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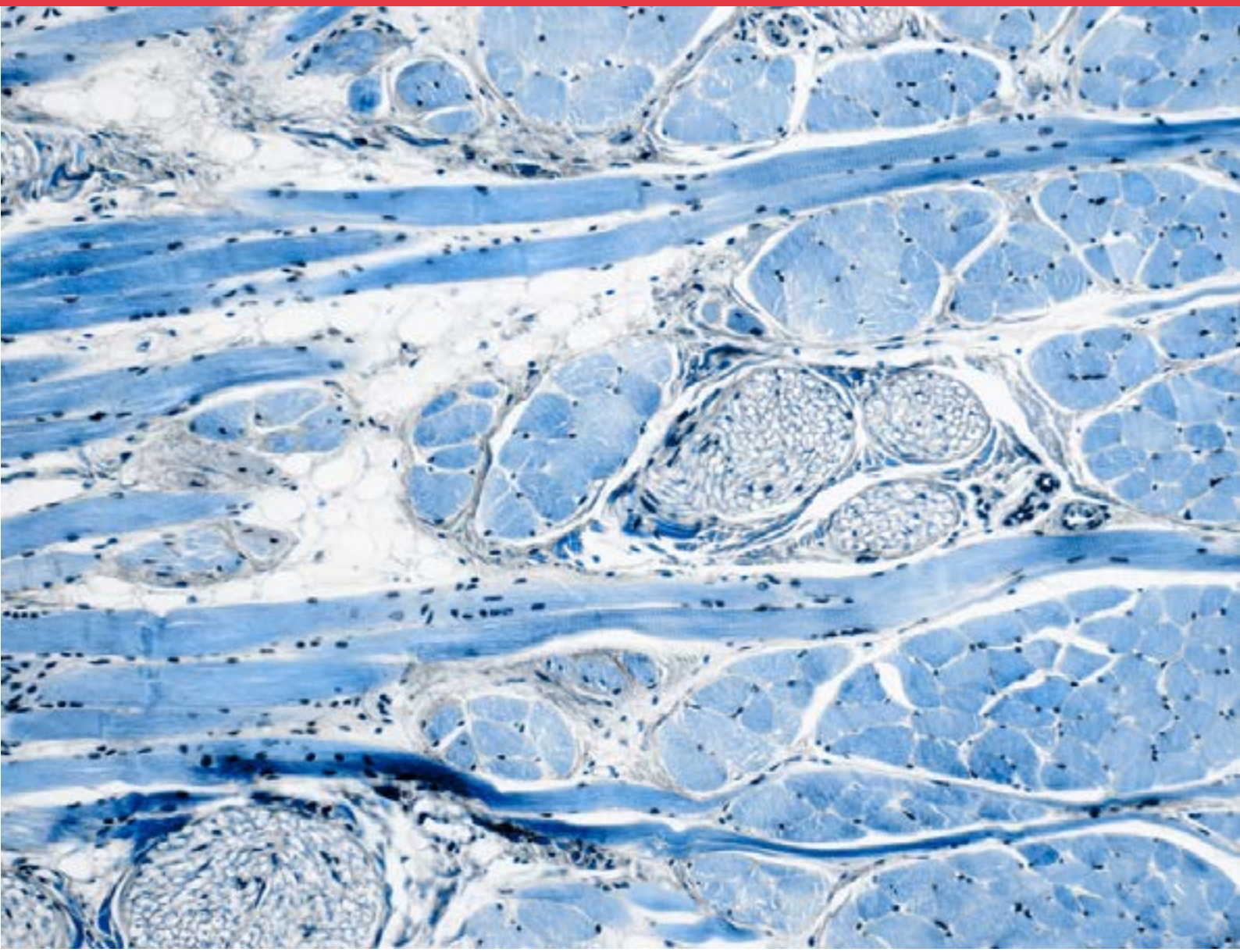

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ELECTROPHYSIOLOGY OF THE MAMMALIAN CYTOSKELETON

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Abstract

The cell's cytoskeleton consists of a dynamic structure containing actin-based filaments (F-actin), tubulin-based microtubules (MTs) and intermediate filaments. While it is well-known for maintaining cell shape and providing mechanical support, these cytoskeletal elements also have important electrical properties that may play a crucial role in electrical signaling and information processing within the cell. F-actin and MTs possess a large uncompensated charge, which give rise to nonlinear electrical properties, explaining the high sensitivity of cells to electric fields both in vitro and in vivo. Remarkably, the polymers of the cytoskeleton enable the generation of ionic condensation-based waves in F-actin and exhibit behavior analogous to transistors in MTs. This review summarizes three decades of research from our laboratory, elucidating the fundamentals and methodologies of cytoskeletal electrophysiology. The electrophysiology of the cytoskeleton is an emerging field of study that investigates the electrical properties and behavior of the various elements of the cytoskeleton and their implications for various areas of biology and medicine. The electrical properties of the cytoskeleton contribute to a new paradigm of cell physiology. They might be implicated in cell signaling and regulation, and associated with the sensory properties of the cell.

Keywords: Actin, Tubulin, Microtubules, Electrophysiology, Oscillations

Resumen

El citoesqueleto celular es una estructura dinámica que incluye filamentos de actina (F-actina), microtúbulos (MTs) basados en dímeros de tubulina y filamentos intermedios. Si bien se le conoce principalmente por mantener la forma celular y proporcionar soporte mecánico, investigaciones recientes han revelado importantes propiedades eléctricas de los polímeros que componen el citoesqueleto, que podrían desempeñar un papel crucial en la señalización eléctrica y el procesamiento de información celular. Tanto los filamentos de F-actina como los MTs poseen una gran carga no compensada, lo que genera propiedades eléctricas no lineales, y explicaría la alta sensibilidad de las células a los campos eléctricos tanto in vitro como in vivo. En particular, estos polímeros generan propiedades que permiten la generación de ondas iónicas basadas en condensación iónica en la F-actina, y un comportamiento similar al de un transistor en los MTs. Esta revisión resume tres décadas de investigación realizada en nuestro laboratorio, con el objetivo de dilucidar los fundamentos y las metodologías para el estudio de la electrofisiología del citoesqueleto, un campo de estudio emergente que investiga las propiedades eléctricas y el comportamiento de los diversos elementos del citoesqueleto y sus implicaciones en diversas áreas de la biología y la medicina. Las propiedades eléctricas del citoesqueleto contribuyen a un nuevo paradigma de la fisiología celular. Estarían implicadas en la señalización y regulación celulares y asociadas a sus propiedades sensoriales.

Palabras clave: Actina, Tubulina, Microtúbulos, Electrofisiología, Oscilaciones

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Introduction

The cytoskeleton comprises three main types of filaments: F-actin, MTs and intermediate filaments, which undergo constant reorganization, allowing cells to adapt and respond to the various environments, and a diversity of stimuli. Known for its contribution to the mechanical properties and stability of the cell, the cytoskeleton is implicated in various essential structural functions, including cell shape, contraction and motility, and functions as cell division and the transport of cargo. However, F-actin and MTs also exhibit novel electrical properties that may be implicated in the formation, maintenance, and sensing properties of specialized actin structures like filopodia, lamellipodia, microvilli, dendritic spines, and cilia and flagella in the case of MTs. Investigating the electrical properties of the cytoskeleton provides valuable insights into their role in cell function.

The electrical properties of actin

Actin is the most abundant protein of the cytoplasm (~10-20%) that plays an essential role in cell shape and locomotion [1]. Monomeric (globular) actin (G-actin) is a 45 kDa peptide that polymerizes into noncovalent helical filaments (F-actin). While actin is primarily known for its structural and mechanical functions, it also possesses interesting electrical properties. Actin is a charged protein due to the presence of charged amino acid residues [2]. At neutral pH, each F-actin subunit bears 14 excess negative charges, where roughly three histidines per monomer are likely protonated [3]. The linear charge density of F-actin is calculated at 4 *e*/nm[1], such that it makes possible counterion condensation.

[1]*Linear charge density in macromolecular polymers is expressed in unitary electron charge (1.60217662 × 10^{-19} Coulombs) per nanometer.*

To determine the electrical contribution of F-actin in solution, [4] measured the Donnan potential developed by the polymer in an osmotic experiment designed to constrain F-actin into a dialysis bag. Polymerized actin (5 mg/ml) induced a -3.93 mV spontaneous potential from which a calculated linear charge density of 1.65 x 10^5 *e*/μm was obtained, in agreement with a reported value of 75 Debye/monomer[2] (~5 x 10^5 *e*/μm) from birefringence studies of electric field-oriented F-actin [5]. Interestingly, much higher values were reported for F-actin oriented by shear flow [5], which may be explained by the helical nature of F-actin [6] that generates nonuniform counterion distributions arranged in peaks and troughs along the polymer. To explore this phenomenon, the actual concentration and distribution of net charge in bundles of F-actin, [7] combined atomic force microscopy (AFM) imaging and surface potential microscopy (SPM) to map their surface potential. An uneven spatial charge distribution was detected, where surface potential showed strong nonlinearity in charge distribution that decayed exponentially over 100 nm, with accumulated charge of 2.39 x10^{-18} C, with excess ions in the order of 15/nm[3].

[2]*The Debye is a CGS unit (a non-SI metric unit) of electric dipole moment defined as 1×10^{-18} statcoulomb-centimeter, where the statcoulomb, also known as the franklin or esu (electrostatic unit) of charge, is a unit of electric charge in the CGS electromagnetic unit system, equivalent to approximately 3.3356 × 10^{-10} coulombs in the International System of Units (SI).*

Ionic traveling waves in actin filaments

The observed values by SPM indicated that the condensed charge around the polymer is actually much higher than the expected value based on a theoretical charge density of ~4 *e*/nm. As a consequence, significant ionic movements will occur within this ionic cloud, resulting in a highly conductive medium [8] electrically shielded from the bulk solution [9]. Thus, F-actin may act as a biological "electrical wire" capable of propagating nonlinear dispersive waves and solitons [10]. [11] used the "patch-clamp" to explore this electrodynamic behavior. An actin filament in solution (Fig. 1) was “connected” at both ends, by gluing through myosin-loaded pipettes [12] to respective patch clamp amplifiers. Electrical signals were observed under high (physiological) and low ionic strength conditions, proving that the

conductive medium was the ionic cloud around the polymer. Actin indeed behaved as a biological "electrical wire" (Fig. 1).

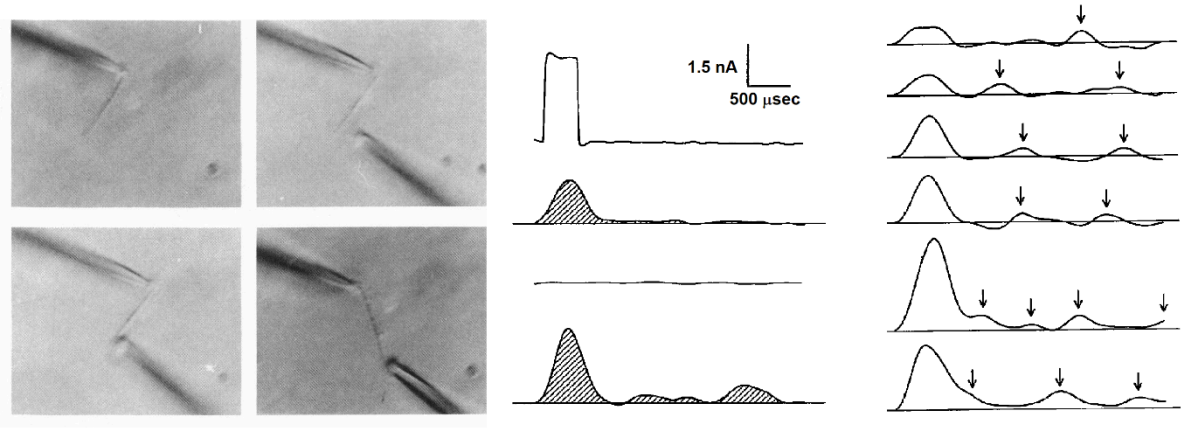

Figure 1. *Electrical recordings from actin filaments*. A. Left. An actin filament is attached consecutively to two myosin-containing pipettes connected to respective patch-clamp amplifiers. A. Middle. Data are shown for the recorded pulse in the stimulus (A) and collection pipette (B) prior to attaching F-actin. There is no signal in the absence of stimulus once attached (C), but a collection of waves is observed after stimulation (D). B. Examples of waves from square voltage pulses of different magnitude. Reproduced from Lin and Cantiello 1993 [11].

The observed wave patterns in F-actin resembled solitary waveforms and solitons recorded in nonlinear transmission lines [10]. Solitons are well established in nonlinear transmission lines modeled by discrete lumped circuits [13]. The input square pulse decomposes in a finite number of solitons and a low-amplitude oscillatory tail (Fig. 1). Adapting the discrete transmission line model to F-actin entails that each actin monomer represents an electrical node, where the collecting pipette is "connected" to the nth one. The total charge propagated via F-actin was calculated around 200 pC. Ionic wave propagation under low ionic strength conditions confirmed that the "condensed" ionic cloud was the conductive medium [11]. Thus, actin filaments are electrical transmission lines, that can be modelled electrically where each monomer is an electric element with capacitive, inductive, and resistive properties [14]. Nonlinear partial differential equations can be derived for the actin ionic wave propagation that can have a relevant role in information processing, especially in neurons.

Piezoelectricity and nonlinear electrical properties of actin

Actin is a major component of the cytoskeleton, providing structural support and facilitating various cellular processes such as cell motility, division, and intracellular transport. F-actin also produces interesting paracrystalline structures by exposure to lanthanides and other high ionic strength conditions [15]. Actin paracrystals typically form within the cytoplasm of eukaryotic cells [16], [17], [18]. Recently [19] assessed the electrical properties of purified $MgCl_2$- or $GdCl_3$-induced actin paracrystals. The voltage-clamped crystals displayed strong rectification with a nonlinear conductance under symmetrical conditions, with positive-to-negative conductance ratios ranging from 4.18 to 9.00. The current-to-voltage responses could be fitted with double Schottky diode equations. This phenomenon may be associated with the piezoelectric properties of actin [20], which can cause electrical potentials in response to mechanical forces [21], linking actin's mechanical and electrical functions within cells. Several conditions bring about actin crystalline structures, including interactions with actin-binding proteins, where 3D co-crystals have been found both *in vivo* and *in vitro* [22]. Actin paracrystals are commonly observed in areas associated with dynamic rearrangements of the cytoskeleton, such as the cell cortex near the cell membrane and, especially in regions where cell

adhesion, migration, or cell-cell interactions occur ([16], [17], [18]). Actin-rich structures such as filopodia, lamellipodia, and microvilli are also hotspots for actin polymerization where actin paracrystals may form during cellular movements or in response to extracellular signals ([23], [24], [26]). Actin paracrystals can also associate with certain organelles, including the Golgi apparatus or endoplasmic reticulum. In cells undergoing processes such as cytokinesis or response to mechanical stress, actin paracrystals may form within stress fibers or contractile rings, which are contractile bundles of F-actin.

One of the main contributions of the electrical properties of the actin cytoskeleton may be implicated in the regulation of ion channels contributing to physiological processes such as signal transduction, cell-cell communication, and ion transport [25]. Lader et al. (1999) [27] found that F-actin organization strongly controlled L-type Ca^{2+} channel currents in neonatal mouse cardiac myocytes from both wild-type mice and mice genetically devoid of the F-actin severing protein gelsolin. In vascular smooth muscle cells, for example, F-actin can directly interact with mechanosensitive ion channels like stretch-activated ion channels (SACs) to regulate their gating in response to mechanical forces, thereby influencing processes such as vascular tone regulation and endothelial barrier function [28]. In epithelial cells, the actin cytoskeleton has been implicated in the regulation of ENaC activity that plays a critical role in sodium reabsorption and fluid homeostasis [29]. Actin dynamics can modulate ENaC activity through various mechanisms, including direct physical interactions between actin filaments and ENaC subunits, as well as indirect effects on membrane trafficking and channel localization [30].

Actin cytoskeleton remodeling impacts on the function and localization of voltage-gated Na^+, K^+ and Ca^{2+} channels. In neurons, actin dynamics clusters and anchors ion channels at specific sites along the axon and dendrites, which are crucial for action potential generation and propagation ([31], [32], [33], [34]).

Although the structural/biochemical interaction between actin and ion channels is well established, the possibility that these interactions may be of an electrical nature is likely, and with an important contribution to the electrical gating of membrane transport.

Electric properties of tubulin and microtubules

Microtubules (MTs) are tubulin-based polymers, with a diameter of 25 nm and several micrometers in length [35]. Heterodimers of αβ-tubulins of 55 kDa each form linear strings of protofilaments that arrange in parallel, most often thirteen, which close in a cylindrical shape. The lateral arrangement of protofilaments generates nanopores that have a ionic conductivity [36]. MTs produce mechanical oscillations ([37], [38]) that may affect the topological features of the nanopores and, thus, their ion permeability.

[38] determined the electronic charge and dipole moment of monomeric tubulin, which is highly negatively charged at physiological pH. As much as 40% of the overall charge, is concentrated on the carboxy (C)-terminus. Without their C-termini a tubulin dimer has about 10*e* and an overall dipole moment of ~1714 Debye. At neutral pH, the negative charge maintains extended the C-terminus that is reduced and more compacted folded form under acidic conditions. Tubulin presents several dipoles in saline solution [38], including a double layer between bound dimers that place their positively and negatively charged ends to form a net longitudinal dipole moment. [38] predicted the emergence of an anti-ferroelectric system with permanent dipoles placed almost perpendicular to the surface of the MT and almost canceling each other due to rotational symmetry.

Electrical amplification by microtubules. A biopolymer transistor

Priel et al., (2006) [39] determined the electrodynamic properties of isolated, paclitaxel-stabilized MTs. Isolated MTs were connected at each end to respective patch-clamp amplifiers (Fig. 2a), where electrical stimulation was applied to one of them. Applied voltage pulses at one end resulted in

electrical signals that were collected at the opposite end of the MT. The currents measured at the collection site were a strictly inverse ohmic response, i.e., linear amplification occurred. Thus, the MT acts as a biomolecular transistor, where Nernst potentials arising from asymmetries in the ionic distributions between the intra- and extra-MT environments polarize the polymer where the biased junctions of the intramolecular transistor allow amplification of axially transferred signals.

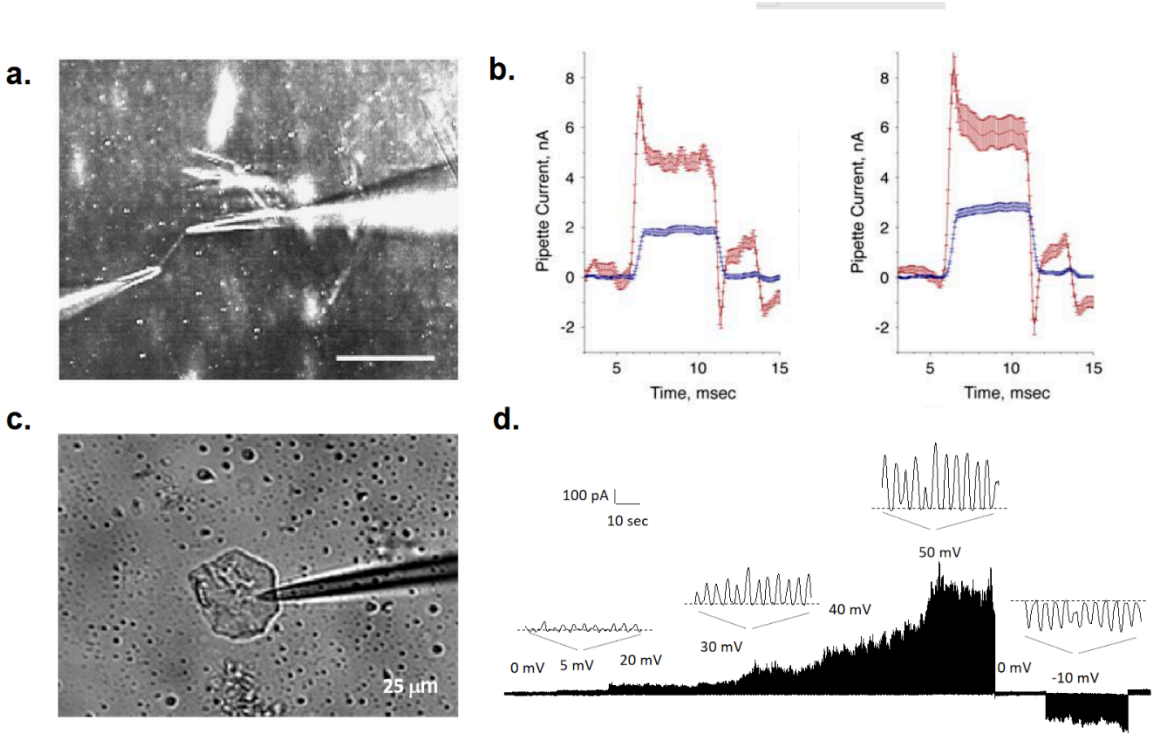

Figure 2. *Electrical recordings of MTs in different conformations.* **a,b.** Left, Electrical amplification by isolated MTs. A free-floating MT was "connected" to two patch clamp amplifiers through respective recording pipettes. A voltage pulse was first applied to the saline solution's "stimulus" pipette, obtaining the electrical coupling by the "collection" pipette. A similar approach was repeated after MT attachment. The resulting currents were higher after attachment to the MT than saline solution. Reproduced from Priel et al., 2006 [39]. **c,d.** A patch pipette recorded electrical signals from a sheet of brain MTs. Electrical oscillations were observed that changed direction with voltage polarity. Reproduced from Cantero et al., 2016.

Electrical oscillations of microtubule structures

To explore the role of the nanopores present at the MT wall [40], explored the electrical properties of MT sheets of bovine brain (Fig. 2b) with the patch clamping technique. Surprisingly, MT sheets displayed spontaneous, self-sustained electrical oscillations that responded directly to the magnitude of the stimulus (Fig. 2b, Right). Conversely, current-clamped MT sheets also displayed voltage oscillations that resembled action potentials [41]. A linear mean conductance was observed, while a nonlinear electrical response was observed in the peak frequency currents that were modeled with an Esaki diode current equation, displaying a "tunneling" effect. The role of the nanopores in the electrical oscillations, was tested by adding paclitaxel, an anti-mitotic drug that diffuses through and interacts with the nanopores [42]. Increasing paclitaxel concentrations elicited a dose-dependent decrease in current amplitude, with complete inhibition at ~10 µM, and a K_D of 1.29 µM. Interestingly, the

paclitaxel-MT sheet interaction was entirely voltage-dependent, such that an increase in the voltage clamping potential recovered the oscillatory activity.

The MT wall behaves as an electrical oscillator with a remarkably constant frequency independent of holding potential and ionic strength conditions. The synchronized electrical currents may be explained by the opening and closing of individual oscillators, possibly coordinated by mechanical changes in the tubulin dimers. Freedman et al. (2010) [36] calculated the ionic conductance of the nanopores in the MT wall, concluding that they have a large cationic conductance. The electrical oscillations were recently confirmed in isolated MTs [43], and thus likely play a relevant role in biological signaling events, such as the transport of electrical information in neurons, and MT-driven organelles such as cilia and flagella.

Bundles of brain microtubules generate electrical oscillations

To investigate whether different assemblies of MTs had different oscillatory response, bundles of brain MTs were also patch-clamped [41], showing electrical oscillations and bursts of electrical activity similar to action potentials. Voltage-clamped membrane-permeabilized neurites of cultured adult mouse hippocampal neurons (Fig. 3) confirmed this finding [41], where electrical oscillations propagated along the cytoskeleton. Thus, electrical oscillations may have important implications in the propagation of electrical information, and possibly the gating and regulation of cytoskeleton-regulated excitable ion channels that may contribute to higher brain functions such as memory and consciousness.

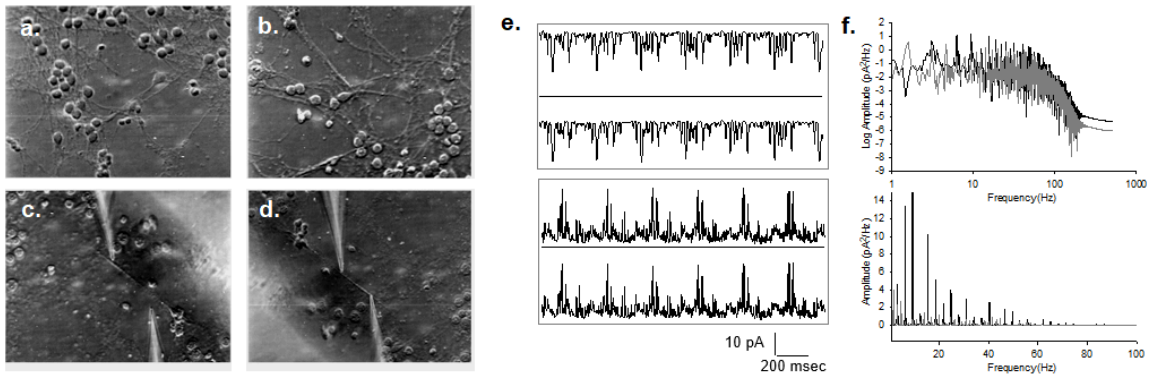

Figure 3. *Cytoskeletal electrical oscillations in hippocampal neurons*. **a,b.** Images of one-week old cultured adult mouse hippocampal neurons (x20), before and after cell membrane permeabilization with Triton X. **c,d.** Permeabilized neurites shown before and after double patching with patch-clamp pipettes. (e) Spontaneous electrical oscillations observed in one pipette and mirror images collected on the second pipette. **f.** Power spectra of the tracings shown on **e.**, for the positive (Black) and negative (Gray) biased signals, respectively. Linear-Linear plots for respective spectra are also shown (Bottom). Reproduced from Cantero et al., 2018 [41].

Microtubules as memristive devices

To explore the molecular steps implicated in the onset of the oscillatory behavior, [44] assessed the electrical response of non-oscillating rat brain MT sheets, observing a complex voltage-dependent nonlinear charge movement. This included a small, saturating, voltage-dependent capacitance with a maximum charge displacement in the range of 4 fC/μm^2, and a second, major contribution as a non-saturating voltage-dependent charge transfer, consistent with the properties of a multistep memristive device ([45], [46]). The memristive capabilities of MTs could drive the oscillatory behavior, enabling voltage-driven neuromorphic circuits and architectures within neurons [47]. The spiking events were phenomenologically characterized, and well fitted with an equation similar the Mem-Con model of memristive devices that explains neuron spikes ([48], [44]).

Coupling of electrical activity between F-actin and brain microtubules

Actin filaments and MTs interact in various dynamic cellular processes. In neurons, this synergistic activity provides intrinsic structural support throughout development and the transition into mature neurons [49]). Cantero et al. (2020) [50] explored the electrical connection between F-actin and MTs by evaluating the effect of various conformations of actin on the electrical oscillations of brain MT sheets [50]. G-actin elicited a time-lagged increase in the electrical oscillations while the addition of pre-polymerized F-actin elicited a faster and higher stimulatory effect. Thus, F-actin helped amplify the electrodynamic properties of tubulin structures. Although MT-associated proteins (MAPs) including MAP2 and Tau bind both actin and tubulin [51], electrostatic interactions also occur between F-actin and tubulin. The MT's surface may offer an electrostatic environment for actin interaction. [50] observed that F-actin produced a time-dependent shift in reversal potential of up to 12 mV, consistent with a strong electrostatic potential (see Fig. 5 in [50]), despite no change in chemical potential.

Conclusion. Electrical contributions of the cytoskeleton to cell function

Actin and tubulin present interesting electrical properties that may contribute to the assembly, stability and dynamics of the cytoskeleton that play critical roles in various cellular processes, including the maintenance of cell shape and cell migration and muscle contraction. The electrical properties of actin and tubulin may be implicated in neuronal signaling and the modulation of neuronal activity [52]. The resting potential of a cell establishes extremely large electric fields of the order of 100 kV/cm. Because very small electric fields, on the order of 10 mV/cm are capable of inducing cellular responses [53], it is entirely possible that changes in plasma membrane-originated electrical responses may be directed into the cytoplasm by cytoskeletal structures. Most ion transport mechanisms, including ion channels and transporters are linked to cytoskeletal structures that elicit an electrical signaling mechanism. Here we summarized experimental evidence for novel electrical properties of F-actin and MTs, also establishing a functional link between them. The data are consistent with novel properties of the cytoskeleton that can be viewed as an intracellular computing device [54] whose properties remain to be largely defined.

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About authors

El Dr. Horacio Cantiello, se recibió de Médico Veterinario en la Facultad de Ciencias Veterinarias de la Universidad de Buenos Aires en 1978. Siendo aún estudiante y ayudante de la Cátedra de Física Biológica, se incorporó al grupo del Dr. Ignacio Reisin, investigador del CONICET, en el Centro de Investigaciones Médicas "Albert Einstein", Buenos Aires Argentina, con quien realizaría su Tesis Doctoral. Para dichos estudios obtuvo una beca doctoral de la Comisión de Investigaciones de la Provincia de Buenos Aires, obteniendo el título de Dr. en Ciencias Veterinarias de la Universidad Nacional de La Plata en 1981.
A la espera de una posición postdoctoral en el extranjero, fue contratado como Investigador por CONICET bajo la dirección del Dr. Mario Fernández Villamil en el Instituto de Investigaciones Cardiológicas "Prof. Dr. Alberto C. Taquini" de la Facultad de Medicina, UBA. Un año después concursó y obtuvo la beca del Programa Fogarty International de los Institutos Nacionales de Salud de los EEUU (NIH), cuyo comité local estaba presidido por el Dr. Luis Federico Leloir. Esta beca para realizar estudios de transporte iónico en células epiteliales renales en la Unidad Renal del Massachusetts General Hospital, Harvard Medical School, lo llevó a EEUU en lo que sería una estancia de casi 30 años enteramente dedicada a la Biofísica experimental en temas de transporte iónico.
Durante ese período, fue también Asociado Posdoctoral en la División de Medicina Comparada del Massachusetts Institute of Technology (MIT, 1984-1986). Posteriormente, desarrolló sus actividades científicas ocupando distintos cargos desde Instructor hasta Profesor Asociado en la División de Nefrología de los Hospitales Brigham and Women´s and Massachusetts General Hospital, ambos asociados a la Harvard Medical School. Durante su prolongada estancia en el exterior tuvo la oportunidad de llevar a cabo la formación de RRHH en todos los niveles, estudiantes de grado y posgrado e investigadores formados. En la Argentina ha dirigido siete Tesis Doctorales y codirigido otras dos. Fue investigador invitado en varias ocasiones al Mount Desert Island Biological Laboratory en Maine, USA.
En el año 2010, decidió retornar definitivamente a nuestro país, incorporándose como Investigador Principal del CONICET, originalmente en Buenos Aires, y posteriormente hasta la actualidad, en la provincia de Santiago del Estero, donde es Director del Instituto Multidisciplinario de Salud, Tecnología y Desarrollo (IMSaTeD, UNSE-CONICET). Actualmente, es Investigador Superior de CONICET y ha publicado ciento diez trabajos en revistas internacionales.
En paralelo, es de destacar su actividad gestión y docente, ya que fue Miembro del Consejo Directivo del Centro Científico Tecnológico Tucumán (CCT Tucumán), CONICET (2018-), Director del Servicio de lectrofisiología del Massachusetts General Hospital, MA, USA (2006-2009), Director Adjunto del Servicio Nacional de Sonda Electrónica para Análisis de Células, NIH, MA USA (1988-1989, Profesor Asociado, Harvard Medical School, MA, USA (1998-2014), Profesor Asistente de Medicina, Harvard Medical School, MA, USA (1991-98) e Instructor en Medicina, Harvard Medical School, MA, USA (1988-1991), Profesor Regular Adjunto, Facultad de Odontología, UBA (2012-2018) y Profesor Asociado, Facultad de Ciencias Médicas, UNSE (2017-2021) hasta que la Facultad le discontinó su contrato docente. Junto con los Drs. Tabatadze DR, Zamecnik PC y Raychowdhury MK, desarrolló una patente Oligonucleotide complex compositions and methods of use as gene alteration tools (US 8,841,271 B2) para el tratamiento de la fibrosis quística. Actualmente, está iniciando una compañía de desarrollo biotecnológico junto con miembros de su laboratorio.

La **Dra. María del Rocío Cantero**, se recibió de Farmacéutica en la Facultad de Farmacia y Bioquímica (FFyB) de la Universidad de Buenos Aires en 2007. Entre los años 2003 y 2005 trabajó en la industria farmacéutica hasta que decidió seguir su vocación científica y docente. Siendo aún estudiante y ayudante de la Cátedra de Química General e Inorgánica, se incorporó al grupo originalmente conducido por el Dr. Ignacio Reisin en la FFyB, desarrollando su Tesis doctoral bajo la Dirección del Dr. Horacio Cantiello con una beca de CONICET. Sus estudios en el área de biofísica y fisiología se centraron en el estudio de los aspectos regulatorios de la policistina-2, un canal de la familia TRP, cuya disfunción se

relaciona con la poliquistosis renal autosómica dominante. En el 2012, obtuvo el título de Doctora de la UBA en el área de Farmacia y Bioquímica en la misma Facultad de la que se graduó como Farmacéutica.

Durante el desarrollo de su Tesis, realizó tres pasantías en el exterior, en la División de Nefrología del Massachusetts General Hospital, en Boston, Estados Unidos. Obtuvo una Beca posdoctoral de CONICET y posteriormente ingresó a carrera de Investigador Científico en la misma institución en 2017. Durante estos años fue Ayudante de Segunda en la Cátedra de Química General e Inorgánica, FFyB (2003-2008), Ayudante de Primera en el Departamento de Fisiología, Biología Molecular y Celular, Facultad de Ciencias Exactas y Naturales, UBA (2008-2009), Ayudante de Primera, Cátedra de Biofísica, Facultad de Odontología, UBA (FOUBA) (2010-2011), Jefe de Trabajos Prácticos Regular, Cátedra de Biofísica, FOUBA (2011-2017), Profesora Adjunta en Metodología de la Investigación, Facultad de Ciencias Médicas de la Universidad Nacional de Santiago del Estero (UNSE) (2017-2018) y Profesora Asociada de Farmacología General, Facultad de Ciencias Médicas, UNSE (2018-2021), hasta que la Facultad le discontinuó su contrato docente. Fue becada en el año 2019 para participar y presentar sus resultados en el Workshop "Emerging Concepts of the Neuronal Cytoskeleton" organizado por la European Molecular Biology Organization llevado a cabo en Chile, que posteriormente se plasmaron en un artículo por invitación en la revista Cytoskeleton.

La Dra. Cantero ha sido invitada a brindar conferencias en la Sociedad Argentina de Fisiología, donde fue también Vocal en representación de la región Centro, tiene numerosas presentaciones a congresos y más de 25 publicaciones con referato internacional. Es miembro de la Sociedad Argentina de Biofísica y de la Biophysical Society (Estados Unidos). Desde su incorporación a la CIC CONICET se ha enfocado en el estudio de las propiedades electrodinámicas de los microtúbulos y del citoesqueleto de actina, iniciando un nuevo campo del conocimiento con relevancia tantos en desarrollos biotecnológicos como en medicina. Este área solo contaba con desarrollo teórico, con lo que junto con el Dr. Cantiello, son pioneros en el campo. Actualmente es Vicedirectora del Instituto Multidisciplinario de Salud, Tecnología y Desarrollo (IMSaTeD, UNSE-CONICET) en Santiago del Estero e Investigadora Independiente de CONICET. La Dra. Cantero está iniciando una compañía de desarrollo biotecnológico junto con miembros de su laboratorio.