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A quantum biological hypothesis of human secondary dentinogenesis

M.L. Moss[a,b,*], L. Moss-Salentijn[a,b], G. Hasselgren[b], H. Ling[c]

[a] *College of Physicians and Surgeons, Columbia University, 630 West 168th Street, New York, NY 10032, USA*
[b] *School of Dental and Oral Surgery, Columbia University, 630 West 168th Street, New York, NY 10032, USA*
[c] *Department of Civil Engineering and Engineering Mechanics, Fu Foundation School of Engineering and Applied Sciences, Columbia University, 500 West 120th Street, New York, NY 10027, USA*

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Summary It is hypothesized that human coronal secondary dentin (SD) is a final classical mechanical (CM) response to a chain of prior quantum mechanical (QM) transductions of the information of initial CM occlusal loadings of enamel. Such CM energy is transduced into QM quanta (as protons) that are translocated centripetally via clustered water (CW), (as ''proton wires''), that is structurally related to both enamel prism sheath and hydroxyapatite crystal hydration shells.

These quanta pass into odontoblastic cell processes (OP), lying within dentinal tubules (DT). OP's contain abundant parallel arrays of cylindrical microtubules (MT). These are the sites of two further CW-related QM events: (i) proton translocation associated with conformal changes of MT tubulin protein dimers; and (ii) coherent energetic oscillations within the CW filling the MT's hollow cores.

Finally, these quanta pass into the odontoblastic soma, where QM wave function collapse transduces this information into a final CM state that initiates the processes of SD formation.

A critical portion of this hypothesis may be experimentally tested.

Introduction

A theoretical, scale constrained, dichotomy underlies contemporary science. One category holds that supra-atomic phenomena manifest deterministic actions of macroscopic CM processes; the other, that they express insensible, stochastic, microscopic, QM processes occurring at more fundamental levels. Most biomedical sciences, and explicitly mineralized tissue research, study macroscopic CM phenomena. Microscopic problems involve a series of quantum disciplines [1]. For example, one biomedical quantum biological hypothesis suggests

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[*] Corresponding author. Address: Department of Anatomy and Cell Biology, Columbia University, 630 West 168th Street, New York, NY 10032, USA. Tel./fax: +1 212 305 5647.
E-mail address: mlm7@columbia.edu (M.L. Moss).

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that human consciousness is associated with QM events occurring in molecular structures located within, or adjacent to, neurons [2—4].

While a comprehensive explanation of information processing in mineralized tissues is absent in extant CM literature [5—7], parsimony suggests the hypothesis that QM processes may act similarly in human neurons and scleroblasts. The theoretical and experimental bases of this hypothesis are sketched here, with the role of odontoblasts in the formation of secondary dentin serving as an explicit example.

Secondary dentin

The literature uniformly describes odontoblastic dentinogenesis solely as a series of CM processes [8,9].

Secondary dentin (SD) commonly is formed in erupted, functionally occlusal, non-carious, permanent human teeth (Fig. 1), after the completion of normal dentinogenesis. Characteristically it is deposited, in discreet areas of the pulpal wall, by odontoblasts subjacent to a specified functionally loaded enamel surface [10].

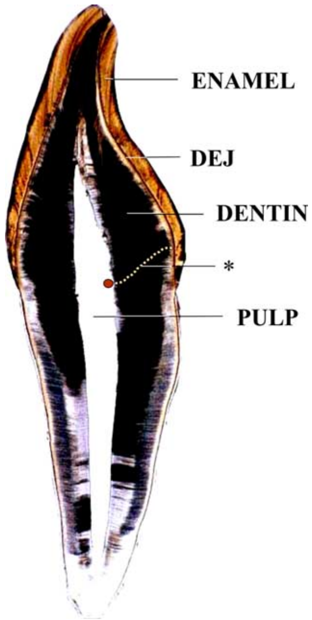

Figure 1 Central section through an incisor tooth showing an enamel-covered crown and a cementum-covered root. Dentin and pulp comprise most of the volume of the tooth. DEJ: dentino-enamel junction. $*$: course of a dentinal tubule. The ovoid marks the location of the related dentin-forming cell (odontoblast) at the pulpal surface of the dentin.

SD differs etiologically and histologically from the tertiary (reactive, reparative, irregular secondary) dentin that is a response to pathological stimuli (e.g., dental caries); as textually described [11].

The structural bases in enamel for QM proton translocation

Enamel

Intact vital enamel has a minute, yet operationally significant, amount of organic materials and ''water'' [12]. It lacks collagen and any microscopic ''tubular'' or ''canalicular'' structure: its ''porosity'' is of a different order and structure from that of bone [13].

Enamel prisms

Enamel is organized as prisms (rods) formed by ameloblasts. They are oriented as a 3-D continuum, that neither branch nor merge, but run from the outer tooth surface to the DEJ. Prisms may be several millimeter long; with diameters of 4—5 μm.

Enamel prism sheaths

Organic sheaths surround individual prisms, averaging 0.1—0.2 μm wide. They are composed of the O-linked glycosylated protein ameloblastin (amelin, sheathlin). Postsecretion, this is proteolytically cleaved, and accumulates in these interprismatic sheaths.

Prismatic hydroxyapatite crystallites

Prisms are domains of highly ordered bundles of finer-scaled biological crystallites. Each crystallite is associated structurally with the protein enamelin, whose fragments remain attached to individual crystallite surfaces after normal postsecretory cleavage. Each crystallite is surrounded by a hydration shell.

Clustered water in enamel

Enamel's clustered water (CW) exists at two structural levels: prism sheaths and hydration shells. CW is alternatively termed: confined water, constitutional water, highly restricted water, cytoplasmic water, vincial water, low and high density water, ordered water, interstitial water, bound water, supramolecular aggregates or clusters [14—16]. CW is preferred here since it semantically suggests its molecular geometrical structure.

CW differs uniquely from the bulk water in both its physical and chemical attributes [14]. CW exhibits long-range order; it may form an infinite hydrogen-bonded network, with localized, supramolecular aggregates or clusters: ''the assumption that essentially all intracellular water has ideal osmotic and motional behavior is not supported by experimental findings'' [17].

Proton transmission

Proton transmission through CW is a QM phenomenon [18]. CW's hydrogen bonds acts as quasi one-dimensional pathways for the translocation of protons over large distances in proteins. The postulated mechanism for proton wires is ''... that a proton is deposited at one end of a water chain and is transported to the other end of the chain through a series of proton transfer steps.'' [18,19].

And, ''... proton transfer through a hydrogen bond is a ubiquitous phenomenon, influencing dynamical behavior in a wide variety of systems ranging from materials science to biochemistry. For example, ... water wires are crucial in the function of membrane protein channels ... (that) ... utilize proton transduction as one of its fundamental steps'' [20].

QM events in enamel associated proton translocation

Imposition of CM occlusal loads

Imposed mechanical loads is one mechanism capable of initiating proton transmission through CW. ''Information'' is created by the application of CM occlusal loading forces of normal magnitudes (20—100 N) to the coronal enamel.

The initial QM transduction

Enamel's CW responds to such loads by initiating quantum proton currents within the nanoscaled microdomains of CW associated with both prism sheath proteins and crystallite hydration shell. This QM event transduces CM energy into QM informational quanta.

Importantly, very weak signals of mechanical pressure are readily amplified and propagated by a modulation of proton currents. Both CW sites act as a proton wire through which the proton currents flow pulpally (centripetally).

Proton transmission of information

While ''information'' is not consensually defined, ''... energy and information are interconvertible ... all expenditures of energy lead to a change (of) information status.''; and importantly, ''... information, like energy, may exist in a variety of forms. Two major classes of energy are structural and kinetic'' [21].

Dentino-enamel junction

The present QM hypothesis posits the passage of informational quanta through the dentino-enamel junction (DEJ): the common plane from which ameloblasts and odontoblasts move oppositely during odontogenesis. Hydroxyapatite mineralizes both compositionally different organic matrices; albeit quantitatively differently [22].

While DEJ structure is uncertain, a nanoscale approximation of the two crystalline domains is certain. In one view, the two domains are continuous; ''such areas of crystal intimacy show a co-localization of calcium and phosphorous extending from the calcified collagen fibers to enamel sheaths'' [23]. While an alternate view, suggesting no interdomain continuity [24], notes the ''existence of a proteinaceous continuum between enamel and dentin'' [25].

The present hypothesis requires the transmission of informational quanta across the DEJ, whether or not there is direct crystallite continuity. It is possible that either of the two enamel CW sites (prism sheaths and/or crystallite hydration shells) connect directly with analogous sites in dentinal crystallites, or protons could cross the DEJ through CW associated with the proteinaceous continuum.

Dentinal structures associated with proton translocation

The phylogeny, histology and composition of dentin is closely similar, but not identical, with bone [26].

Dentin's mineralized organic matrix contains abundant DT, each enclosing an odontoblastic process (OP); a state similar to an osseous intralacunar canaliculus containing an osteocytic cell process. OP's have an abundant parallel longitudinal array of MT, similar to that of neuronal axons [9]; it is not known if they are similarly polarized. CW is intimately associated with the OP's MT's; and also with the hydration shells of the matrices' collagen fibers and hydroxyapatite crystallites.

Dentinal tubules

As in all mineralized matrices, dentinal tubules (DTs) form about preexistent organic structures; i.e., the original diameter of the DT closely approximates that of its original OP. A periprocessal space, (PS) (0.2—0.4 μm) is between the OP membrane and the DT wall.

DT and its enclosed OP, while structurally more complex and of greater diameter, are operationally similar to bone canaliculi and cell processes [6,27,28].

Odontoblastic process

Typical odontoblasts are unipolar, and best-typified coronally. In orthodentinogenesis, each cell moves centripetally from the DEJ, trailing a single OP filled with microfilaments and MT.

The extent of the mature OP

Initially a DT contains an OP along its entire length; with occasional nerve fibers, lipid droplets and ''fibrillar materials'' in the PS. The extent of the OP is unsettled. Some hold that the OP initially fills the entire DT; while in mature dentin, due to some centripetal ''retraction'', the OP extends only into the inner 1/4 of tubule length [29], and the remaining DT is filled with dense concentrations of fine granular ''materials''; including tubulin and actin. Others report and depict that the OP is continuously present through the entire DT length, including all its branches [30]. Such published photomicrographic data suggests that the OP is present, and functional, through the entire DT in mature, healthy dentin; since 'no preparation method is known to cause the OP to extend peripherally beyond its normal biological length.' The pernicious influence of preparation artifacts on cytoplasmic structure is well established.

Mantle dentin

This layer, subjacent to the DEJ, exhibits extensive, arborizing, ''delta'', peripheral branching; offering many pathways for information flowing across the DEJ; accordingly each OP is connected to a DEJ surface area larger than its own diameter.

Odontoblastic soma

The fully differentiated human odontoblast is a polarized columnar cell, approximately 50 μm tall, with non-secretory (basal, proximal) and secretory (apical, distal) ends. The nucleus is located basally, mitochondria and organelles associated with protein synthesis (well developed RER and Golgi complexes) are found apically. Odontoblasts are connected extensively with each other, and with a subodontoblastic layer, by desmosomes and gap junctions.

The OP and the soma are separated by a ''terminal web'' of microfilaments. Normally vital odontoblasts remain throughout life on the dentin's pulpal surface, although there are distinct age related, and topological, histological differences.

Correspondence between odontoblasts and neurons

The axons and dendrites, of all neuronal cell types, function identically to transmit information, either to or from the soma. In addition to dentinogenesis, odontoblasts similarly transmit, or are involved in, many other types of CM (and probably QM) physiological activities not considered further here.

Odontoblastic shapes resemble certain neurons whose soma also ''... has one primary process that may give rise to many branches... these cells predominate in invertebrate nervous systems, but may also occur in certain ganglia of the vertebrate autonomic nervous system.'' [31].

MT in OP

MT's are the most prominent cytoskeletal element in the OP [32] associated with actin and intermediate filaments. Human OP-MT have a dense parallel array similar to that in neurons [9,31]. The generalized CM cellular physiological functions of MT are independent of their QM roles considered here [33].

An MT is a hexagonal lattice polymer of subunit tubulin globular dimers (8 nm × 4 nm × 4 nm), consisting of alternately arrayed subunits of α-tubulin and β-tubulin. These dimers are electrolets, with oriented assemblies of dipoles with piezoelectric and ferroelectric properties [34]. Their structure, location and composition are determined by 3-D X-ray crystallography and by immunofluorescence staining, among other methods [35].

MT's are polarized with (−) and (+) ends; terminating with α and β subunits respectively [36]. New dimers assemble at the faster growing (+) end. Tubulin subunit structure (GTP with α and GDP with β) was reviewed recently [37]. Each has a large hydrophobic region, a non-polar pocket of amino acid side groups within which additional quantum mechanical activities regulate protein conformational changes.

Microtubule associated protein

MT's are intimately attached to microtubule associated proteins (MAP), forming 3-D, MT-MAP networks that define cell architecture and functions. Significantly, MAP, forming the interconnections between successive MT in the OP, creates an uninterrupted structural pathway within which QM events (protons) may pass centripetally into the odontoblastic soma [38].

In a typical human axon all MT's have a parallel array and similar polarity, (−) ends towards soma; this is not true in dendrites (111). Axonal information flow from the soma (whether by membrane depolarization or by MT's) is unidirectional, paralleling the MT orientation and from (−) to (+).

Parsimony suggests a similar correlation between OP-MT arrays and direction of information flow in SD genesis. Below we describe an experimental test of the hypothesis that the MT in OP have their (+) ends facing the odontoblastic soma. That is, that the QM informational flow, regulative of SD, passes to the soma through MT from (−) to (+).

QM events in MT associated with proton translocation

Six MT attributes support QM events: i.e., (i) high prevalence, (ii) functional importance, (iii) periodic, crystal-like structure with long-range repeat, (iv) ability to be transiently isolated from external interaction/observation, (v) functionally coupled to quantum-level events, and, (vi) suitable for information processing (2).

Several modes of MT information processing offer intuitively comprehensible biological concepts, and are the bases for the present hypothesis [2,3,15,39–42]. These models suggest that two topographically distinct QM events may occur in the OP MT; both are hypothesized to transmit information through the dentin into the odontoblastic soma.

These sites are (i) the unit elements (tubulin dimers) of the cylindrical MT ''wall''; and (ii) the enclosed spatial volume of that same cylinder. (i) involves proton transmission associated with changes of protein conformational charge of tubulin dimers; (ii) involves quantum coherent oscillations of pumped protons. The QM superpositioned states, in both sites, arise, are isolated in, and ''collapse'' in MT. Both sites, MT wall dimers and MT internal cylinder volume, are associated with CW.

CW in MT of dentin

MT's are embedded in ''cages'' of CW that act to isolate MT, their information, and the quantum events within them, from ''environmental effects''. With respect to the MT external surface, all vital biochemical reactions take place within 2 nm of a protein surface. The equivalent of two to eight layers of CW molecules extend beyond these surfaces, existing as transient ''flicker clusters''.

With respect to coherent oscillations, CW fills the core of neuronal MT: presumably true also for OP MT. This is the structural basis for the oscillations that arise from an interaction between the electric dipole field of the confined CW in the core and the electromagnetic field of the MT wall dimers [2,3,15,40,41].

QM events in MT dimers

Tubulin dimers exhibit two alternate molecular conformations, termed and depicted as ''open'' and ''closed''. These two dimer states reflect alternate positions of a pair of quantum coupled protons (or electrons); a condition correlated with the presence of the aromatic amino acid residues of tryptophan and histidine.

These residues have a highly polarizable and resonant ring structure, in which protons (and electrons) are mobile, and transfer occurs within and among them. The residue locations in MT are arrayed in pathways that match the helical patterns of the tubulin lattice structure; patterns suggested to ''... lead to topological quantum effects resistant to decoherence'': this model is extensively discussed and sketched [3].

Information is transmitted along tubulin chains. Cooperation among tubulins bound in MT locations could coordinate conformational changes, and thus support the propagation of wave-like signals in the MT [2].

The alternate dimer configurations permits their quantum superposition before one is ''selected'';

i.e., it is the site of a QM wave function collapse [41–45].

The conformational state of each dimer allows all kinds of informational messages to be propagated and processed along the length of each MT. These signals are transmitted by the various interconnections between neighboring MT's; in the form of bridge-like MAP's.

MT dimer protein folding

The alternate conformational states of tubulin dimers is a specific example of the general topic of the role of protein folding and QM informational processing.

The main driving force in protein folding is produced as uncharged non-polar amino acid groups joined together, repelled by solvent water, causing the formation of hydrophobic groups in the protein molecule. Such groups mutually attract, and reside in the protein's interior, as hydrophobic pockets.

QM events in MT core

This section is based upon concepts developed by Jibu [40,41,44].

The ordered water within the hollow MT core is coupled to the MT walls. This is the postulated site of wave-like coherent oscillations. This is produced by an interaction between the electric dipole fields of the CW in the MT core, producing a quantitized electromagnetic field. In this sense the MT acts as a non-linear coherent optical device; i.e., like a wave guide. This creates a QM ordering phenomenon producing coherent quantum oscillations, followed by a collapse of wave function.

'It is significant that the inner diameter of the MT hollow core (15 nm) is precisely that calculated to be the radius of self-focusing filamentous energy beams of coherent electrical waves within MT' [46].

There is experimental evidence for such coherent oscillations in biological systems [47–50].

Quantum-classical transduction

When the information, transduced and transmitted by the QM events and processes sketched above, reach the odontoblastic soma, a final QM-CM transduction occurs. This is the operational equivalent of a ''collapse of wave function''. It is in this CM form that the information now enters the molecular pathways that initiate the genomically regulated processes formative of SD: these matters are beyond our present scope.

It is noted that an identical theoretical sequence of informational transformations with respect to consciousness is hypothesized [2]; i.e., an initial CM state leads first to a QM state of superposition that, in turn, is followed by a collapse to a final CM outcome state. A similar CM—QM—CM chain is postulated to occur in SD formation.

Pertinently, recent studies indicate that certain, relatively large, biomolecules exhibit QM wave behavior under specific experimental conditions; e.g., C_{60}, ''... an almost a classical body'', exhibits quantum wave superposition [51].

The implications of the present hypothesis for the further study of other mineralized tissues are noted.

Proposed immuno-fluorescent testing of odontoblastic MT

It is of interest to determine if MT orientation is identical in axons and OP. Fluorescent cytoskeletal fusion proteins will visualize their locations and orientations in living cells [52,53]. Explicitly, the (+) end of MT selectively stain with a specific fluorescent tubulin preparation: tetramethylrhodamine-labeled tubulin and GTP-coated beads prepared with green-fluorescent microspheres [54].

Should the OP MT exhibit an orientation similar to that of axons, topics of significant interest will emerge.

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