## Biomechanical and bioelectrical effects regulate the adaptation processes in cortical bone

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**Cortical bone adaptation** is a summary of physiologically permissible processes that are aimed to maintain and preserve the genetically predetermined (defined) homeostasis. **Bone tissue adaptation processes** are primarily influenced by external and internal biomechanical effects (at all eight structural levels) that initiate the both biochemical and bioelectrical processes at the nano level. **Adaptation processes in bone tissue** can be classified from a time point of view as short-lived processes (lasting several months) and long-lived processes -evolutionary (ongoing in a chain of several generations, i.e. decades / centuries). **Short-term adaptation** processes are tissue modelling, while preserving genetically predetermined anatomical shapes and functions. **Long-term adaptation processes** are considered processes of evolution.

## Biomechanoelectric effects can be briefly described by the following axioms:

(1) External mechanical stimuli (i.e. forces, bending moments, torsional moments) initiate in differential element ( $dx_i dy_i dz_i$ , i = 1, 2, 3...8) of each i-th bone level (**Fig. 1**) the stress/strain states (generally). These states can be defined by tensors exactly.

NANOSTRUCTURE			SUBMICROSTRUCTURE		MICROSTRUCTURE	MEZOSTRUCTURE	MACROSTRUCTURE
1. level	2. level	3. level	4. level	5. level	6. level	7. level	8, level
< 1µm			1 – 10 µm		10 - 500 µm	500 µm - 10 mm	> 10 mm
tropocollagen molecule + HA crystal /crystals	system of sub- nanofibrils	system of parallel mineralized nanofibrils (nanorods)	system of mineralized nanoshalls	system of mineralized microfibres	system of osteonal lamellas	system of asteans	femoral bone
50x25x3 nm	80 - 140 nm		R				Y
subnanofibril diameter of 1,23 nm)	mineralized nanofibrii (nanorod), diameter of ca 80 - 140 nm	mineralized nanoshali	mineralizad microfibre (microcolumn)	lamella of osteon/ (mineralized column wall)	osteon	population of osteons	proximal diaphysis
		Stru	ctural levels	in cortical fer	noral bone		

**Fig. 1** Structural levels in cortical femoral bone. Each structural level is defined by one (typical) structural domain, which is always shown below each figure. Populations of the same domains at a lower structural level create a new domain at a next higher structural level.



(2) Structural domains on the 8<sup>th</sup> structural level (i.e. the macro-level) create the anisotropic right-handed and left-handed helical structures, **Fig. 2**).

Fig. 2 The scheme of orientations of principal (main) longitudinal axes of osteons in the walls of the femur.

- (3) In the left wall of the *right* femoral diaphysis, the longitudinal osteon axes are tangents to the left-handed helix and, in the right wall, to the right-handed helix, **Fig. 2**.
- (4) Longitudinal axes of osteons in the Haversian bone are oriented in the directions of *dominant* 1<sup>st</sup> principal stresses and ca in the directions of *dominant* 1<sup>st</sup> principal deformations also (Fig. 3). Note: The meaning of the word "dominant" means "long-acting" principal (main) stresses / strains.

- (5) The 1<sup>st</sup> principal stresses in the ideal state of the bone remodeling equilibrium are approximately identical with the first principal axis of anisotrophy, with the longitudinal axis of osteon and with the directions of dominant 1<sup>st</sup> principal strains at the point (i.e. in the differential element/subelements (dxidyidzi, i = 1,2,3...8) of each i-th bone level (Fig. 3, Fig. 1).
- (6) <u>Mechanoelectric synergies</u> activate the intensity and quality of dynamic remodeling and modeling processes in the bone tissue *at all structural levels*.



Fig. 3 The scheme of bone remodelling equilibrium in the point A and the state of bone remodelling *unbalance* in the point B. The first axes of the principal stress  $\mathbf{a}_{\sigma 1}$  and the principal deformation  $\mathbf{a}_{\epsilon 1}$  (in the point/element A) are approximately identical (in 3D) with the principal

axis of the material domain (i.e. in our case with the longitudinal axis  $\mathbf{a}_s$  of the osteon), resp. with the first axis of anisotropy. The first axes of the principal stress  $\mathbf{a}_{\sigma 1}$  and the principal deformation  $\mathbf{a}_{\epsilon 1}$  (in the point/element **B**) are NOT identical in **3D** with the principal axis of the material domain (i.e. in our case with the longitudinal axis  $\mathbf{a}_s$  of the osteon), resp. with the first axis of anisotropy.

- (7) Mechanoelectric couplings regulate adaptation processes in bone tissue.
- (8) Hydroxyapatite nanocrystals (HAPs) in the natural form and tropocollagen molecules (TCMs) are domains of main nano structural bone components. *Basic nano structural module* consists of a pair of domains: HAP + TCM. *Haverty et al.* (*in 2005*) proposed for HAP two polar symmetries: a monoclinic P<sub>21</sub> and hexagonal P<sub>63</sub> which do not possess any centre symmetry.
- (9) When on the HAP is applied a principal strain-load, having the principal direction parallel/identical with the electrical axis, the electrical charges are initiated and located on the surfaces of hydroxyapatite crystal.
- (10) Mineralisation by the HAP plateaus is considered in the gap zones and on the surfaces of some TCMs mainly.
- (11) Compressed crystals of HAP initiate the piezoelectric effects in the bone nanostructure.

(12) Tensile stresses in tropocollagen molecules initiate transports of streaming potentials (ions).

(13) The second fundamental nano structural domain - TCM is considered as a dielectric bioelectric material exhibits the polar uniaxial orientation of molecular dipoles in its nano structure.

(14) TCMs are bound to HAP plateaus via bonds and tensile forces in TCMs are transmitted to HAP by shear forces (i.e. by the shear nano stresses, resp. by the shear nano strains). Covalent ties in 1st and 2nd structural level ensure the biomechanical stability of bone tissue.

(15) Mechanochemical covalent ties among adjacent TCMs provide the transversal stability of TCMs and their complexity.

(16) The stability in the lateral direction is provided by the *electrical strengthening* as the consequence of electric currents. The electric currents create around TCMs the electromagnetic nano force lines, which *attract neighbour* TCMs.

(17) The electric current in the TCMs initiates not only the strong contraction of helical nanostructure of tropocollagen molecules (see: *the electrical strengthening*) but also contributes to the reduction of extreme tensile strains in helical tropocollagen fibres.

(18) The extreme compressive strength, tensile strength and flexural strength of all the structural domains (within the all structural levels of the cortical bone) contribute to the high load-bearing capacity, as well as to the processes of *hydraulic strengthening and electrical strengthening* of the bone tissue.

(19) The *hydraulic strengthening* in bone depends on fully hydrated nanostructure (by bound water) and on the presence of extracellular fluid containing non-collagenous proteins, proteoglycans, glycosaminoglycans and other components.

(20) The *principle of synergy* (integrating biomechanical, bioelectrical and biochemical processes) in bone tissue is the proof of the law on conservation energies and their changes during the bone adaptation in all structural levels.

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