

CARDIAC ELECTRO-MECHANICS & MEF: THE STRESS-ASSISTED DIFFUSION 'SAD' APPROACH

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NONLINEAR PHYSICS AND MATHEMATICAL MODELING LAB WWW.MULTIPHYSICA.IT



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ACTIVE DEFORMABLE MEDIA

ELECTRO-ACTIVE POLIMERS (EAP)



Ion exchange resins



Multiple materials





ELECTRO-ACTIVE POLYMER (EAP) ARE BASED ON ION-EXCHANGE PROPERTIES OF RESINS

EAP ARE USED IN SEVERAL CHEMICAL & ROBOTIC APPLICATIONS - ARTIFICIAL MUSCLES



Electroactive Polymer (EAP) Actuators as Artificial Muscles Reserverses

ACTIVE DEFORMABLE MEDIA

BIOLOGICAL TISSUES





BIOLOGICAL ACTIVE TISSUES: HEART, SKELETAL MUSCLE, GASTRO-INTESTINE, EYE'S IRIS...

- SHOW THE ABILITY TO DEVELOP CONTRACTIONS, PRODUCING THE MECHANICAL FORCES NECESSARY TO THE ORGAN'S FUNCTION.
- CONTRACTIONS ORIGINATED BY AN ELECTRIC POTENTIAL DUE TO TRANSMEMBRANE (K-, NA-) AND INTRACELLULAR IONS (CA++)

EXCITATION-CONTRACTION

MACROSCOPIC CORRELATION BETWEEN:

Biophysical Motivation

- * THE 5 ECG PHASES
- * THETRANSMEMBRANE POTENTIAL
- * THE CONTRACTION WAVE FOR A MUSCULAR FIBER (CALCIUM)
- MICROSCOPIC RELATION BETWEEN: ACTIVE PASSIVE CONTRIBUTIONS



ATRIAL MEF

Biophysical Motivation

- ROLE OF MECHANO-ELECTRIC FEEDBACK (MEF) IN ARRHYTHMOGENESIS
- **STRETCH** CONTRIBUTES TO:
 - * I) FOCAL ARRHYTHMIAS BY INDUCING EARLY AFTER-DEPOLARIZATIONS
 - * 2) <u>REENTRANT ARRHYTHMIAS</u> BY
 - ✦ SHORTENING THE CONDUCTION VELOCITY
 - ✦ SHORTENING REFRACTORY PERIOD INCREASING SPATIAL DISPERSION



ATRIAL MEF

Biophysical Motivation



RAVELLI 2003

ATRIAL MEF



SVT is supraventricular tachycardia, ΔP the average change in mean atrial pressure, RP refractory period. The parameter measured increased (\uparrow), decreased (\downarrow), or did not change (\leftrightarrow).

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Dog

Balloon inflation

RAVELLI 2003

Solti et al. (1989)

ACTIVE ELECTRO-MECHANICS (EM)

ELECTRO-ACTIVE SYSTEMS' CHARACTERS:

- * DEFORMATIONS MAY INDUCE A CHANGE OF THE EVENTUAL INITIAL ISOTROPY OF A BODY
- * AN **INTERMEDIATE NON COMPATIBLE CONFIGURATION** IS USUALLY ACCOUNTED FOR (<u>MULTIPLICATIVE DECOMPOSITION</u>)
- GENERALIZED CONSTITUTIVE EQUATIONS USUALLY IMPLY MULTIPLE PHYSICAL COUPLINGS (VISCOSITY, DAMAGE, GROWTH, TEMPERATURE)

ELECTRO-ACTIVE BIOLOGICAL SYSTEMS' CHARACTERS:

* THE INTERNAL ACTIN-MYOSIN BINDING (EXCITATION-CONTRACTION - MEF) CAN BE CONSIDERED AS A MICRO-STRUCTURAL ALTERATION OF THE INTERNAL KINEMATIC STATE OF THE MUSCLE FIBRE, WHICH LEADS TO CHANGES IN THE MACROSCOPIC BEHAVIOR

> GIZZI ET AL. 2015 YANG ET AL. 2006

ACTIVE ELECTRO-MECHANICS (EM)

- ACTIVE STRESS (NASH & PANFILOV 2004)
 - **MOST USED APPROACH IN CARDIAC ELECTRO-MECHANICS**
- ACTIVE STRAIN (CHERUBINI ET AL. 2008, AMBROSI ET AL. 2011, RUIZ-BAIER ET AL. 2012)
 - REPRESENTS AN EIGENDEFORMATION APPROACH WELL ESTABLISHED FOR REALISTIC CARDIAC ELECTRO-MECHANICAL APPLICATIONS
 - * MULTIPLICATIVE DECOMPOSITION OF THE DEFORMATION GRADIENT TENSOR
- THERMODYNAMIC APPROACH (GIZZI ET AL. 2015)
 - RELATES THE CONCEPTS OF ACTIVE DEFORMATION & ACTIVE STRESS THROUGH <u>THERMODYNAMICAL ARGUMENTS</u>
 - *** ADDITIVE DECOMPOSITION OF THE STRAIN ENERGY**
 - *** MAXWELL ELECTRO-STATICS**





The active stress model does not derive from thermodynamical arguments

ADVANTAGES

Easy to implement in numerical codes for a proof of concept theoretical study

Proof of Concept

DIFFUSION IN SOLIDS

INFINITESIMAL ELECTRO-DYNAMICS

- RATIONALIZE DIFFUSION IN SOLIDS BASED ON <u>CONSERVATION OF MOMENTUM</u> FOR THE DIFFUSING SPECIES
- THE BALANCE EQUATION CONTAINS:
 - *** STRESS SUPPORTED BY THE DIFFUSING SPECIES**
 - DIFFUSIVE FORCE VECTOR FOR THE EXCHANGE OF MOMENTUM BETWEEN THE DIFFUSING SPECIES AND THE SOLID MATRIX

INTERDIFFUSING MATERIALS ARE ACCOUNTED FOR BY THE CONSTITUTIVE PRESCRIPTIONS (APPLIED TO <u>METALLURGY</u>, <u>POLYMER PHYSICS</u>, <u>GEOPHYSICS</u>)

THESE TWO QUANTITIES ARE NOT IDENTIFIED IN THE CLASSICAL DIFFUSION INTERPRETATION

Homemade Proof of Concept





E							JOURNAL OF POLYMER SCIENCE: Polymer Physics Edition VOL. 11 (
l							On the	Stress-Depen	dent Diffusion Equation	1	
	Acta Mechanica 37, 26	- 284 (1980) ACTA MECHANICA G by Springer-Werlag 1980	Acta Mechanica 45, 27	5—293 (1962)	ACTA MECHANICA (a) by Springer-Veriag 1982	Acta Mechazies 47, 117-151 [1983]		-151 (1983)	ACTA MEC © by Springer-Ver	ACTA MECHANICA © by Springer-Verlag 1963	
L		On the Problem of Diffusion in Solids By		On the Theor	y of Stress-Assisted Diffusion, I			On the Theory of Stress-Assisted Diffusion, I		iffusion, II	
L				By					By		
		E. C. Aifantis, Urbana, Illinois		R. K. Wilso	n azd E.C. Aifantis, Urbana, Illinois			D. J. Unger and	d E. C. Aifantis, Minneapol	is, Minnesota	

STRETCHED VENTRICLES



STRESS-ASSISTED DIFFUSION 'SAD'

- THE **BASIC PHENOMENOLOGY** IS THE SAME EITHER IF "MICROPOROSITY" OR "MACROPOROSITY" IS INVOLVED.
- DIFFUSION OF A DILUTE SOLUTE IN A SOLID MATRIX.
- GENERALIZE THE THEORETICAL WORK OF FICK (A PHENOMENOLOGICAL DESCRIPTION OF DIFFUSION THAT PRECEDES ANY EXPERIMENTAL WORK) WHICH IS CURRENTLY APPLIED IN ANY ELECTROPHYSIOLOGICAL MODELING (CABLE EQUATION).
- THE THEORY OF CONTINUOUSLY DISTRIBUTED MATTER (EULER'S AXIOMS) LEADS TO THE BALANCE OF MOMENTUM.
- CONSTITUTIVE EQUATIONS WILL DIFFERENTIATE BETWEEN:
 - *** DIFFUSION IN STRESSED SOLIDS**
 - *** DIFFUSION OF VISCOUS SOLUTE**
 - *** DIFFUSION IN ELASTIC & INELASTIC MATERIALS**
- FRAMED WITHIN THE **THEORY OF MIXTURES**: ATKIN & CRAINE, BOWEN, TRUSDELL, MAXWELL'S GASES THEORY



Voltage Membrane

as

"continuum"

Diffusion process strongly dependent on the mechanical state



'SAD' THEORETICAL DERIVATION



EM-SAD: A MINIMAL MODEL

2v Reaction-Diffusion (RD) Model (Nash & Panfilov 2004)

RD Constitutive Equations

Classical cubic

"Bistable" function

$$\frac{\partial V}{\partial t} = \frac{\partial}{\partial x_i} d_{ij}(\sigma_{ij}) \frac{\partial V}{\partial x_j} + I_{ion}(V,r) \bigstar \qquad I_{ion} = -kV(V-a)(V-1) - rV$$

$$\frac{dr}{dt} = f(V,r) \qquad \qquad \text{No sac} \qquad f(V,r) = \left(\varepsilon + \frac{\mu_1 r}{\mu_2 + V}\right) (-r - kV(V-b-1)) + V$$

$$\text{Nonlinear} \qquad \text{Nonlinear}$$

$$\text{"Recovery" dynamics}$$

Active Stress Formulation (Nash & Panfilov 2004)

$$\frac{\partial T_a}{\partial t} = \epsilon(V)(k_{T_a}V - T_a)$$

Equilibrium

$$\frac{\partial \sigma_{ij}}{\partial x_i} = 0 \qquad J = 1$$

Representation Formula for
2nd Order Isotropic TensorsTwo additional
Material Parameters
$$d_{ij}(\sigma_{ij}) = D_0 \left(\delta_{ij} + D_1 \sigma_{ij} + D_2 \sigma_{ik} \sigma_{kj}\right)$$

Isotropic Stress-Assisted Diffusion Model

$$\sigma_{ij} = \sigma_{ij}^{\text{passive}} + \sigma_{ij}^{\text{active}} \quad \dots \quad \flat \quad \sigma_{ij} = 2c_1b_{ij} - 2c_2b_{ij}^{-1} - p\delta_{ij} + T_a\delta_{ij}$$

Passive Neo-Hookean material with ISOTROPIC diffusion & ACTIVE stress



 $\sigma_1 = 1 \text{ or } \sigma_2 = 1$





$$d_{ij}] = \begin{bmatrix} 1 + D_1 \sigma_1 + D_2 \sigma_1^2 & 0\\ 0 & 1 + D_1 \sigma_2 + D_2 \sigma_2^2 \end{bmatrix}$$

Ellipticity regime (Non-negative diffusion)

$$1 + D_1 \sigma_1 + D_2 \sigma_1^2 > 0, \quad \to \quad 4D_2 > D_1^2$$





$$d_{ij}(\sigma_{ij}) = D_0 \left(\delta_{ij} + D_1 \sigma_{ij} + D_2 \sigma_{ik} \sigma_{kj} \right)$$

- 1. Calculate the <u>Conduction Velocity</u> of the <u>Excitation Wave</u> (Voltage) for different combinations of the Material Parameters
- 2. Compute the ratio CVx/CVy











EM-SAD: ENHANCED MEANDERING



EM - SAD & SAC (MINIMAL)

2v Reaction-Diffusion (RD) Model

RD Constitutive Equations

Active Stress Formulation

$$\frac{\partial V}{\partial t} = \frac{\partial}{\partial x_i} d_{ij}(\sigma_{ij}) \frac{\partial V}{\partial x_j} + I_{ion}(V, r) + I_{sac}(\lambda, V)$$
$$\frac{dr}{dt} = f(V, r)$$

 $\frac{\partial T_a}{\partial t} = \epsilon(V)(k_{T_a}V - T_a)$

Isotropic Stress-Assisted Diffusion Model

$$I_{\text{ion}} = -kV(V-a)(V-1) - rV$$
$$f(V,r) = \left(\varepsilon + \frac{\mu_1 r}{\mu_2 + V}\right)(-r - kV(V-b-1))$$

 $I_{\rm sac}$

$$d_{ij}(\sigma_{ij}) = D_0 \left(\delta_{ij} + D_1 \sigma_{ij} + D_2 \sigma_{ik} \sigma_{kj} \right)$$

$$(\lambda, V) = G_s H_{\text{sac}}(\lambda - 1)(V_{\text{sac}} - V)$$

YES SAC

Minimal model of Stretch-Activated Currents

$$\frac{\partial \sigma_{ij}}{\partial x_i} = 0 \qquad J =$$

$$\sigma_{ij} = 2c_1 b_{ij} - 2c_2 b_{ij}^{-1} - p\delta_{ij} + T_a \delta_{ij}$$

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EM - SAD & SAC

Spiral Tip Meandering





SAD stabilizes meandering

SAC generates irregular behavior

Static/Dynamic & Displacement/Traction BCs conduct to different scenarios

EM - SAD & SAC ... ?



LIMITATIONS...

GENERALIZED ELECTRO-MECHANICAL FRAMEWORK

STRESS-ASSISTED DIFFUSION

V

SAC VS. SAD

SOTROPIC HYPERELASTIC MATERIALS CAN UNDERGO ANISOTROPIC REACTION-DIFFUSION DYNAMICS

MINIMAL PROOF OF CONCEPT

OPEN QUESTIONS...

MULTISCALE MODELING

FROM <u>CELL-CELL COUPLING</u> TO TISSUE SCALE (EMERGENT PHENOMENA)

D PHYSIOLOGICAL MODELING (ROLE OF CALCIUM)

MODEL VALIDATION: SACESAD LIMITS



RUIZ-BAIER, AG ET AL. 2014

Π....

LENARDA, AG, PAGGI 2018

HURTADO, CASTRO, AG 2016

A. T. WINFREE, 2000

PRINCETON GRADUATE SCHOOL CENTENNIAL



ANUBIS IN THE DESERT EST OF EGYPT - 3RD MILLENNIUM BCE

"Weighing the heart against the feather of Truth"



we are still trying...

EM-SAD: INDUCED ANISOTROPY



Eigenvalue/Eigenvector rendering of the a Second Order Tensor in a two-dimensional view

Solve local eigenvalue problems using the tensor at hand and display an ellipsoid whose shape and size depend on the local eigendirection

$$\sigma_{ij} = 2c_1 b_{ij} - 2c_2 b_{ij}^{-1} - p\delta_{ij} + T_a \delta_{ij}$$

 $d_{ij}(\sigma_{ij}) = D_0 \left(\delta_{ij} + D_1 \sigma_{ij} + D_2 \sigma_{ik} \sigma_{kj} \right)$