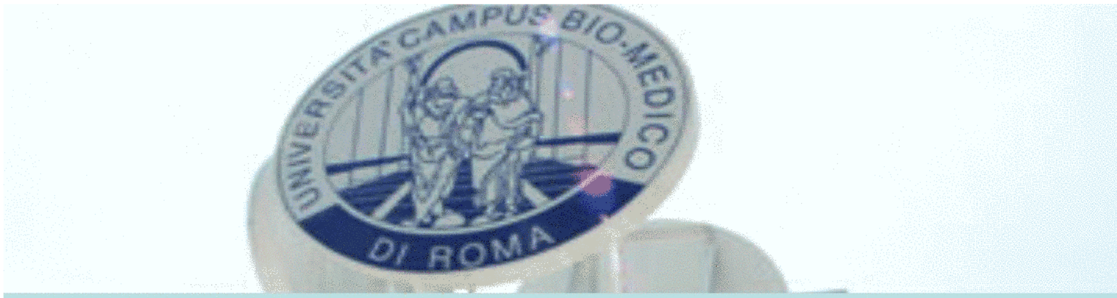

FitzHugh-Nagumo model with a) viscoelastic coupling b) thermal coupling

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AREA DI FISICA

a) An extended FitzHugh-Nagumo model including viscoelasticity is derived in general and studied in detail in the one-dimensional case.

- Bini et al. PHYSICAL REVIEW E **72**, 041929 (2005)

Newton's law for an isotropic solid medium with viscoelasticity in interaction with an electric field

(A. M. Kosevich, E. M. Lifshitz, L. D. Landau, and L. P. Pitaevskii, *Theory of Elasticity*, 3rd ed. 1986, Vol.7, E. M. Lifshitz, L. D. Landau, and L. P. Pitaevskii, *Electrodynamics of Continuous Media*, 2nd ed. 1984, Vol.8.)

$$\rho \frac{\partial^2 u_i}{\partial t^2} = \frac{\partial \sigma_{ik}}{\partial x_k},$$

$x_i' = x_i + u_i$,
u_i deformation

$$\sigma_{ik} = \sigma_{ik}^{(0)} + \sigma_{ik}'^{(0)} + \frac{2\varepsilon_0 - a_1}{8\pi} \mathcal{E}_i \mathcal{E}_k - \frac{\varepsilon_0 + a_2}{8\pi} \mathcal{E}_j^2 \delta_{ik},$$

$\mathcal{E}_i$ represents the electric field related to external potential via $\mathcal{E}_i = -\partial V / \partial x_i$.

$\sigma_{ik}^{(0)}$ stress tensor in absence of electric in teractions

$$\sigma_{ik}^{(0)} = \frac{E}{1+\lambda}\left(u_{ik} + \frac{\lambda}{1-2\lambda} u_{ll} \delta_{ik}\right),$$

λ is Poisson's co efficient

E Young modulus

$u_{ik} = \frac{1}{2}(\partial u_i / \partial x_k + \partial u_k / \partial x_i)$ (linear elasticity deformation tensor)

ε_0 dielectric permittivity

viscous contribution

$$\sigma_{ik}'^{(0)} = 2\eta\left(\frac{\partial u_{ik}}{\partial t} - \frac{1}{n}\delta_{ik}\frac{\partial u_{ll}}{\partial t}\right) + \zeta \frac{\partial u_{ll}}{\partial t}\delta_{ik},$$

dielectric tensor in terms of u_{ik},

$$\varepsilon_{ik} = \varepsilon_0 \delta_{ik} + a_1 u_{ik} + a_2 u_{ll} \delta_{ik}.$$

Diffusion coefficient in FitzHugh-Nagumo equations expanded analogously as the dielectric tensor

$$D_{ik} = D_0 \delta_{ik} + b_1 u_{ik} + b_2 u_{ll} \delta_{ik},$$

in viscoelastic Fitzhugh-Nagumo model,
contrac tion and extension of the medium backreacts with its electric properties.

ONE-DIMENSIONAL FIBER

Propagation of longitudinal compressional waves in the viscoelastic medium
Final form of equations for coupled interacting "electroviscoelastic signals"

$$\frac{\partial^2 w}{\partial \tau^2} - \frac{e_1^2}{\alpha^2}\frac{\partial^2 w}{\partial X^2} = s\frac{\partial^3 w}{\partial \tau \partial X^2} + e_2 \frac{\partial \mathcal{V}}{\partial X}\frac{\partial^2 \mathcal{V}}{\partial X^2}$$

$$\frac{\partial \mathcal{V}}{\partial \tau} = \mathcal{V}(1-\mathcal{V})(\mathcal{V}-\alpha) - \mathcal{U} + I_{\text{ext}} + \left[D + D_1 \frac{\partial w}{\partial X}\right]\frac{\partial^2 \mathcal{V}}{\partial X^2} + D_1 \frac{\partial \mathcal{V}}{\partial X}\frac{\partial^2 w}{\partial X^2}$$

$$\frac{\partial \mathcal{U}}{\partial \tau} = e_1(\mathcal{V} - a\mathcal{U} - \mathcal{V}_0)\,,$$

— mechanoelectric coupling

$X \in [0, L]$ $\qquad X' = X + w(\tau, X)$

Equations in dimensionless units: *w* =*deformation*, *V* =*membrane potential*, τ = *time*, *X* = *spatial coordinate*

PARAMETERS

$L = 5, \quad e_1 = 0.01, \quad \alpha = 0.1, \quad a = 2.5, \quad D = 1, \quad \mathcal{V}_0 = 0$

1) Free insulated fiber activated by an initial Gaussian distribution of action potential

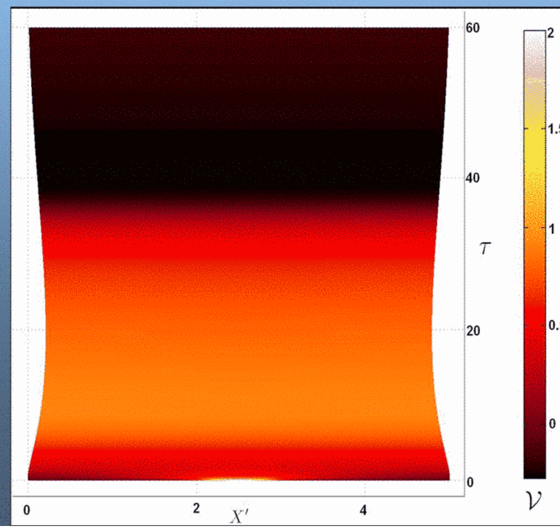
2) Clamped fiber stimulated by two counter phased currents, located at both ends of the space domain.

1) Free insulated fiber activated by an initial Gaussian distribution of action potential

Parameters: $D_1 = 1.5, \quad e_2 = 0.3, \quad s = 0.2, \quad I_{ext}=0$

initial data $w=\mathcal{U}=0$ and $\mathcal{V}=Je^{-r(X-L/2)^2}$ with $J=2$ and $r=5$.

Boundary conditions:
Neumann zero flux



Given a point X at $\tau=0$, its (adimensional) position during the dynamics will be $X'=X+w(\tau,X)$.

The Action potential in function of time in *X*=1,

- elastic case (dotted)
- nonelastic standard Fitzhugh-Nagumo (continuous curve)

Electrical activity is not affected by elasticity.

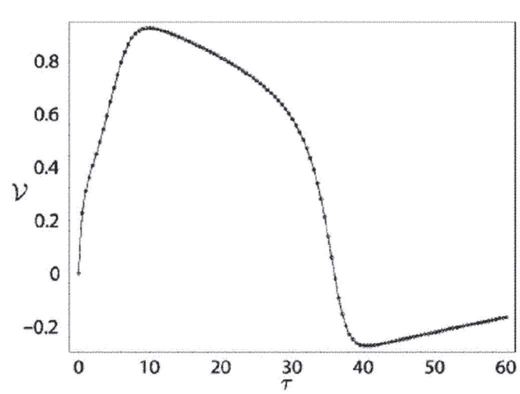


FIG. 3. Plot of the quantity $\mathcal{V}$ (the action potential) in function of τ taken in $X=1$, both in the elastic case (dotted) and the nonelastic one (continuous curve).

Dimensionless displacement *w* of the fiber's point initially located in *X*=1 in function of time.

As expected the point *X*=1 is pushed towards the center of the fiber and then comes back to its rest position when $w \to 0$ at late times.

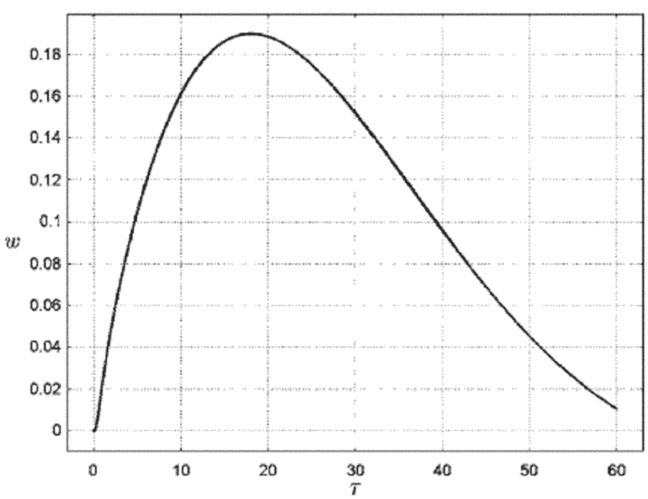


FIG. 4. Plot the adimensionalized displacement w of the point initially located in $X=1$ in a function of τ.

Clamped stimulated fiber

External currents:

$$I_{\text{ext}}(\tau,X) = B\sin(2\pi f\tau)e^{-\lambda X^2} + B\sin(2\pi f\tau+\phi)e^{-\lambda(X-L)^2}$$

$\phi=\pi, \quad \lambda=1000, \quad B=-30, \quad f=0.0125.$

$D_1=0.36, \quad e_2=-0.36, \quad s=0.9,$

The initial data are $\mathcal{U}=\mathcal{V}=w=0$ for $\tau=0$.

boundary conditions

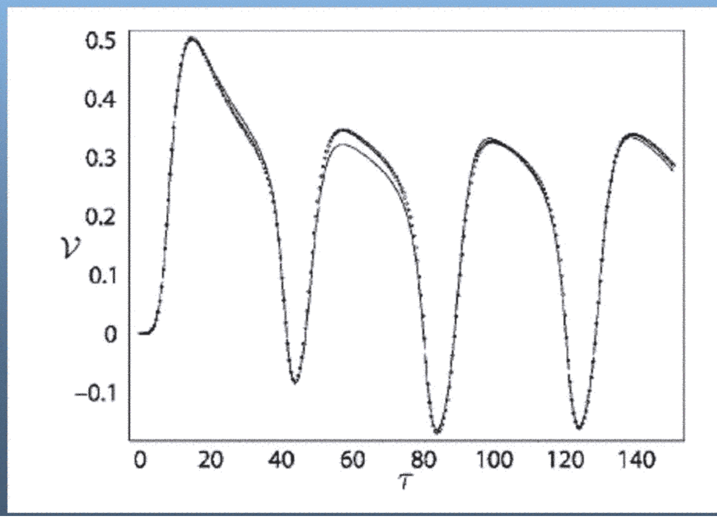
zero flux Neumann
for $\mathcal{U}$ and $\mathcal{V}$, i.e., $\partial\mathcal{U}/\partial X=\partial\mathcal{V}/\partial X=0$ both in $X=0$ and $X=L$.

null Dirichlet condition $w=\dfrac{\partial w}{\partial\tau}=0$ on the extremal points

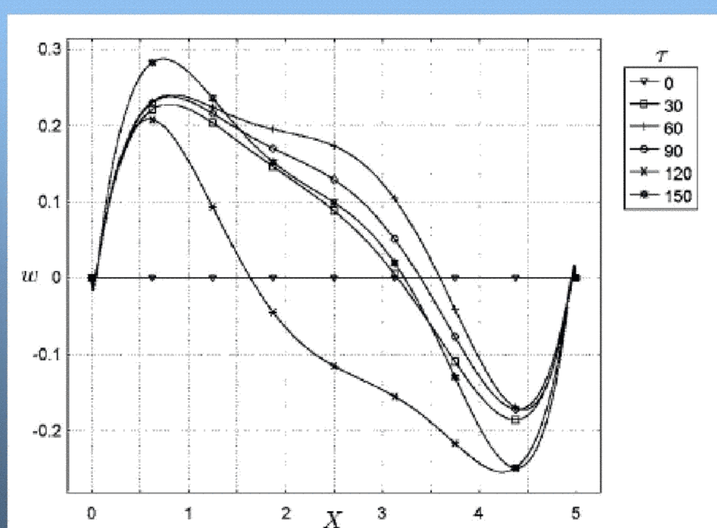
The action potential in function of time: the signal is taken in the center of the fiber.

- in the elastic case (dotted)
- the non-elastic (continuous curve).

Due to the strong external electrical stimulation, the action potential is modified with respect to the non-elastic case.

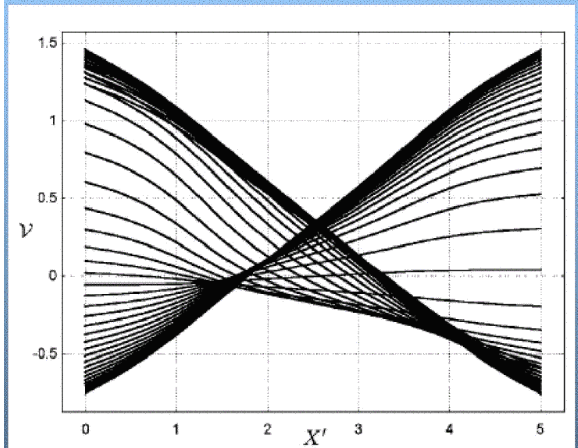


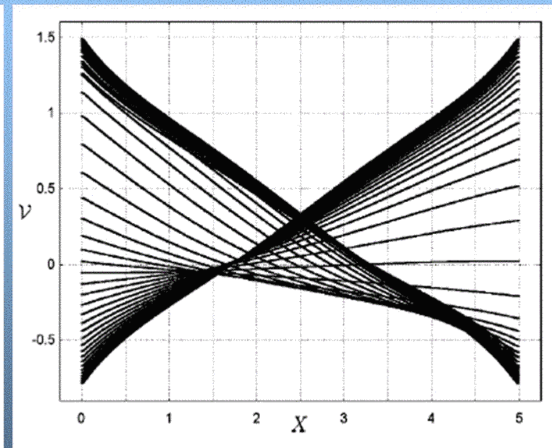
Plot of *w (deformation)* respect to *X*



The action potential in viscoelastic FHN with respect to *X'* at different values of time

The action potential in FHN with respect to *X* at different values of time





The central node (position and amplitude) unaffected by the elastic addition.
Slightly modified the behavior of the signals far from the center.

These results show that:

- Contraction is strongly affected by electrical activity
- The action potential does not backreact unless the fiber is strongly electrically stimulated.
- If one wants to change the nodal structure of two interacting external currents, it would require the use of the nonlinear elasticity theory (finite elasticity, additional nonlinear term) including density variations.

$$u_{ik}=\frac{1}{2}\left[\partial u_i/\partial x_k+\partial u_k/\partial x_i+(\partial u_l/\partial x_i)(\partial u_l/\partial x_k)\right].$$

Heat transfer in FitzHugh-Nagumo model

- Hodgkin and Katz 1949: on the global effects of temperature on the electrical activity of the giant axon of the squid.
- Abbott, Hill and Hovarth 1958: a single nerve impulse is closely associated with membranal temperature changes.
- Chapman 1967: experiments on the squid giant axon were performed to explore the effects of temperature on the conduction velocity of the action potential.
- Tasaki et al. 1989, 1992, 1999: the thermal response starts and reaches a peak on the order of some μ◦C nearly simultaneously with the electric response. The phase of heat production is followed immediately by the phase of heat absorption and no net heat release after passage of the action potential.

Pennes heat equation and Generalized FHN model

$$\underbrace{\nabla_i(k_{il}\nabla_l T)}_{\text{conduction}} + \underbrace{w_b c_b (T_a - T)}_{\text{perfusion}} + \underbrace{\sigma_{ik}\nabla_i V \nabla_k V + q_m}_{\text{heat sources/sinks}} = \underbrace{\rho c_p \partial_t T}_{\text{energy storage rate}}$$

For the giant squid axon modeled by HH, the perfusion term can be interpreted as the rate of heat transfer between a sea water-bath around the axon having temperature T_a and the axon itself. The quantity q_m is the metabolic heat term (which accounts for production and reabsorption of heat due to effects associated with the molecular structure of the cell), ρ is the tissue density, c_p is the heat capacity of the tissue and $\hat{\sigma} \equiv \sigma_{ik}$ is the electrical specific conductivity tensor (per unit volume), measured in $Siemens/m$.

Generalized FHN model

$$\frac{\partial v}{\partial \tau} = \frac{1}{\chi}\{D_1\nabla^2 v + (1+b\Theta)[\Sigma v(1-v)(v-\alpha)-w]-w_0\},$$

$$\frac{\partial w}{\partial \tau} = \frac{1}{\chi}3^{\Theta}\epsilon_{21}(v-v_0-\gamma w),$$

$$\frac{\partial \Theta}{\partial \tau} = \frac{1}{\chi}\{\epsilon_{24}\nabla^2\Theta + \epsilon_{25}\sigma_1\nabla v\cdot\nabla v - \epsilon_{23}(\Theta-\Theta_*)\}.$$

Typical choice of temperature independent FHN parameters

Parameter	Value
χ	1
D_1	1
b	0.6
Σ	1
α	0.1
γ	2
v_0	0
ϵ_{21}	0.005
ϵ_{23}	0.05
ϵ_{24}	10^{-7}
$\epsilon_{25}\sigma_1$	$5 \cdot 10^{-6}$
Θ_*	various choices

Elongated fiber

In order to simulate an axon as an elongated fiber, we have built a domain D of 200x1 space units. We have then implemented heat exchanges with the boundary. Zero flux boundary conditions have been imposed for:

$$\hat{n}\cdot\nabla v = \hat{n}\cdot\nabla w = 0, \qquad \vec{X} \in \partial\mathcal{D}$$

Dirichlet conditions on the boundary for:

$$\Theta = \Theta_*, \qquad \vec{X} \in \partial\mathcal{D},$$

(a thermostat is assumed to be located on D).

The initial data are $v(0,\vec{X}) = w(0,\vec{X}) = 0, \quad \Theta(0,\vec{X}) = \Theta_*.$

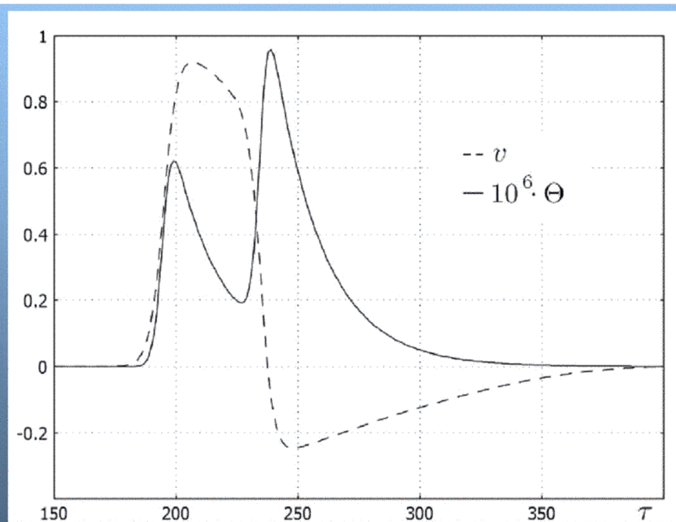
The action potential is initiated by a stimulus located at one extreme of the fiber, with a smooth Gaussian profile centered on it and damped in time,

$$w_0 = e^{-f(X-X_c)^2-g\tau^2}.$$

with $f = 1$, $X_c = 100$ and $g = 2$.

Thermal and electrical response

FIG. 1: Superimposed plots of the dimensionless action potential v and temperature Θ in function of dimensionless time τ taken in the center of the fiber, in the case of $T_* = 6.3°C$, $(\Theta_* = 0)$.

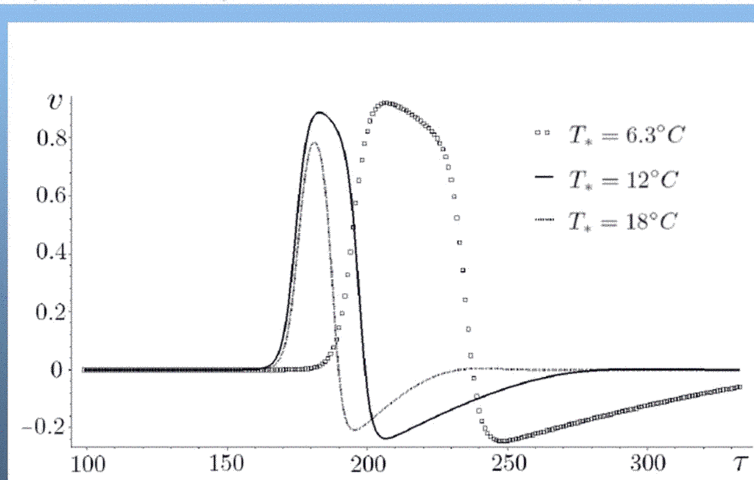


Due to heat coupling, a temperature gradient is associated with action potential propagation. As expected, the heat production and the following re-absorption is in phase with the action potential, in agreement with experiments.

Global effects of temperature on action potential

The effect of temperature on the action potential produced by a single current pulse is studied by setting the thermostat at different values of temperature.

$T_* = (6.3, 12, 18, 19)°C$, equivalent to $\Theta_* = (0, 0.57, 1.17, 1.27)$



J. Physiol. (1949) 109, 240–249 612.014.43:612.813

THE EFFECT OF TEMPERATURE ON THE ELECTRICAL ACTIVITY OF THE GIANT AXON OF THE SQUID

By A. L. HODGKIN and B. KATZ

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Experimental results

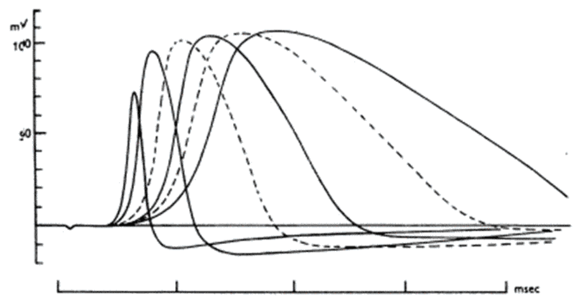


Fig. 4. Superimposed tracings of six spikes at the following temperatures: 32·5, 20·2, 13·3 (broken line), 9·8, 6·3 (broken line) and 3·6° C.

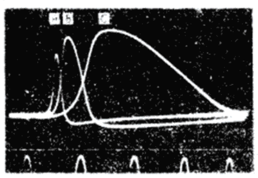
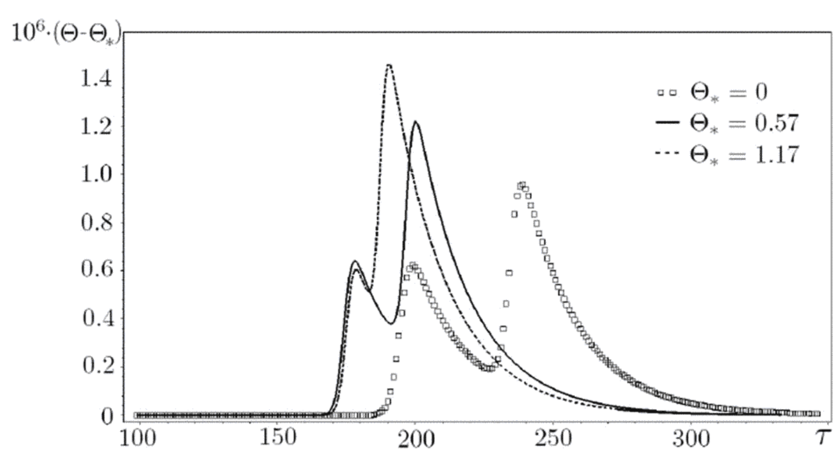
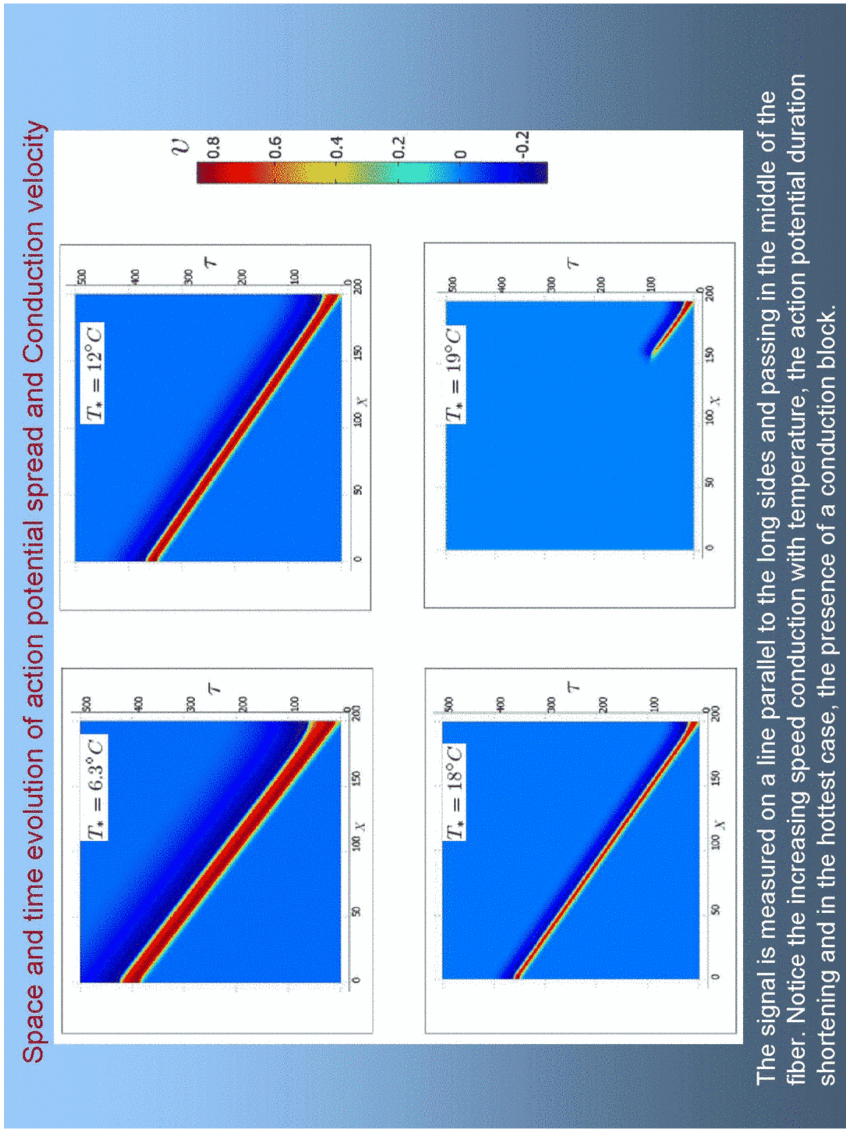


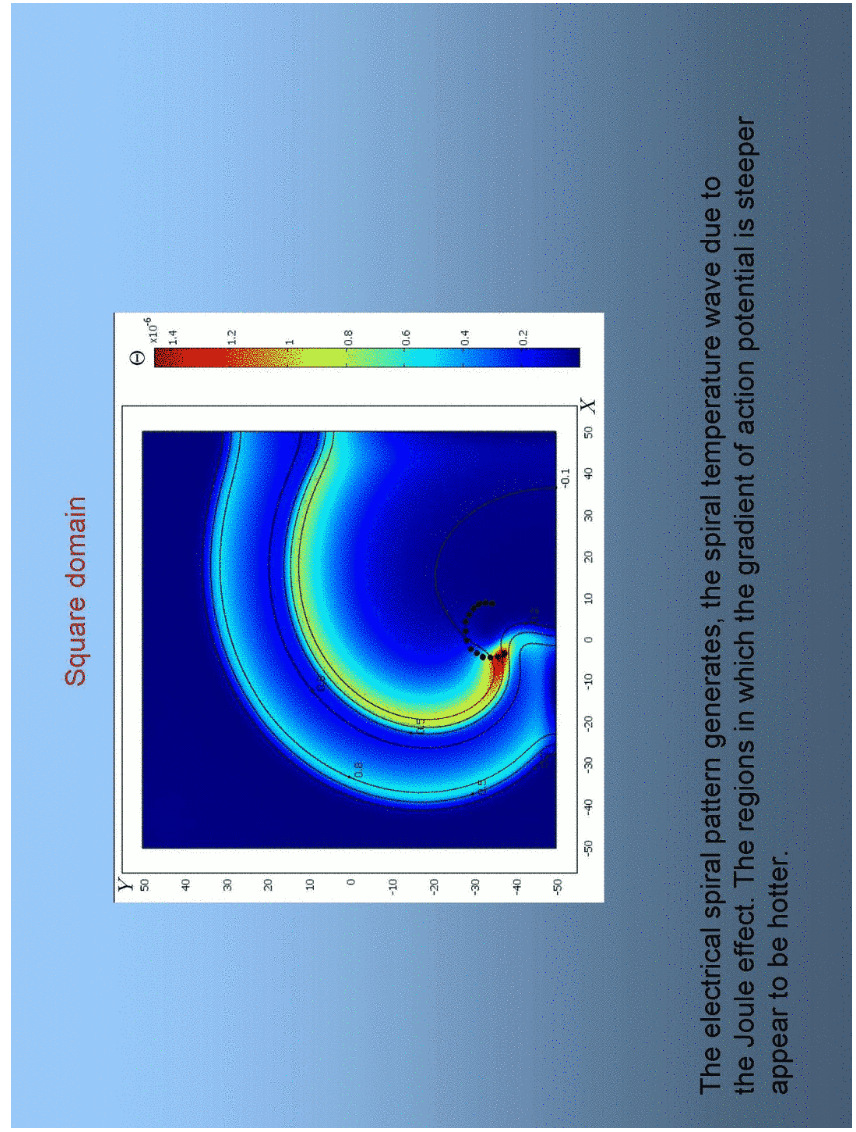
Fig. 3. Records of action potentials at three temperatures, superimposed on the same base-line and stimulus artefact. Temperatures and amplitudes, respectively: *A*, 32·5° C., 74·5 mV.; *B*, 18·5° C., 99 mV.; *C*, 5° C., 108·5 mV. Time marks: 1 msec.

Heat release and re-absorption

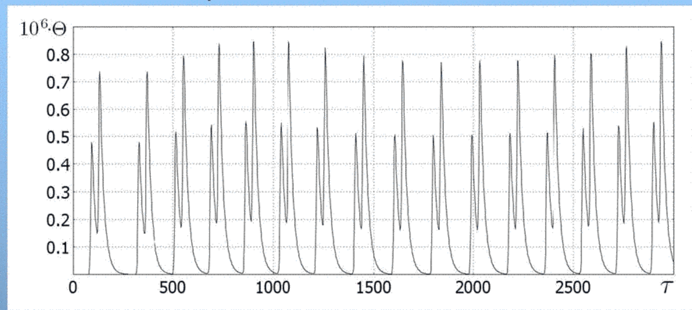


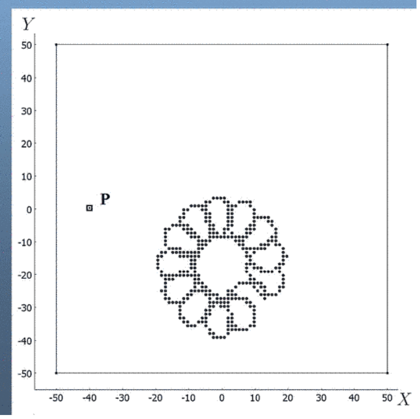
In Figure (4) we have plotted $\Theta - \Theta_*$ versus τ, taken in the center of the fiber, superimposed for the cases $T_* = 6.3°C, T_* = 12°C, T_* = 18°C$. As expected a traveling pulse of action potential, in the case of a thermostat temperature T_* in the range $T_* = 6.3°C - T_* = 18°C$, produces a corresponding temperature variation of $10 - 15\mu K$.


Space and time evolution of action potential spread and Conduction velocity
$T_* = 6.3°C$
$T_* = 12°C$
$T_* = 18°C$
$T_* = 19°C$
τ
X
v
The signal is measured on a line parallel to the long sides and passing in the middle of the fiber. Notice the increasing speed conduction with temperature, the action potential duration shortening and in the hottest case, the presence of a conduction block.


Square domain
Θ
X
Y
The electrical spiral pattern generates, the spiral temperature wave due to the Joule effect. The regions in which the gradient of action potential is steeper appear to be hotter.

A modulation effect in the temperature is present and this fact can be explained by spiral's tip meandering such that the spiral tip (the hotter area) can be far from or close to the observation point P.





SUMMARY

- APD shortening and AP amplitude decreasing as temperature is raised
- CV increasing with temperature
- Conduction block at sufficiently high temperature
- Heat release and re-absorption in phase with AP
- Temperature variation ~10 μ C