

The Unified Mechanical Model of Neurotransmission: A Mechanical-First Hypothesis of Continuous Axonal Signal Propagation and Pressure-Differential Ion-Channel Gating

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Abstract

Neural transmission is conventionally understood primarily as an electrical process in which voltage-dependent ion channels generate and regenerate action potentials along neuronal membranes. The Unified Mechanical Model of Neurotransmission (UMMN) proposes an alternative physical interpretation of axonal signal propagation.

The central hypothesis of UMMN is that the primary signal travelling along the axon is a continuously propagating mechanical pressure wave, termed the Action Pressure Wave (APW). The electrical events conventionally recorded as action potentials are proposed to represent local electrical manifestations of this mechanically propagating signal rather than the primary long-range carrier of neural information.

The model does not dispute the existence or importance of ion channels, ionic currents, membrane potentials, or action potentials. Instead, it proposes a different causal interpretation of their activation during propagation.

Specifically, UMMN hypothesizes that the relevant ion-channel gates are mechanically influenced by a transient pressure differential across the gating structure. During the phase in which intra-axonal pressure falls below its resting value, extracellular pressure is proposed to become transiently greater than intracellular pressure, producing a mechanical force capable of displacing the channel gate and permitting ionic influx.

The proposed causal sequence is therefore:

Pressure differential → mechanical gate displacement → ion-channel opening → ionic current → change in internal charge relative to its resting value → local electrical potential change (action potential)

A second defining feature of UMMN concerns myelinated axons. The model does not propose that the primary neural signal travels by electrically jumping from one Node of

Ranvier to another. Instead, the APW is hypothesized to propagate continuously through the entire axonal pathway, including the internodal regions. The Nodes of Ranvier are proposed to be specialized sites where the continuously propagating mechanical wave interacts with the membrane and ion-channel structures, producing localized electrical responses.

The model further proposes that electrical initiation occurs at the axon hillock, where a mechanically active cytoskeletal structure may generate the initial APW. A candidate mechanism is described as a hypothetical "nano-piston," although this component remains speculative and requires direct experimental investigation.

The principal experimental prediction of UMMN is that the pressure change responsible for channel activation should precede the corresponding ionic current and the change in internal charge relative to its resting value, at the axon hillock, at each node of Ranvier, and at the terminal bouton. This temporal sequence constitutes the central experimental test of the model.

UMMN is therefore presented as a falsifiable hypothesis rather than an established mechanism. Its validity depends on direct experimental demonstration of mechanical precedence, quantitative sufficiency, causal influence on ion-channel gating, and continuous mechanical propagation along the axon.

Keywords: *Action Pressure Wave; mechanical neurotransmission; axonal conduction; pressure-differential gating; ion channels; Nodes of Ranvier; myelin; mechanotransduction; action potential*

1. Introduction

The action potential is one of the most extensively investigated phenomena in neuroscience. The classical Hodgkin-Huxley framework provided a quantitative description of electrical excitation in which changes in membrane potential alter the conductance of voltage-dependent ion channels, generating the characteristic action-potential waveform. This framework has successfully explained a vast body of electrophysiological observations and remains the dominant theoretical description of neuronal excitability.

The present hypothesis does not challenge the existence of these electrical phenomena. Instead, it asks a more fundamental physical question: What is the primary signal that physically travels along the axon?

The conventional interpretation assumes that the action potential itself constitutes the propagating signal. According to this view, changes in membrane potential activate voltage-dependent ion channels, and the resulting ionic currents regenerate the action potential along the axonal membrane.

UMMN proposes an alternative causal architecture. It hypothesizes that the primary long-range signal is mechanical rather than electrical. Specifically, it proposes the existence of a continuously propagating Action Pressure Wave (APW), whose interaction with neuronal structures generates the electrical events observed during axonal excitation.

The distinction is not between "electrical" and "mechanical" observations. Both are accepted. The distinction concerns their causal order.

The conventional interpretation can be summarized conceptually as:

Electrical excitation → ion-channel activation → ionic current → propagation of electrical excitation.

UMMN proposes instead:

Mechanical propagation → pressure-dependent channel activation → ionic current → local electrical manifestation

This represents a fundamentally different interpretation of the same physiological observations.

2. Relationship to Established Neuroscience

UMMN accepts the established existence of ion channels, ionic currents, membrane potentials, action potentials, sodium and calcium influx, myelinated axons, Nodes of Ranvier, synaptic transmission, and neurotransmitter release.

The model does not claim that these phenomena are imaginary, unnecessary, or incorrectly measured. The proposed departure concerns their causal role in axonal propagation.

In particular, UMMN does not assume that the voltage change conventionally identified as the action potential is necessarily the immediate physical stimulus

responsible for opening the relevant ion-channel gates during propagation. Instead, it proposes that the transiently inverted pressure differential generated by the APW may provide the immediate gating stimulus. This distinction is central to the present hypothesis.

The existence of voltage-gated ion channels is an established experimental fact. The additional proposition that transient pressure differentials contribute directly and causally to their activation during axonal propagation is a testable hypothesis.

3. Definition of the Action Pressure Wave

The Action Pressure Wave (APW) is defined in UMMN as a transient mechanical pressure disturbance that propagates along the axonal pathway. The term "pressure wave" is used to emphasize the proposed primary physical variable, rather than to imply a particular mathematical waveform before experimental measurements have established its precise characteristics.

The APW is expected to involve spatial and temporal changes in pressure within the axon. For the purposes of the present hypothesis, pressure is considered relative to two reference values: the local resting pressure within the axoplasm, and the pressure on the opposite (extracellular) side of the membrane.

The propagating wave is characterized by a biphasic pressure profile consisting of a positive-pressure front followed by a negative-pressure tail. Here, zero pressure is referenced to the resting intra-axonal pressure, which is physiologically maintained at a higher value. Accordingly, the negative-pressure phase of the wave represents a transient decrease in intra-axonal pressure below its elevated resting value, rather than an absolute negative pressure.

At rest, the intra-axonal pressure exceeds the extracellular pressure. During the negative-pressure phase of the wave, however, this relationship is transiently reversed: the intra-axonal pressure falls below the extracellular pressure, such that the pressure differential across the membrane inverts and the extracellular pressure now exceeds the intra-axonal pressure.

The term "pressure differential" is used throughout this model to denote the pressure difference between the intra-axonal and extracellular compartments, both at rest and during neural transmission.

It is this transiently inverted pressure differential – arising during the negative-pressure phase of the wave – that is hypothesized to generate a mechanical force acting on the channel-gating structures. This transient inversion of the pressure differential is the specific mechanical event proposed to trigger channel gating, and its temporal relationship to electrical activation is the subject of the Golden Test.

4. The Central Hypothesis

The central hypothesis of UMMN is that the primary long-range signal in an axon is a continuously propagating mechanical pressure wave.

Electrical activity remains essential for neuronal function, but during axonal propagation it is proposed to represent the local electrical consequence of a mechanically transmitted signal. This distinction constitutes the central conceptual innovation of UMMN. The electrical signal is therefore not eliminated from the model. Its role is reinterpreted.

The proposed causal sequence is:

Action Pressure Wave → transiently inverted pressure differential → mechanical channel-gate displacement → ion-channel opening → ionic current → change in internal charge → local electrical potential change (action potential)

5. Three Functional Phases of Neural Transmission

UMMN divides neural transmission into three broad functional phases:

Phase I – Electrical Initiation: *Synaptic inputs produce electrical changes in the dendritic and somatic compartments. When the integrated electrical activity reaches the axon hillock and threshold conditions are met, the mechanical transmission process is proposed to begin.*

Phase II – Mechanical Axonal Transmission: *A primary APW originates at the axon hillock and propagates continuously along the axon. The model does not*

propose that the primary signal disappears between Nodes of Ranvier, nor that it must be regenerated independently at each node; rather, the same continuously propagating mechanical disturbance travels through both internodal and nodal regions.

Phase III — Electrical Termination: *When the APW reaches the presynaptic terminal, its mechanical interaction with the terminal membrane and calcium-channel structures is proposed to generate calcium influx and the downstream events responsible for neurotransmitter release.*

The overall sequence is therefore:

Electrical input → mechanical transmission → electrical/chemical output

6. Proposed Initiation of the Action Pressure Wave

6.1 The axon hillock

*The axon hillock represents the proposed transition zone between electrical integration and mechanical axonal transmission. UMMN hypothesizes that the specialized cytoskeletal organization of this region generates two distinct mechanical events: a transient, soma-confined disturbance termed the **Central Action Pressure Wave**, and the propagating **Action Pressure Wave (APW)** that carries neural information along the axon.*

The candidate mechanism for both events is a microtubule-associated structure functioning as a mechanically active "nano-piston." This term is descriptive and hypothetical; it does not imply that a conventional piston-like structure has already been demonstrated experimentally in neurons. The mechanism by which this piston is proposed to operate is described in Section 6.2.

6.2 The nano-piston hypothesis

According to this proposal, the microtubular formation within the axon hillock operates as a mechanically active piston that generates all fluid displacements within the axon. Its operation is proposed to unfold in two stages.

In the first stage, an incoming electrical pulse drives the piston backward. This backward displacement generates the Central Action Pressure Wave, which sweeps through the somatic compartment and reflects from the somatic boundary.

In the second stage, the returning wave strikes the piston, driving it forward and restoring it to its initial position. This forward displacement generates the propagating Action Pressure Wave (APW).

The piston therefore operates in two distinct phases – a backward displacement generating the soma-confined central wave, and a forward displacement triggered by the wave's reflection generating the axonal APW. This mechanism remains one of the speculative components of UMMN and should be treated separately from the core proposition that a mechanical wave may propagate along the axon.

7. Proposed Generation of the Action Potentials

7.1 General Mechanism

The electrical event is hypothesized to arise when a mechanical pressure disturbance reaches a membrane region containing ion channels. This mechanism is proposed to operate at all three excitable sites along the pathway – the axon hillock, each node of Ranvier, and the terminal bouton – although the source of the negative pressure differs between sites.

*In all cases, the resulting negative-pressure phase is proposed to exert a **dual mechanical action**:*

- 1. **On the channel gate.** The pressure differential mechanically displaces the channel gate, opening the pore.*
- 2. **On the ions.** The same pressure differential draws positively charged ions inward **through the opened pore**, supplementing the electrochemical driving forces already present across the membrane.*

*The displacement of the gate and the suction of ions are therefore not two separate events in time: both are consequences of the same transient pressure inversion. The gate displacement, however, is the **necessary precondition** for ion flow, since no ions can pass while the pore remains closed.*

The resulting ionic current – driven by the combined action of the electrochemical driving forces and the suction force of the negative-pressure phase – produces a change in the internal charge of the cell relative to its resting value. This change in internal charge is in turn manifested as the local electrical potential change recorded at that site.

The proposed sequence is:

Negative-pressure phase → transiently inverted pressure differential → mechanical gate displacement → ion-channel opening → ionic current (driven by electrochemical forces and suction) → change in internal charge → local electrical potential change

This sequence is a hypothesis and requires direct experimental verification.

7.2 Site-Specific Differences in the Source of Negative Pressure

At the axon hillock, the negative pressure does not arise from an APW tail, since the APW has not yet been generated at this stage. Instead, it results directly from the backward displacement of the nano-piston, driven by the incoming electrical pulse. This backward displacement creates a local pressure reduction in the axoplasm of the hillock.

At the nodes of Ranvier and the terminal bouton, the negative pressure is generated by the tail of the propagating Action Pressure Wave. When the APW reaches these sites, its front produces a transient pressure increase, followed by the negative-pressure phase of its tail.

The specific ions involved differ by location – sodium at the axon hillock and nodes of Ranvier, calcium at the terminal bouton – but the underlying mechanical mechanism is proposed to be the same.

7.3 Types of Action Potentials in Neural Transmission

UMMN proposes that the same mechanical mechanism – a transiently inverted pressure differential acting on channel gates – generates three distinct electrical events at three distinct sites:

<i>Electrical Event</i>	<i>Site</i>	<i>Source of Negative Pressure</i>
<i>Initial Action Potential</i>	<i>Axon Hillock</i>	<i>Backward displacement of the nano-piston</i>
<i>Standard Action Potential</i>	<i>Each node of Ranvier</i>	<i>Tail of the propagating APW</i>
<i>Terminal Action Potential</i>	<i>Presynaptic bouton</i>	<i>Tail of the propagating APW</i>

Although the source of the negative pressure differs by site, the gating mechanism is proposed to be identical. The three events therefore share a common physical origin but differ in their anatomical location, their initiating trigger, and their downstream consequences.

8. Role of Electrical Activity

UMMN does not regard electrical activity as irrelevant after the initial mechanical event. Electrical activity is proposed to serve a specific function: preparing the pathway ahead of the propagating wave.

The proposed mechanism is as follows. When the APW reaches a Node of Ranvier (node N), its negative-pressure tail opens ion channels and recruits ions, building a positive polarity within the nodal plasma. This positive polarity faces an innate negative polarity present in the plasma of the immediately following internodal segment (segment N→N+1), that is, the segment lying ahead of the wave in its direction of propagation. The resulting potential difference generates an action potential whose effect is confined to that segment.

It is well established that action potentials can organize molecules within their field of influence. UMMN proposes that this molecular alignment and ordering increase the conductivity of the axoplasmic medium for mechanical wave transmission. In this way, the action potential prepares the pathway for the Action Pressure Wave

before the wave arrives, reducing energy losses and preserving its propagation speed.

A secondary hypothesis, termed the "liquid highway," formalizes this proposed facilitation mechanism. It is not required for the central model unless experimentally supported. Failure to demonstrate transient molecular reorganization would therefore require modification of the proposed facilitation mechanism, but would not, by itself, falsify the mechanical-first hypothesis.

9. Ion Channels and the Proposed Mechanical Gating Mechanism

The UMMN does not deny that neuronal ion channels are voltage-sensitive. The term "voltage-gated channel" remains appropriate as a description of their experimentally characterized voltage dependence.

*The hypothesis concerns the possibility that these channels may also respond mechanically to pressure differences under physiological conditions. Accordingly, UMMN proposes that the **transiently inverted pressure differential** may contribute directly to channel activation during axonal propagation.*

This proposition generates a clear experimental question, which is addressed by the Golden Test: Can the physiological transiently inverted pressure differential produce channel-gate displacement and channel opening independently of the membrane-voltage change that normally accompanies the action potential?

The answer to this question is critical. If the pressure differential is too small to influence channel gating, the proposed mechanism would require substantial revision. If, however, pressure change is sufficient and temporally precedes channel activation, the mechanical contribution would require serious consideration.

10. Ionic Currents in the UMMN Framework

UMMN explicitly accepts ionic currents as essential physiological phenomena. The proposed difference is their position in the causal chain.

In the conventional interpretation, ionic currents generated by voltage-dependent channels constitute the fundamental mechanism by which the action potential is propagated.

In UMMN, ionic currents are proposed to be local consequences of mechanically induced channel opening.

The distinction can therefore be stated simply:

Conventional interpretation:

Voltage change → channel activation → ionic current → electrical propagation

UMMN interpretation:

Pressure change → channel activation → ionic current → local electrical response

The ionic current therefore remains real and physiologically important. The proposed change concerns what initiates it.

11. Continuous Propagation of the Action Pressure Wave

Continuous propagation is a defining principle of UMMN. The model does not propose that the primary signal travels by jumping from one Node of Ranvier to another. Instead, the APW is proposed to travel continuously along the entire axonal pathway, including the initial axon, internodal regions, Nodes of Ranvier, and terminal axonal segments.

The wave therefore remains physically continuous even though the electrical manifestations associated with it may occur preferentially at specialized anatomical sites.

*This distinction is central to the model. The sequence of electrical action potentials observed at successive Nodes of Ranvier is therefore interpreted as a series of local electrical manifestations generated by a continuously propagating **Action Pressure Wave**.*

12. Nodes of Ranvier

The Node of Ranvier is proposed to function as a specialized mechanical-electrical transformation site rather than as a gap between successive electrical signals.

UMMN proposes three potential nodal functions:

I. Mechanical interaction: *The arriving APW interacts with the local membrane and structural environment.*

II. Wave regulation: The nodal architecture may influence the local shape, amplitude, or propagation characteristics of the APW, contributing to the standardization of the mechanical waveform as it travels between nodes.

III. Electrical manifestation: The negative-pressure phase produces the proposed pressure differential that mechanically influences sodium-channel gating. The resulting sodium current produces the local electrical action potential. The mechanical wave then continues beyond the node.

The overall nodal sequence can therefore be summarized as:

Continuous APW → nodal mechanical interaction → local pressure-dependent channel activation → local electrical response → continued APW propagation

The electrical response is therefore local, while the mechanical carrier remains continuous.

13. The Standard Action Pressure Wave

UMMN proposes that the APW originating at the axon hillock is initially irregular in waveform, reflecting the turbulent conditions of its generation. Its parameters – amplitude, duration, and spatial extent – are therefore proposed to be elevated and variable at this early stage.

The **first Node of Ranvier** is proposed to function as a calibration site: it transforms the irregular wave into a more reproducible waveform whose parameters are adjusted to standard values specific to each nerve fiber. This hypothetical waveform is termed the **Standard Action Pressure Wave**. This proposal extends the concept of wave regulation introduced in Section 12. II.

The term "Standard" parallels the designation of the Standard Action Potential at each node, reflecting the proposed standardization of both the mechanical waveform and its local electrical manifestation.

Subsequent nodes are proposed to serve a different function: rather than recalibrating the wave, they maintain its standard parameters and contribute to the regulation of its propagation pathway.

The term does not imply that the waveform has already been experimentally characterized. Its proposed features include:

- a positive-pressure phase;*
- a negative-pressure phase;*
- a characteristic duration, spatial extent, and propagation velocity.*

The Node of Ranvier may contribute to the stabilization or shaping of these parameters. This proposal should be investigated experimentally rather than assumed.

14. Myelin and Mechanical Propagation

Myelin has well-established electrical effects on axonal conduction. These include increased membrane resistance and reduced effective membrane capacitance, contributing to rapid conduction in myelinated fibers. UMMN does not dispute these effects. It proposes an additional possibility:

Myelin may influence the mechanical environment in which the APW propagates. Potential mechanical effects include:

- modification of axonal wall compliance (potentially reducing wall elasticity and thereby limiting radial dissipation of the pressure wave);*
- mechanical confinement of the axonal compartment;*
- resistance to morphological deformation of the axon during the passage of the pressure wave;*
- alteration of mechanical impedance;*
- reduction of mechanical energy loss;*
- stabilization and maintenance of the propagating pressure wave.*

In this interpretation, myelin may contribute not only to the speed of propagation but also to the preservation of the Standard Action Pressure Wave between successive nodes, complementing the maintenance function attributed to the nodes themselves.

Thus, myelin may have both electrical and mechanical relevance. The mechanical role remains hypothetical and requires quantitative investigation.

15. Why UMMN Does Not Invoke Saltatory Propagation of the Primary Signal

*As established in Section 11, the primary signal in UMMN is the Action Pressure Wave, which propagates continuously along the axon. The present section addresses a related but distinct question: what is the **nature** of the electrical events associated with this mechanical propagation, and how does UMMN's interpretation differ from the conventional concept of saltatory conduction?*

In the conventional description, the electrical action potential is regenerated at successive Nodes of Ranvier, and conduction is described as "jumping" from node to node. UMMN proposes a different interpretation, based on three principles.

First, the electrical events are secondary. *They are not the primary carrier of neural information, but local products generated when the continuously propagating APW interacts with excitable membrane regions.*

Second, the electrical events are local. *Their effects do not themselves extend along the axon. The electrical action potential recorded at a given node is a local manifestation; it is the mechanical wave – not the electrical event – that carries the signal forward to the next node.*

Third, the electrical events are functional. *They are not merely epiphenomena. As developed in Section 8, they serve a specific purpose: preparing the pathway for the Action Pressure Wave by organizing the molecular environment of the immediately following internodal segment, thereby facilitating mechanical propagation.*

This distinction can be summarized as follows:

<i>Aspect</i>	<i>Character</i>
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<i>Electrical manifestation</i>	<i>Secondary, local, and functional</i>
<i>Mechanical propagation</i>	<i>Primary and continuous</i>

The model therefore does not deny that electrical action potentials occur preferentially at Nodes of Ranvier. It proposes that these events are local products of a continuous mechanical process, and that their function is to facilitate the continued propagation of the APW itself.

16. Axonal Diameter and Conduction Velocity

Axonal diameter is known to influence conduction velocity. Within a mechanical framework, this relationship may acquire additional significance.

Changes in axonal diameter could influence:

- intracellular fluid resistance;*
- mechanical impedance of the axonal wall and surrounding medium;*
- wall compliance;*
- pressure-wave velocity;*
- attenuation;*
- dispersion.*

A larger axonal diameter permits a greater total mass of axoplasm per unit length of the axon. When accompanied – as it typically is in the living organism – by a thicker and stiffer myelin sheath, this geometry may allow the establishment of a higher resting intra-axonal pressure, and consequently the generation of Action Pressure Waves with greater amplitude, energy, and propagation velocity. The association between large axonal diameter and thicker myelin is therefore proposed to serve a functional mechanical role, reinforcing the conditions required for efficient pressure-wave propagation.

UMMN therefore predicts that some established relationships between axonal geometry and conduction velocity may be partly explainable through mechanical parameters. This is a quantitative prediction that should be tested rather than assumed.

17. Propagation Through Internodal Regions

A crucial prediction of UMMN is that an APW should exist within the myelinated internodal segments. The wave should not disappear after leaving one node and reappear at the next. Instead, it should remain continuously detectable.

A particularly important experiment would therefore measure the mechanical signal at multiple locations:

Node 1 → internodal region → Node 2

If the APW is the primary carrier, the mechanical waveform should show a continuous temporal progression between these sites, with the wave's arrival time at each location increasing monotonically along the axonal path.

Conversely, if the mechanical signal disappears in the internodal region and reappears only at the next node, this would support a purely nodal mechanism and challenge the continuous-propagation principle of UMMN.

This experiment could therefore provide an important distinction between a continuously propagating mechanical signal and a purely nodal electrical regeneration model. While the Golden Test addresses the temporal relationship between mechanical and electrical events at a single node, the present experiment addresses the spatial continuity of the mechanical signal between nodes.

18. Terminal Propagation and Calcium Entry

At the presynaptic terminal, the APW is proposed to interact with calcium-channel structures. The model predicts that the negative-pressure phase of the APW generates a **transiently inverted pressure differential** capable of mechanically displacing the calcium-channel gate.

The proposed sequence is:

Transiently inverted pressure differential → calcium-channel gate displacement → calcium influx (driven by electrochemical forces and suction) → terminal electrical response (the Terminal Action Potential)

This is conceptually analogous to the proposed sodium-channel mechanism along the axon, but the ionic species and physiological consequences differ.

The terminal mechanism remains experimentally unproven and should therefore be treated as a testable prediction.

19. Synaptic Transmission

The present model does not claim that the Action Pressure Wave is capable of crossing an open extracellular space, as is the case at the synaptic cleft; such a crossing lies beyond its capacity, since the Action Pressure Wave presupposes a confined medium capable of supporting its propagation.

It does, however, affirm the importance of the mechanical signal – embodied in the Action Pressure Wave – in generating a pressure differential at the level of the terminal bouton. This pressure differential is capable of opening calcium-channel gates and generating a Terminal Action Potential. The latter is responsible for ensuring the transmission of the neural signal to the opposite side of the synaptic cleft.

Thus, the neural impulse that reached the neuron as an electrical pulse departs from it as an electrical pulse as well. What occurs within the axon – between entry and exit – is purely mechanical transmission, and this is what distinguishes UMMN from the conventional model. The Action Pressure Wave is the sole carrier of the signal from its origin at the axon hillock to its endpoint at the terminal bouton.

The present manuscript does not address the role of the chemical neurotransmitter in synaptic transmission; this is the subject of a separate manuscript, to be presented in due course.

20. Proposed Functional Sequence

The complete UMMN sequence can be stated in plain language:

At the axon hillock:

- 1. Synaptic input produces electrical activity in the neuron.*
- 2. The integrated electrical signal reaches the axon hillock.*
- 3. An incoming electrical pulse drives the nano-piston backward.*
- 4. The backward displacement creates a local pressure reduction that opens sodium channels, generating the Initial Action Potential.*
- 5. The same backward displacement generates the Central Action Pressure Wave, which sweeps through the soma and reflects.*
- 6. The returning wave drives the piston forward, generating the Action Pressure Wave (APW).*

Along the axon:

- 7. The APW propagates continuously along the axon.*
- 8. At each Node of Ranvier, its negative-pressure phase generates a transiently inverted pressure differential across ion-channel gating structures.*
- 9. The pressure differential mechanically displaces the channel gate and draws ions inward through the opened pore.*
- 10. Ionic current occurs locally.*
- 11. The ionic current produces a change in the internal charge of the cell relative to its resting value.*
- 12. This change in internal charge is manifested as the local electrical potential change recorded as the Standard Action Potential.*
- 13. The APW continues through the next internodal region, and the process is repeated at subsequent Nodes of Ranvier.*

At the presynaptic terminal:

- 14. The APW reaches the presynaptic terminal.*

15. Mechanical activation of calcium-channel structures produces calcium influx.

16. The resulting Terminal Action Potential ensures transmission of the signal across the synaptic cleft.

This sequence represents the proposed causal architecture of UMMN.

21. Comparison With the Conventional Framework

<i>Feature</i>	<i>Conventional interpretation</i>	<i>UMMN</i>
<i>Primary long-range carrier</i>	<i>Electrical action potential</i>	<i>Mechanical Action Pressure Wave</i>
<i>Ion-channel activation</i>	<i>Primarily voltage-dependent</i>	<i>Proposed contribution from pressure differential</i>
<i>Ionic current</i>	<i>Central component of propagation</i>	<i>Local consequence of channel activation</i>
<i>Membrane potential</i>	<i>Central electrical variable</i>	<i>Local electrical manifestation and physiological participant</i>
<i>Myelinated conduction</i>	<i>Saltatory electrical conduction</i>	<i>Continuous mechanical propagation with nodal electrical manifestations</i>
<i>Node of Ranvier</i>	<i>Site of action-potential regeneration</i>	<i>Mechanical-electrical transformation site</i>
<i>Internodal region</i>	<i>Site of passive electrical</i>	<i>Proposed pathway of continuous APW</i>

	<i>spread</i>	<i>propagation</i>
<i>Myelin</i>	<i>Electrical insulation and capacitance control</i>	<i>Established electrical role plus proposed mechanical role</i>
<i>Long-range signal</i>	<i>Successive electrical action potentials</i>	<i>One continuously propagating mechanical wave</i>
<i>Central experimental discriminator</i>	<i>Electrical sequence</i>	<i>Pressure-gating-current-voltage sequence</i>

The table summarizes the principal conceptual difference.

UMMN does not merely add mechanical phenomena to conventional neuroscience. It proposes a different causal hierarchy.

22. Existing Evidence for Mechanical Events During Neural Excitation

Mechanical changes associated with neural excitation have been experimentally observed. Earlier studies reported transient changes in nerve-fiber dimensions and mechanical pressure during action potentials.

Subsequent work demonstrated that mechanical waves can accompany action-potential propagation. The existence of these mechanical phenomena provides an important basis for considering mechanical contributions to neural conduction.

However, correlation does not establish causation. The observation that a mechanical signal accompanies an action potential does not by itself demonstrate that the mechanical signal causes the electrical event.

UMMN therefore requires a stronger test: Does the mechanical pressure change precede and causally influence ion-channel activation?

This is the central unresolved question – and the central question addressed by the Golden Test described in Section 25.

23. Distinction From Existing Electromechanical Models

Several theoretical models have proposed interactions between electrical and mechanical processes in nerve fibers. These models provide an important conceptual background for UMMN.

The principal distinction is the causal role assigned to the mechanical component. Three broad possibilities can be distinguished:

- I. **Electrical-first:** electrical excitation produces mechanical effects.*
- II. **Bidirectional coupling:** electrical and mechanical processes influence each other, without either being assigned causal primacy.*
- III. **Mechanical-first:** mechanical propagation produces the electrical manifestations.*

UMMN belongs to the third category. Its central proposition is therefore not simply that "action potentials have mechanical correlates." It is that the mechanical component is proposed to constitute the primary long-range carrier.

24. The Central Experimental Test

The decisive experiment should focus initially on a single Node of Ranvier – the most technically accessible site – and simultaneously measure:

- 1. local intracellular and extracellular pressure;*
- 2. intracellular charge;*
- 3. ionic current;*
- 4. where technically feasible, ion-channel conformational or gating dynamics.*

The predicted temporal sequence is:

***Transiently inverted pressure differential → mechanical gate displacement
→ ion-channel opening → ionic current → change in internal charge***

The experiment must control carefully for:

- sensor latency;*

- *spatial separation between measurements;*
- *signal-processing delays;*
- *filtering artifacts;*
- *mechanical disturbance caused by the measuring apparatus;*
- *temperature effects;*
- *membrane damage;*
- *alterations caused by the experimental preparation itself.*

While the initial experiment should focus on a single Node of Ranvier, the same protocol should subsequently be applied to the axon hillock and the terminal bouton.

Temporal precedence alone would not be sufficient. The pressure differential must also be quantitatively capable of influencing channel gating, and experimental manipulation of the pressure should predictably alter channel activation.

25. The Golden Test

The most important proposed test of UMMN is therefore: At a Node of Ranvier, does the APW-associated pressure change occur before ion-channel activation and the resulting ionic current and change in internal charge?

A strong positive result would require all of the following:

- *reproducible mechanical precedence;*
- *direct evidence of channel-gate response;*
- *sufficient pressure magnitude;*
- *predictable changes in channel activation when pressure is experimentally manipulated;*
- *persistence of the relationship across multiple nodes.*

Such evidence would provide strong support for a mechanical-first interpretation of axonal conduction. Conversely, failure to demonstrate reproducible mechanical

precedence, or failure of mechanical manipulation to alter channel activation, would challenge the mechanical-first hypothesis and support an electrical-first or bidirectional interpretation.

26. Falsifiability

UMMN is explicitly intended to be falsifiable. The following observations would challenge or potentially falsify the central model.

26.1 Electrical precedence

If electrical activation consistently occurs before the relevant pressure change, the proposed mechanical-first sequence would be strongly contradicted.

26.2 Insufficient pressure

If measured physiological pressure changes are quantitatively incapable of influencing ion-channel gating, the proposed mechanism would require rejection or major revision.

26.3 Absence of continuous APW

If a mechanical wave cannot be demonstrated to propagate continuously through internodal regions, a central prediction of the model would fail.

26.4 Independence of electrical propagation

If electrical action potentials can propagate normally despite experimental elimination or substantial disruption of the proposed APW, the proposed causal hierarchy would be weakened substantially.

26.5 Lack of pressure dependence

If experimentally changing the relevant pressure change has no effect on channel activation under otherwise controlled conditions, the proposed pressure-gating mechanism would be challenged directly.

27. Experimental Program

A progressive experimental strategy is proposed.

Stage 1 – Detection: *Develop methods capable of measuring the APW with high temporal and spatial resolution.*

Stage 2 – Propagation: *Measure the mechanical waveform at multiple locations along the same axon, including internodal regions.*

Stage 3 – Temporal ordering: *Determine whether mechanical changes precede electrical activation.*

Stage 4 – Channel gating: *Measure channel-gating dynamics relative to the pressure waveform.*

Stage 5 – Mechanical manipulation: *Manipulate the pressure change independently of membrane voltage wherever technically possible.*

Stage 6 – Causal validation: *Determine whether changes in the mechanical signal predictably alter ionic currents and electrical activation.*

Stages 3 through 6 correspond directly to the Golden Test described in Section 25, which addresses the temporal and causal relationship between pressure change and electrical activation. The later stages are essential because detection and correlation alone cannot establish causation.

28. Auxiliary Hypotheses

Several components of UMMN are potentially important but are not necessary to establish the central hypothesis.

These include:

- the proposed nano-piston mechanism at the axon hillock;*
- mechanical shaping of the APW by Nodes of Ranvier;*
- mechanical stabilization by myelin.*

These should be tested independently. Separating the core hypothesis from auxiliary mechanisms is important for rigorous scientific evaluation.

29. Limitations

The UMMN remains a hypothesis and contains several speculative elements.

First, the proposed APW must be characterized quantitatively in living axons.

Second, the magnitude of physiological pressure changes must be measured directly.

Third, it must be demonstrated that these pressure changes are sufficient to influence the gating of relevant ion channels.

Fourth, continuous APW propagation through internodal regions must be demonstrated.

Fifth, the proposed nano-piston mechanism remains hypothetical.

Sixth, the exact mechanical role of myelin and Nodes of Ranvier remains to be established.

These limitations correspond directly to the experimental stages outlined in Section 27, which are designed to address each of them systematically.

Finally, even if a mechanical wave precedes electrical activity, this would not automatically prove that it is the sole mechanism of neural conduction. Neural signaling may ultimately prove to involve a coupled electromechanical system in which both components contribute causally.

UMMN should therefore be evaluated experimentally rather than treated as an established replacement for electrophysiological theory.

30. Discussion

The principal contribution of UMMN is a change in causal perspective. The model does not dispute the extensive experimental evidence demonstrating voltage changes, ion-channel activation, ionic currents, and action potentials. Instead, it asks whether these phenomena necessarily define the primary physical carrier of information along the axon.

The existence of mechanical changes during excitation provides a plausible basis for investigating this possibility. The central question is not whether electrical and mechanical phenomena coexist. They clearly do.

The central question is: Which process is causally upstream during axonal propagation?

If the sequence is:

Voltage change → channel opening → ionic current → propagation

then the conventional electrical framework remains sufficient.

If instead the sequence is:

Pressure change → channel gating → ionic current → change in internal charge → voltage change

and the pressure wave propagates continuously along the axon, then the causal architecture of axonal transmission would be substantially different from the conventional interpretation.

UMMN proposes that this second sequence is the correct one, and that the experimental program outlined in this manuscript is designed to test this proposition directly.

31. Potential Significance

If experimentally validated, UMMN would have implications for several areas of neuroscience. It could provide a unified physical framework connecting:

- axonal mechanics;*
- ion-channel gating;*
- ionic currents;*
- action potentials;*
- myelin;*
- Nodes of Ranvier;*
- axonal geometry;*
- and synaptic transmission.*

It could also provide a new perspective on why mechanical changes accompany action potentials and why axonal structural properties influence conduction velocity.

However, these implications should not be regarded as established consequences until the central mechanical mechanism has been experimentally demonstrated.

32. Conclusion

The Unified Mechanical Model of Neurotransmission proposes that the primary signal travelling along an axon is a continuously propagating Action Pressure Wave.

The model accepts the established existence and physiological importance of ion channels, ionic currents, membrane potentials, and action potentials.

Its central proposal is a different causal interpretation.

*The APW is proposed to generate a **transiently inverted** pressure differential across ion-channel gating structures. During the negative-pressure phase, extracellular pressure **is proposed to** transiently exceed intracellular pressure across the relevant gate. This pressure differential is hypothesized to mechanically displace the gate and draw ions inward through the opened pore. The resulting ionic current then produces a change in the internal charge of the cell, which is manifested as the local electrical event detected as an action potential.*

The proposed sequence is therefore:

Action Pressure Wave → transiently inverted pressure differential → mechanical gate displacement → ion-channel opening → ionic current → change in internal charge → local electrical potential change (action potential)

The mechanical signal is proposed to propagate continuously along the axon, including through internodal regions.

The Nodes of Ranvier are therefore not proposed to be gaps between which the primary signal jumps. Rather, they are proposed to be specialized sites where the

continuously propagating mechanical signal produces localized electrical manifestations.

The central prediction of UMMN is experimentally precise:

The mechanical pressure change should precede the relevant channel-gating event, ionic current, and change in internal charge.

This prediction can be tested. The model should therefore not be accepted or rejected solely on theoretical grounds. Its scientific status should ultimately depend on direct measurements capable of resolving the temporal and causal relationship between pressure, channel gating, ionic current, and the local electrical potential change.

If such experiments demonstrate mechanical precedence, quantitative sufficiency, and causal control of channel activation, the results would provide significant support for a mechanical-first interpretation of neural conduction.

If they fail to do so, the hypothesis must be revised or rejected.

The essential proposition of UMMN is therefore: The electrical action potential may be the local electrical expression of a continuously propagating mechanical signal rather than the primary physical carrier of that signal.

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