates, $\overline{m}, \overline{h}, \overline{n}$ are their equilibria, and $\tau_{m,h,n}$ are their time scales.

On the front, $E$ is rapidly raised by two large currents, the Na current and the intercellular current described by the diffusion term. Elsewhere, $E$ is changed only by the smaller currents. To describe the front only, we consider the limit of large $g_{\mathrm{Na}}$, and disregard all ionic currents but Na. Thus, only $m$ and $h$ which are responsible for the Na current remain, while $n$, as well as many other variables in more complicated models, become irrelevant.

Values of $\tau_m(E)$ at the front are very small compared to other characteristic time scales of the problem. Thus $m$ is always close to its quasistationary value $\overline{m}(E)$. The differential equation for $m$ is therefore eliminated.

Thus we get a system of two equations,

$$\begin{aligned} \partial_t E &= \partial_x^2 E + I_{\mathrm{Na}}(E)\overline{m}^3(E)h, \\ \partial_t h &= [\overline{h}(E) - h]/\tau_h(E), \end{aligned} \tag{5}$$

where $I_{\mathrm{Na}}(E) = g_{\mathrm{Na}}(E_{\mathrm{Na}} - E)$. This system is intended to describe the propagation of the excitation front (the fast process) only, leaving all other processes, such as action potential and recovery (the slow processes), out of the scope. Compared to the FHN model, this system plays the same role as the first equation in (2), but here we do not assume $h$ to be much slower than $E$, thus two fast equations in place of one.

So far we exploited small parameters available in the model, and (5) can be expected to be in a reasonable quantitative agreement with the full system. Further simplifications are based on qualitative considerations, and do not claim to produce quantitative results. We note that $\overline{m}(E)$ and $\overline{h}(E)$ are steplike functions, taking values either close to 0 or close to 1 (see Fig. 2). Thus we replace them with

$$\overline{m}(E) = \theta(E - E_m) = \overline{m}^3(E), \qquad \overline{h}(E) = \theta(E_h - E),$$

where $\theta(a)$ is the Heaviside step function.

Further, we replace $\tau_h(E)$ and $I_{\mathrm{Na}}(E)$ by constants as their dependence on $E$ is not essential here. So, growth of $E$ stops when $h$ or $m$ close down, not when $E$ reaches $E_{\mathrm{Na}}$, and the maximal voltage in a front is usually significantly lower than $E_{\mathrm{Na}}$ (in CRN, by more than 60 mV).

After scaling $E$ so that $E_h = 0$ and $E_m = 1$, and $t$ so that $I_{\mathrm{Na}} = 1$ [4], we finally obtain the system

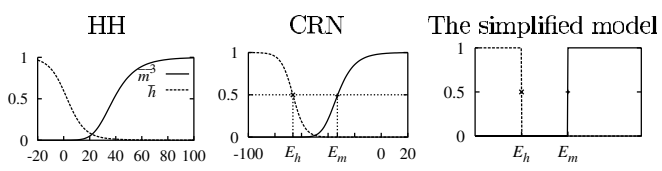


FIG. 2. Dependence of $\overline{m}^3(E)$ and $\overline{h}(E)$ for the Hodgkin-Huxley (HH) (4) [1] and Courtemanche *et al.* (CRN) [7] detailed models and for the proposed simplified model (5).

$$\partial_t E = \partial_x^2 E + \theta(E-1)h, \qquad \partial_t h = [\theta(-E) - h]/\tau, \tag{6}$$

depending on one dimensionless parameter, $\tau$.

Spatially homogeneous equilibria here are not isolated, but form two continua, $(E, h) \in (-\infty, 0) \times \{1\} \cup (0, +\infty) \times \{0\}$. This is due to a disregard of the small ionic currents and the idealization of Na gates as perfect switches. This means that $E$ will remain constant (in reality, slowly vary) as long as the Na channels are closed [12].

*The traveling front solutions.*—A front propagating leftwards with speed $c$ satisfies

$$\begin{aligned} &cE' = E'' + \theta(E-1)h, \qquad ch' = [\theta(-E) - h]/\tau, \\ &E(-\infty) = -\alpha < 0, \qquad E(+\infty) = \omega > 1, \\ &h(-\infty) = 1, \qquad h(+\infty) = 0. \end{aligned} \tag{7}$$

We choose the phase of the front so that $E(0) = 0$, denote $x_1 > 0$ the point where $E(x_1) = 1$, and require that $E(x) \in C^1$ and $h(x) \in C^0$, which implies obvious internal boundary conditions at $x = 0$ and $x = x_1$.

This problem has a family of solutions depending on one parameter, the prefront voltage $\alpha$ (see Fig. 3):

$$\begin{aligned} E(x) &= \begin{cases} -\alpha + \alpha e^{cx} & (x \le x_1), \\ \omega - \frac{\tau^2 c^2}{1+\tau c^2} e^{-x/(\tau c)} & (x \ge x_1), \end{cases} \\ h(x) &= \begin{cases} 1 & (x \le 0), \\ e^{-x/(\tau c)} & (x \ge 0), \end{cases} \end{aligned} \tag{8}$$

where $\omega = 1 + \tau c^2(\alpha + 1)$, $x_1 = \frac{1}{c}\ln(\frac{1+\alpha}{\alpha})$ and $c$ is an implicit function of $\tau$ and $\alpha$,

$$\tau c^2 \ln\left(\frac{(1+\alpha)(1+\tau c^2)}{\tau}\right) + \ln\left(\frac{\alpha+1}{\alpha}\right) = 0. \tag{9}$$

Note that here the postfront voltage $\omega$ depends on $\tau$; this is different from the FHN-type systems where it depends only on the right-hand sides of the equation for $E$.

*Properties of the speed equation.*—Equation (9) is equivalent to the equation of level curves $\ln\tau = g(\beta, \sigma)$ of the function $g(\beta, \sigma) \equiv \ln(1+\sigma) - \ln(1-\beta) - \sigma^{-1}\ln\beta$, where $\sigma = \tau c^2$, $\beta = \alpha/(\alpha+1)$, $(\beta, \sigma) \in S = (0, 1) \times (0, +\infty)$. It can be seen that (i) For every fixed $\beta$, $\partial g/\partial\sigma$ changes sign once as $\sigma$ runs through $(0, +\infty)$. (ii) $g(\beta, \sigma)$ has a local minimum $\sigma_* \approx 1.536\,59\ldots$, $\beta_* \approx 0.394\,23\ldots$, $g_* \approx 2.0378\ldots$, which is its only critical point in $S$. (iii) Function $g(\beta, \sigma)$ has the following lower bounds

$$\begin{aligned} &g(\beta, \sigma) > \ln[\ln(1/\beta)], \qquad g(\beta, \sigma) > \ln[1/(1-\beta)], \\ &g(\beta, \sigma) > \ln(1/\sigma), \qquad g(\beta, \sigma) > \ln\sigma, \qquad \forall\ (\beta, \sigma) \in S. \end{aligned}$$

Using [13], we deduce that for every $C > g_*$, the set $g(\beta, \sigma) = C$ is a simple closed curve, crossing each line $\beta = \text{const}$ at most twice, and $(\beta_*, \sigma_*)$ is a global minimum in $S$. A selection of level curves is shown in Fig. 4.

Thus, for every $\tau > \tau_* = e^{g_*} \approx 7.6740\ldots$, there exists a range of prefront voltages $0 < \alpha_{\min}(\tau) < \alpha < \alpha_{\max}(\tau) < +\infty$, for each of which there are two propagating front solutions (8) with different speeds, and all speeds possible at various prefront voltages span an interval $0 < c_{\min}(\tau) \le c \le c_{\max}(\tau) < +\infty$. Explicit estimates can be obtained in the limit of large $\tau$, e.g.,

$$c_{\min} = e^{1/2}\tau^{-1} + 0.75e^{3/2}\tau^{-2} + O(\tau^{-3}). \tag{10}$$

Existence of a minimal propagation speed implies that the excitation front cannot be stopped or reversed, and is therefore crucial for the phenomenon of front dissipation.

*Some numerical results.*—For every admissible pair of $\tau$ and $\alpha$, except the marginal values of $\alpha$, Eq. (9) gives two values of the speed $c$. Numerical experiment suggests that the faster fronts are stable, and the slower fronts are unstable and either dissipate or develop into the faster solutions (see Fig. 5). This conjecture requires a further investigation.

Figure 6 shows results of computations of (6) with a temporary local excitability block as in Fig. 1. As front propagation is possible if $\tau > \tau_* \approx 7.674$, the block was simulated by a decrease of $\tau$ below this threshold. The front dissipated as soon as it reached the blocked region. When excitability in that region was restored, the front did not resume but continued to spread diffusively. So, the new model behaves similarly to the detailed equations and is different from the FHN model.

*Conclusions.*—Fronts of excitation waves in realistic models of cardiac tissues cannot be stopped or reversed. If they are not allowed to propagate, they dissipate. This is different from FHN-type caricatures, where fronts can

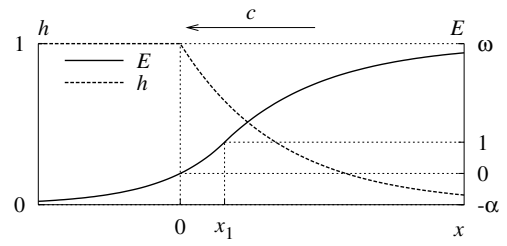


FIG. 3. A propagating front solution (8) and (9) ($\tau = 8$, $\alpha = 1$, $c \approx 0.444$).

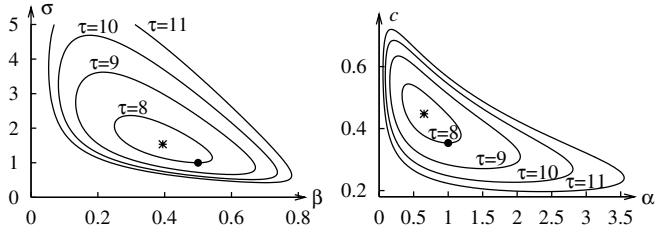


FIG. 4. Prefront voltage vs front speed for a selection of values of $\tau$ (labels on the curves), in $(\beta, \sigma)$ coordinates, and in the original $(\alpha, c)$ coordinates. ( • ): exact solution $\beta = 0.5$, $\sigma = 1$, $\tau = 8$. ( * ): the minimum of $\tau$: $\beta_* \approx 0.394$, $\sigma_* \approx 1.537$, $\tau_* \approx 7.67$.

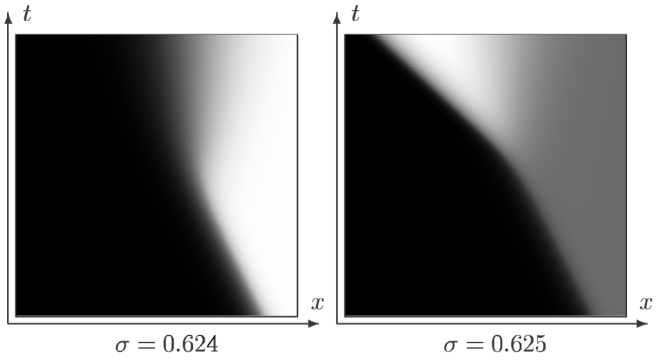


FIG. 5. Solutions of (6) with initial conditions (8), for $\tau = 10$, $\alpha = 1$ and $\sigma$ close to the low speed solution of (9). Space range is 100, and time range is 200. Depending on minute details, the slow front either dissipates or develops into the faster front, corresponding to $\sigma \approx 2.955$.

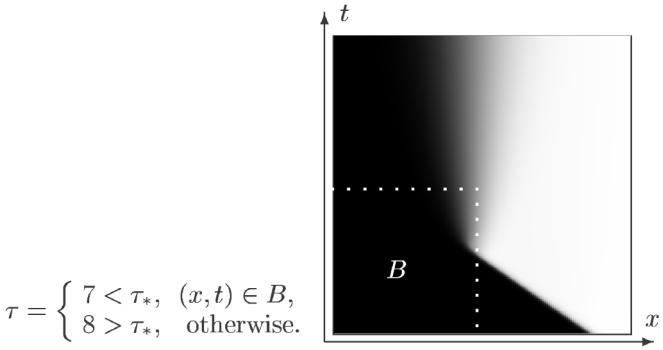


FIG. 6. Temporary local block ($B$, white dots) of the excitation front in the simplified model (6), as in Fig. 1. Front propagation did not resume after the excitability has been restored. Initial conditions (8) with $\tau = 8$, $\alpha = 1$, $c = 0.444$. Time range 1000, space range 300.

slow down indefinitely, or reverse and turn into wave backs. Local propagation blocks can break excitation waves and are essential in fibrillation. An established belief, based on FHN-type models and exemplified by [5], is that a wave break happens when the wave back catches up with the wave front and the length of the excitation wave becomes zero. As we now see, in realistic models the wavelength is irrelevant, and whether or not the wave breaks is decided exclusively by events in its front.

The proposed simplified model (6) captures the main features of realistic models responsible for the propagation and dissipation of the excitation fronts. The main qualitative predictions are the following: (i) Front parameters are determined by the prefront voltage. (ii) The range of prefront voltages at which propagation is possible is bounded from above and from below. (iii) The range of possible propagations speeds is bounded from above and from below. The boundedness of speed from below implies that an excitation front cannot be stopped or reversed, and is therefore crucial for the front dissipation.

Model (6) provides exact analytic solution for the front shape (8) and speed (9), and therefore conditions of front dissipation can be obtained, e.g., (10). For quantitative description, model (5) can be used instead [14], perhaps numerically, with possible exception of qualitative questions like boundedness of the speed spectrum. These models can serve as the fast subsystems in an asymptotic theory of the cardiac excitation waves, which is yet to be developed and to replace, in applications to cardiology, the asymptotic theory of FHN-type systems [8–11].

The key process in front dissipation is the closure of the slow Na gate $h$. Thus any asymptotic or simplified model intended to describe front propagation at low speed or its failure must take dynamics of $h$ into account, along with those of $E$. We now see that this is necessary even if the ratio of characteristic time scales of $E$ and $h$ is rather high, say, around 8.

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[14] Equation (5) does not have prefront ($h = 1$) and postfront ($h = 0$) steady states, so to describe fronts it needs a slight modification: $\overline{m}(E)$ is very small below some $E$, $\overline{h}(E)$ is very small above some $E$, and both are to be replaced by zero in those regions.