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A fundamental basis for all living creatures, *mechanotransduction*, is significantly endangered by periodic exposure to impulsive infrasound and vibration from technical emitters - in particular cardiovascular and embryological functions

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Abstract

Mechanotransduction is *the* common basis for all organisms for converting physical forces into biochemical and biological information. Ongoing PIEZO channel research confirms PIEZ0-I and II channels in numerous other tissues including outside the endothelium. The prerequisite for a inflammatory transformation of the endothelium *is chronic oxidative and oscillatory* stress, as vital regulatory processes depend on an *uninterrupted laminar flow in the* capillary system *and the* integrity of the endothelium. Vascular health, in turn, is closely linked to demand-driven NO bioavailability and its homeostasis.

The latest findings on a growing environmental factor show clear signs of an incompatibility between chronic and impulsive low frequencies and a fundamental information pathway of all organisms. The potentially serious consequences of an interaction, e.g., loss of endothelial integrity, increased blood pressure and tissue remodelling of the heart, reduced fertility, stranding`s and death of whales, decline in animal species and insects and reduction in plant

biomass, have a common basis, which is discussed in this article: *mechanotransduction*. A force that is not demand-oriented can lead to irregular information.

There is an urgent need to reassess the far-reaching effects and consequences of infrasound and vibrations *from technical installations such as biogas plants, heat pumps and* in particular, *large (250 m+) industrial wind turbines* (IWT). '*If you want to discover the secrets of the universe, think in terms of energy, frequencies and vibrations'* (quote from Tesla). Mechanotransduction is a common basis for all life and must be preserved.

Keywords: *mechanotransduction, cardiovascular diseases, embryogenesis, oxidative and oscillatory stress, infrasound and vibration, endothelial integrity, NO homeostasis, PIEZO-channels, biodiversity.*

1. Introduction

For years, researchers have been searching rather unsuccessfully for the pathophysiological mechanism that explains why people living near infrasound-emitting installations exhibit similar symptoms everywhere, domestic animals display conspicuous behaviour and why animals avoid the immediate vicinity of increasingly taller wind turbines or other technical installations that emit infrasound and vibration. The research was for longer times mainly planned, carried out and evaluated by acousticians. Since around 2017, international studies have increasingly pointed to cellular stress effects and serious health impacts from chronic exposure to periodically occurring, low-frequency infrasound and vibrations. The knowledge of the specific properties of this far-reaching environmental factor and the current state of research on endothelial mechanotransduction and PIEZO channels has enabled *a paradigm shift*. The cellular effects could be reclassified.

Ongoing investigations of the PIEZO channel show high concentrations in varying distributions of PIEZO- I and -II channels, even outside the endothelium. The possible effects on the affected organisms are becoming increasingly clear. Sound, whether audible to organisms or not, is subject to the laws of physics.

2. Relevant Foundations

2.1. Structure, Components and Regulation of the Microcirculation System in Mammals

The vascular endothelium serves as *interface* and "*switching point*" between bloodstream and tissue. Endothelial regulation of vasodilation and contraction, vascular permeability and fluid homeostasis, inflammation and immune signalling, are vital for vascular health, which in turn is pivotal to our survival [1]. The endothelium perceives physical and chemical signals from the environment as information and converts them into a response. It consists of the sum of all flat endothelial cells (ED`s), lining all the mammal's vessels - including lymph vessels - as *the body`s largest organ* [2,3]. The ED corresponds in its structure to a somatic cell and is specified for its diverse tasks [3,4]. The surface area of the *endothelium* corresponds approximately to two football pitches – according to new estimates approximately 7,000 square meters for an adult male – and its total weight is estimated at around one and a half kilograms [2]. On the one hand, this enables a nutrient supply that is well adapted to current needs [2,3,4,5], on the other hand, this large surface area also provides a target for *internal and external disruptive factors*. For an overview, which cannot be complete, the complex tasks of endothelial cells are shown in Fig.1. [4].

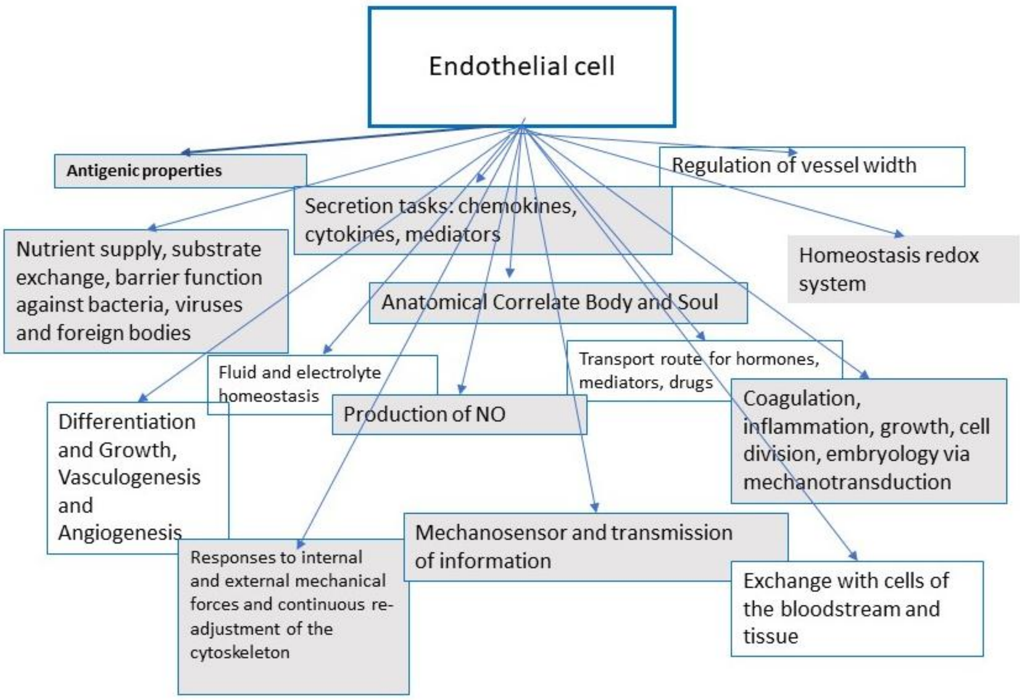

FIG 1: A selection of the most important endothelial functions. Bellut-Staeck UM.2022 [4], translated in English

By regulating the resistance via the upstream arterioles, we physiologically find laminar flow with uniform velocity, strictly bound to vessel size. This is a *crucial precondition* for the diverse and vital tasks of microcirculation and endothelial cells, which take place *in the circuit's low-pressure system* [3,4,6]. Under physical strain, a so-called *capillary recruitment,* according to Moore and Fraser [8], begins by lowering the vascular resistance of upstream arterioles, resulting in a significant increase in the nutrient exchange surface and decrease in the distance between two capillaries [5]. Vascular regulation is controlled by *intrinsic and extrinsic* factors. The autonomic nerve system and vasoactive hormones, e.g., *adrenalin*, *vasopressin*, *angiotensin*, *serotonin,* modulate the intrinsic activity [2,3,7,8]. Vascular segments *are acting in a coordinated manner*, which is attributed to the *Endothelium-derived-hyperpolarising-factor* (*EDHF*) [1]. *EDHF* has a far-reaching effect as vascular response, both upstream and downstream. *Calcium-dependent* activation of potassium efflux by *EDHF* is followed by *hyperpolarisation* with almost simultaneous transmission of electron transfer within the vessel wall via *gap junctions* [11]. This reaction is comparable to *a "school of fish"*, very fast and synchronized [12]. The mechanosensitivity of the capillaries was demonstrated when a positive micro-tactile physical stimulation was confirmed [12]. For further insight in vascular regulation and vasodilating substances [4,10].

2.2. The integrity of the endothelium

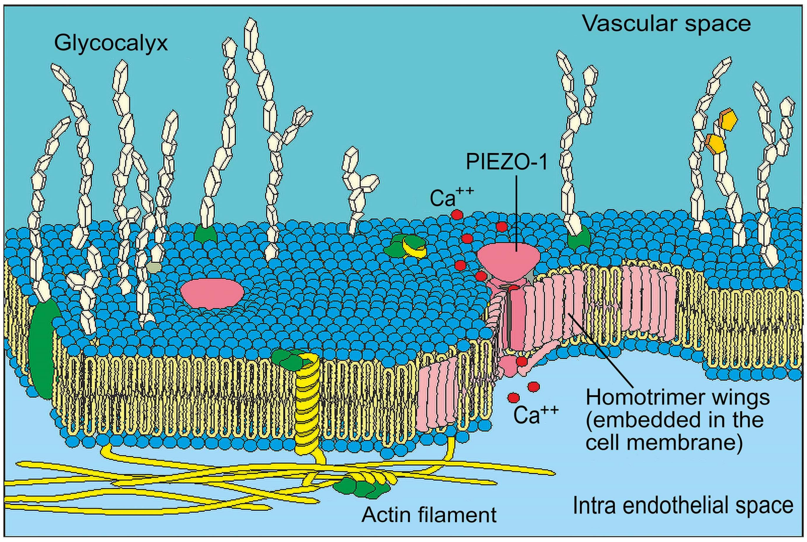

Fig 2 Schematic presentation of the endothelial semipermeable bio membrane with Glycocalyx and PIEZO-I channel, embedded in the endothelial cell membrane. One channel with a triggered Ca^{2+}-inflow. The actin ring (intra-endothelial) is indicated. The wings are moved by mechanical forces on the membrane and release the channel in an opening movement. Blue/Yellow: endothelial bio membrane with lipid bilayer structure [5]

The integrity of the endothelium is crucial for maintaining endothelial functions properly.

a) *Vasomotion*: A fine, non-pulsating vascular movement is extremely typical for a microcirculation with an *intact endothelium.* Even the smallest disturbances can cause *vasomotion* [13] to disappear. Due to its very low movement with sinusoidal changes of 0.1 Hz in the vessel, vasomotion *cannot* be easily observed in *SDF microscopy* [14]. Allowing precise measurements of vasodynamics, authors Zhang et al., 2024, introduced the method of *two-photon microscopy* [15]. As the authors note, vasomotion is crucial for e.g., brain homeostasis. In studies of cerebral blood flow in a mouse model, both native and after occlusion, they showed that vasomotion is of great importance in both the central and peripheral nervous systems. After stress caused by occlusion and reperfusion, vasomotion disappeared for a prolonged period. It was clarified that vasomotion also modulates fluid filtration pressure in the pulmonary vessels and that proper testicular function depends on intact vasomotion. It is expected that the benefits of intact vasomotion can also be demonstrated for the cardiovascular system and other vital systems.

b) *Glycocalyx:* The *glycocalyx* plays a special role in endothelial *integrity*. Only its base is firmly anchored in the endothelium. The part that extends into the bloodstream is subject to constant change, as it is in a continuous state of formation and degradation and at the same time acts as a sensitive mechano-sensor. Damage, known as *shedding*, has been shown to be caused by the effects of increased mechanical and oscillating stress as well as increased free oxygen radicals *(ROS*). In critically ill patients, the extent of *glycocalyx* damage correlates with their morbidity and mortality [2,16,17].

Loss of endothelial integrity:

Other factors that can lead to an oxidative stress syndrome (OSS) include elevated blood sugar levels, increased lipid peroxidation and stress factors, caused by vasoactive substances, e.g., the sympathetic nervous system or angiotensin axis. Elevated cortisol levels also lead to the formation of oxygen radicals (ROS), [5], cap. 8.2. page 54.

Why we must expect more than additive harmful effects with especially big wind turbines of current design is explained below:

The microplastic abrasion from today's wind turbines includes not only epoxy which is 40% Bisphenol-A (BPA), a frequently banned endocrine disruptor, but also per- and polyfluoroalkyl substances (also known as PFAS, PFASs, and sometimes referred to as ‘forever chemicals`) [19]. One of the deleterious effects of *overproduced NO* is Increased susceptibility for radiation, alkylating substances and toxic metals, compare 2.4. TAB 1.

Loss of endothelial integrity: Early atherosclerotic lesions usually develop at vascular bifurcations and curvatures of large and medium-sized arteries, where laminar flow is disturbed and oscillating stresses are present [22]. In [7,18,20,21], the development from an intact endothelium into a state of inflammation*,* is presented. Endothelial dysfunction is both, a consequence *of* and a causal contributor *to* an altered metabolism in the endothelial cell. As a result, the endothelial communication with other cell populations such as macrophages, monocytes and also smooth muscle cells is disrupted, leading to vascular dysfunction and triggering a cascade of intra- and extracellular signals such as endothelial secreted mediators (*cytokines*) [23]. All these factors together lead to easier transport of lipoproteins in the subendothelial space and to the maintenance of chronic inflammation and an increased risk of thrombosis. In case of chronic circulatory disorders and proatherogenic stimuli, endothelial cells partially or completely undergo a transition to *mesenchyma*l cells with corresponding properties. In addition, the pathological activation of PIEZO channels leads to expression of *various pro-inflammatory genes* and also serves as a critical mediator for an inflammatory response [18,24,25], At the same time, an intracellular increase in Ca^{2+} can be registered.

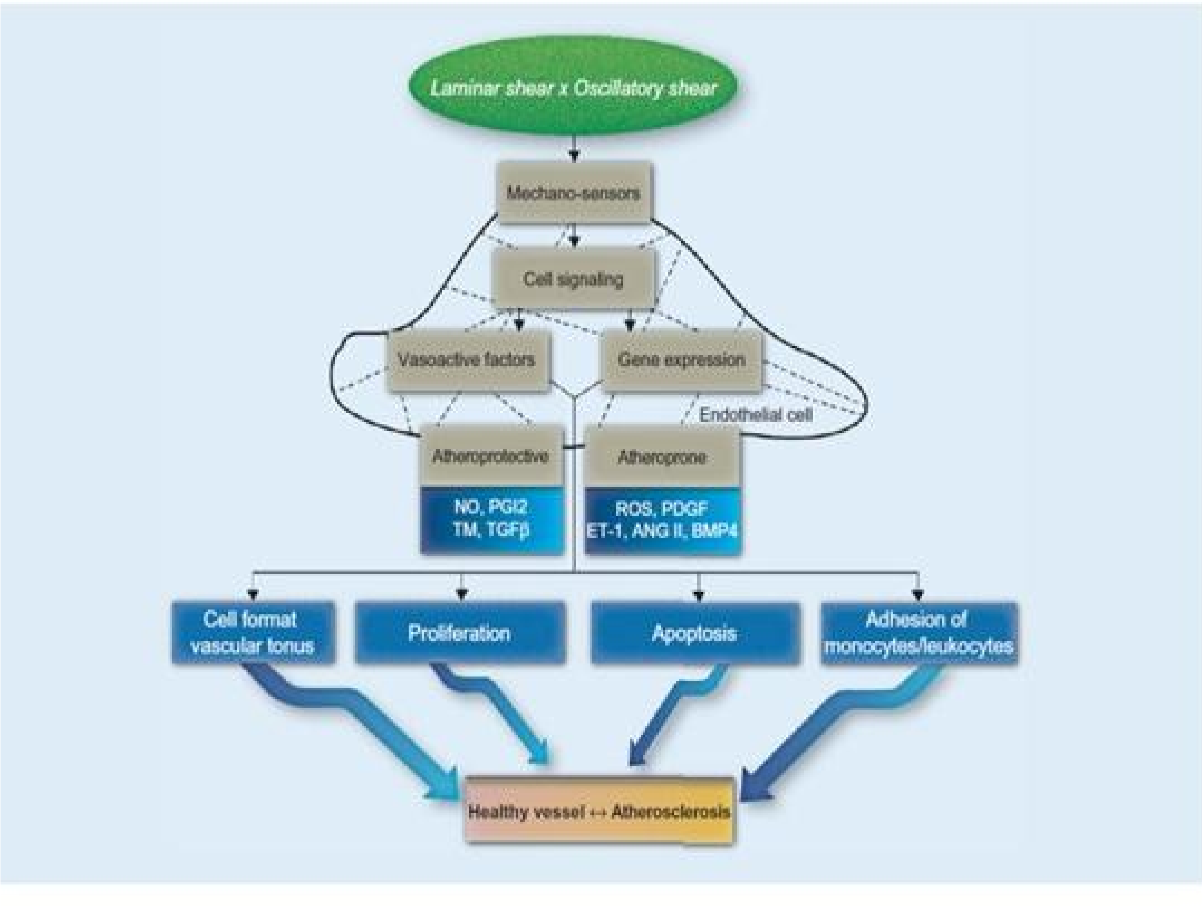

Figure 3 Original description [7]: Different effects of laminar and oscillatory shear on cell function and atherosclerosis. The *dotted lines* represent the endothelial cell cytoskeleton.

Laminar and oscillatory shear forces are recognized in endothelial cells by mechanosensors and the mechanosignals initiate signalling cascades that regulate the production of vasoactive factors and the balance between these factors. While laminar shear stimulates the production of atheroprotective factors, oscillatory shear stimulates the production of atherogenic factors and the balance of these factors determines the vessel tendency to stay healthy or to develop atherogenic plaques. PGI2, prostacyclin; TM, thrombomodulin; TGFb, Transforming Growth Factor beta; PDGF, Platelet-Derived Growth Factor; ET-1, Endothelin-1; BMP4, Bone Morphogenetic Protein 4. Adapted from Jo H, Song H, Mowbray A. Role of NADPH oxidases in disturbed flow- and BMP4-induced inflammation and atherosclerosis. Antioxid Redox Signal 2006; 8: 1609-19. Overview over the different effects of laminar and oscillatory shear stress on cell function and atherosclerosis. Original source [7]: *Fernandes CD, Araujo Thai's S, Laurindo FRM, Tanaka LY. Hemodynamic Forces in the Endothelium. Mechanotransduction to Implications on Development of Atherosclerosis. In: ENDOTHELIUM AND CARDIOVASCULAR DISEASES. Vascular Biology and Clinical Syndromes. Edited by PROTASIO L. DA LUZ.PETER LIBBY ANTONIO C. P. CHAGAS. FRANCISCO R. M. LAURINDO. Publisher: Mica Haley. Sao Paolo. (2018) ISBN 978-0-12-812348-5 Cap. 7 FIG 7.3, p 90*.8 With permission.

2.3. Redox System Homeostasis

NO is one of the most potent antioxidants and plays *a critical role in the homeostasis of overall redox metabolism by interrupting lipid peroxidation and thus reducing ROS* [1,23] (Tab 1]. In all organisms, NO freely diffuses through the membranes [3,5]. The vascular effects of *NO* are either presented *as vascular protective*, *regulatory or damaging* [1,23]. Various factors determine how the effect is realised. Protective effects have an appropriate *NO production* [1], but remarkably, *excessive NO production* is associated with *detrimental effects [1,23]*. NO overproduction leads *to lipid peroxidation*, *depletes antioxidant stores* and *increases susceptibility to radiation, alkylating agents and toxic metals like already mentioned*. It also *inhibits enzyme function and causes DNA damage* (Table 1).

Table 1. The different possible effects of Nitric Oxide as protective, regulatory and deleterious

Protective effects:
• Antioxidant
• Inhibits leucocytes and platelets adhesion

- Protects against toxicity and peroxidation

Regulatory effects:

- Vascular tone
- Cell adhesion
- Vascular permeability
- Neurotransmission
- Bronchodilation
- Inflammation regulation
- Regulation renal function

Deleterious effects

- Inhibits enzymatic function
- Induces DNA damage
- Induces lipid peroxidation
- Increases susceptibility for radiation, alkylating substances, toxic metals
- Depletes reservations of antioxidants

After Original source [23] FIG 1 in WINK AA. MITCHELL J (1998) CHEMICAL BIOLOGY OF NITRIC OXIDE: INSIGHTS INTO REGULATORY, CYTOTOXIC, AND CYTOPROTECTIVE MECHANISMS OF NITRIC OXIDE, Radiation Biology Branch, National Cancer Institute, Bethesda, MD, USA from Book Free Radical Biology & Medicine, Vol. 25, Nos. 4/5, pp. 434-456, 1998. Published by Elsevier Science Inc. 0891-5849/98 $0.00 1.00 reference FIG 1 Page 435.

Crucial for both, a synchronised blood flow regulation and the maintenance of high *NO bioavailability,* is an *adequate release of NO in the right amount, the right place and at the right time.* This is only possible if the triggering forces result in demand-driven information. More details to the whole theme inclusive the involvement of endothelial NO- synthase isoenzymes in redox signalling pathways in orig. articles [1,22,23,26].

2.4. A `Tensegrity Structure` of the Endothelial Cytoskeleton offers the precondition for endothelial mechanotransduction

Named after Fuller [27], the structure combines structural stability, lightness and elasticity *for power transmission*. Actin filaments, microtubules and intermediate filaments as *intercommunicating networks*, take on the *elastic*, the *non-compressible* and *the connecting part*, respectively. Actin filaments serve to maintain the cell shape by forming a ring under the cell membrane [27,28] FIG. 2 which is connected to flow sensors (mechano-sensors) and membrane focal adhesion points (FAS*) – the 'anchor points in the tensegrity model' – as well as the intercellular gap junctions (CCAP)*. The original article [28] provide a more in-depth insight into this topic. In response to contractile stimuli, *actin and myosin filaments* form membrane-bound, parallel-organised units called '*stress fibres*', which stimulate myosin to slide along actin filaments. This leads to an increase in intracellular tension and thus cell contraction according to Wang [29] and Lee [30]. The closing and opening of paracellular gaps in response to inflammation, ischemia and invading substances (*gate-keeper-function*) is essential according to [31].

FIG 4: "Tensegrity" Model "in a schematic presentation [5].

Graphic Bellut-Staeck

2.5. Selected endothelial functions

2.5.1. Inflammation and Fibrosis Homeostasis

To maintain structure and function, an inflammatory response is essential as *a physiological defence mechanism* against, e.g., bacteria, viruses and injuries. All consecutive reactions depend on the *integrity of the endothelium* and involve the *endothelial cytoskeleton.* Since it is a *vital endothelial function*, the complex process of inflammation can be disrupted at any level, Suthahar [32]. Point of no return is the *diapedesis of leucocytes*. The further course leads in the favourable case to a *restitutio ad integrum*, in the unfavourable to a *chronic inflammation* with fibrosis, defect healing and possible organ damage with loss of function. Important works on the state of the science come from Ley [33]and Serhan [34], related work in particular from Nussbaum and Sperando [35,36]. According to these authors, the orderly process in all phases is crucial for its outcome. At the centre of the process is the adequate *gate-keeper-function* of an *endothelium in an integrity state.* In order to *lead to a restitutio ad integrum*, the whole process is dependent on the *absence of increased oxidative and oscillatory stress*, in detail in [4,] in cap.2.4. In clinical medicine, shifts towards chronic inflammation play a major role.[12].

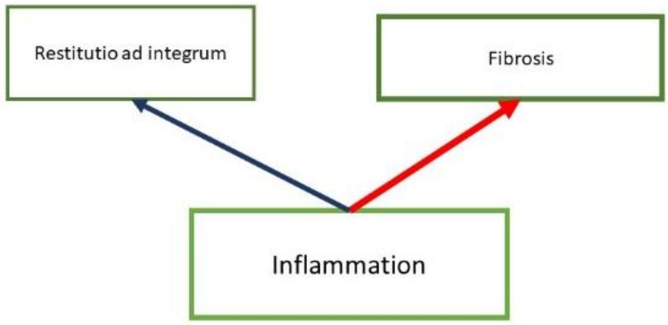

FIG 5: Schematic representation of the homeostasis of inflammation. Disturbance under chronic oscillatory and/or oxidative stress drives shift towards defect healing [5] Graphic 1.4 Bellut-Staeck

The standard works by Buckley [37]and Serhan [34] describe the sequences after the leukocyte diapedesis [5,38]. Failure of such regulatory mechanisms can likewise lead to a state of *chronic inflammation*, causing continuous tissue damage and progressive fibrosis. A classic example is the chronic heart failure by "remodelling" of heart, which can trigger a vicious circle [32, 5]. At heart, immunocompetent myofibroblasts and factors of the ECR actively modulate the development of initially perivascular and later progressive fibrosis. Starting points can be the development of myocarditis into a chronic form, state after myocardial infarction and/or *chronic mechanic pressure load on the he*art (systemic high pressure or pulmonary hypertension). The consequence is the increase in diffusion distance, the decrease in capillary density, an impaired electroconductive system with cardiac arrhythmia, disruption of angiogenesis, leading again to a deteriorated substrate and oxygen supply with a self-reinforcing process: *a vicious circle* [34]. According to the state of PIEZO research, the overstimulation of PIEZO channels can also contribute to this deterioration [24], cap 2.4.

2.5.2. Embryogenesis

According to the current state of knowledge, the importance of external forces, in particular repeated exposure to low frequencies and vibration during the pregnancy, must be classified as significantly more harmful than previously assumed. The high sensitivity is related to various stages particularly of embryonic development which are physiologically based on an undisturbed capillary flow. Examples of particular phases of increased sensitivity are e.g., the *vasculogenesis*. After differentiation of endothelial progenitor cells [4] and their fusion into a primary capillary plexus [31], the growth direction of the vascular tree is essentially regulated by shear *stress* of the blood stream and thus by mechanotransduction, Hahn and Schwartz [40]. PIEZO-I channels play a vital role here, without no embryogenesis would take place. Changes in shear stress pattern drive *immediate vasomotor* changes, which are regulated, as we know, on a '*beat-to-beat*' basis [19,38]. In this way, unexpected force driven disturbances can have *deleterious effects* [19]. Basing on some mutational *human PIEZO- gene* diseases such as the congenital *xerocystosis* or *congenital lymphatic dysplasia,* the erythrocytes and the lymphatic system is highly dependent on adequate forces. The last is characterised clinically by a lymphoedema. The network of lymphatic vessels with its own endothelium regulates the turgor and homeostasis of the interstitium and the lymphatic valve formation by shear forces. In consequence also there is a high sensitivity for an impact with external forces [41].

The neural development process is comparably sensitive to mechanical properties of its environment. One aspect is the alignment of neural stem cells into different *phenotypes* [24] and cap. *3.4. The important role* of Piezo-I in endothelial morphogenesis with dependent endothelial functions, suggests that damaging external forces must be strictly avoided during pregnancy.

In the dissertation "*Acquired flexural deformation of the distal interphalangeal joint in foals*" the influence of deep frequencies and vibration on embryogenesis becomes apparent. With the commissioning of three IWT`s at distances of 350 to 800 meters from the farm in 2008, an increased incidence of flexural deformities – especially 11 individuals affected- was observed, also abnormalities in other tissues were found. Histologically, the most significant alterations were the dissociation of myofibrils of the smooth muscle cells. This was predominantly seen in the small intestine but also in the walls of small capillary vessels, including those of the tendon vasculature [32}.

The chapter PIEZO channels in cap. 3.4. presents current results of PIEZO research on the occurrence and function of PIEZO channels in various organs. This may only be a small part of what influences embryonic development and how is its sensitivity to external and internal forces.

2.5.3. Homeostasis coagulation

Healthy endothelium plays an important anticoagulatory and antithrombotic role. Further insight is provided by ANNICHINO-BIZZACCHI und VINICIUS DE PAULA (2018) [43] in cap. 11, S. 148 and [4] in cap. 4.3.

3 Mechanotransduction

The conversion of mechanical forces into biological information, which is increasingly emerging *as a comprehensive mechanism for all living* things, is represented by the conductivity of biological structures, the presence of mechano-sensors, the conversion process from a physical into a chemical or electrical signal as information and the induced biological and/or biochemical response.

3.1. Hemodynamic Forces

Physiologically, physical forces constantly act on the organism, e.g., *gravidity, pressure, proprioception, shear stress* and *vibration*. The major ones come from the blood flow itself and are tangential forces e.g., *laminar shear stress* or stretching forces e.g., *pulsatile distention* according to Fernandes et al. [19] and Mazzag et al. [44] As described above, *internal oscillatory stressors are physiologically limited in the capillary bed by the vessel size* [1]. As a result, we find *physiologically laminar flow* in the capillary bed. [1,2,19].

3.2. Mechanical Force Transmission via "Biophysical" Pathway"

The observation that many processes take place very much faster than the *mechano-chemical* pathway via *gene expression* and *protein synthesis* would allow – protein synthesis needs a minimum of some seconds – led to intensive research in the "tensegrity" structure of the cytoskeleton and to the definition of the "*biophysical pathway*" [1,44]. *In the example of endothelial mechanotransduction*, this pathway relies on direct physical links between *specific mechano-sensors of* the endothelial surface and the endothelial cytoskeleton. It allows cells to transfer mechanical stimuli over long distances and very importantly, in a "*spatially heterogenic excitation ", quote Mazzag* [44]. Crucial work with important relevance to our work is the research on the dynamics and distribution of transmission in response to "*noisy flow*" from Mazzag and Gouget in [44] and Mazzag and Barakat. in [45]. By "noisy" flow, the authors mean an "*oscillating or turbulent flow* under *conditions with random fluctuations in* *the flow properties of pressure and velocity*", quote Mazzag, Barakat 2010 on page 912 [45]. To the predecessors in the exploration compare [38]. To better understand the dynamics of force transmission via cytoskeletal filaments, several *mathematical models* have been developed. The authors Mazzag and Barakat present an overview with possibilities and limitations in [45].

The "Temporal Network Model 2, as presented in [44] and [45] is based on a *viscoelastic structure* of a *tensegrity model (*FIG 4). The results show that the amplitude of the *oscillations* in the 'noisy' flow is *more strongly answered than its duration, which could be an explanation for why an 'impulse force' is answered more strongly than a constant.*" [45]. A summarising evaluation is provided in Mazzag [44] with further developments of models, e.g., such as the "*spatio-temporal network model*". Important quote on this topic on page 101[44]: *"At sufficiently low oscillatory frequencies*, *the peak deformations match those for constant forcing; however*, *above a threshold frequency*, *the peak deformations drop significantly*. *The analysis demonstrated that this threshold frequency is in the range of* 10^{-5} - 10^{-4} *Hz for microtubules and* 10^{-3}- 10^{-2} *Hz for actin stress fibres*, *suggesting that stress fibres can effectively transmit force over a wider frequency range*."

Na *et al.* [46] confirmed in an experimental study the transfer speeds and effects, predicted by the computer model. The experiment *used infrasound* as physical force. It could be demonstrated, that the *biophysical way* is about 40 times faster–*namely 300 milliseconds*– than the route by pathway of gene expression.

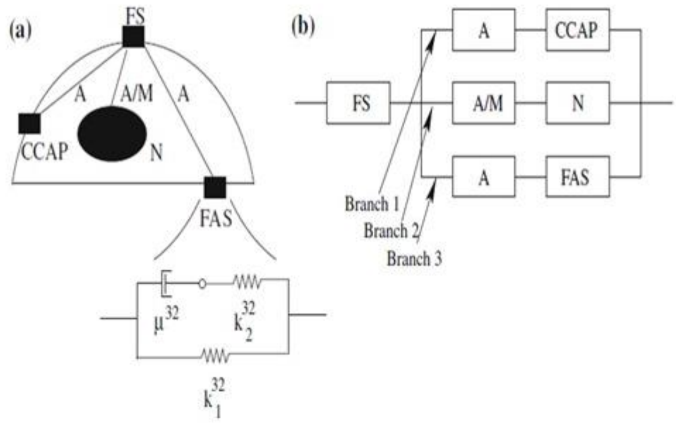

FIG 6. Original description [44,45*]*: Schematic representation of an EC consisting of a mechano-sensor (MS), cytoskeletal elements (either actin stress fibres (a) or microtubules (M)), a nucleus (N), cell-cell adhesion proteins (CCAP), and focal adhesion site (FAS). The inset shows a TPMM (or Kelvin body) representation and the viscoelastic parameters for

FAS. The superscripts '32' on the parameters indicate that this element is the second element on the third branch (see text). (b) Branching network representation of the EC components in panel A. Each cell component corresponds to a TPMM, coupled to other components according to the diagram shown. Actin stress fibre and CCAP connected in series are referred to as Branch 1, actin stress fibre/microtubule in series with the nucleus is Branch 2, and actin stress fibre in series with the FAS is Branch 3. (a) Schematic representation of an endothelial cell consisting of a flow-sensor (FS), cytoskeletal elements actin filament (a) or microtubules (b) and the connections (N), (CCAP), (FAS). (b) Mathematical representation. Original source [44,45]: Temporal Network Model FIG 1 *Bori Mazzag*, *Cecile L. M. Gouget*, *Yongyun Hwang* and *Abdul I. Barakat* (2014) [44] Cap. 5. Page 98 [45] Mechanical Force Transmission via the Cytoskeleton in Vascular Endothelial Cells. In Endothelial Cytoskeleton. *Editors* Juan A. Rosado and Pedro C. Redondo Department of Physiology, University of Extremadura Cáceres, Spain. With permission

3.3. The Mechano-Sensors of the Endothelial Cell

The endothelial *mechanotransduction* occurs *directly*, without delay, as shown in chapter 3.2.

On the side facing the vessel (luminal), mechano-sensors are especially *the cytoskeleton itself* [19], the *glycocalyx*, *integrins*, *cell-cell junctions* (*CCAP*), *caveolae*, *lipid rafts*, *G-protein coupled receptors and PIEZO-I-channels (*designated as ion channels as of 2019, FIG 4 in [1]. They are activated according to their location via shear stress [1,48]. Endothelial mechano-sensors are altered in their microenvironment by shear stress and can activate intracellular signalling pathways in this new formation. The fluidity of microdomains in the plasma membrane is altered after [1]. This leads to a spatial rearrangement of various proteins and thus to the activation of signalling pathways. The *transmission of forces* takes place via the three intercommunicating networks to the basal region of the cytoskeleton (e.g., Integrins) [1,44,45]. One of the most important mechano-sensors is the *glycocalyx* ([1,2]. In critically ill patients, the extent of the *glycocalyx* damage –so called *shedding*– correlates with the severity of disease and mortality [2,21,47].

3.4. A closer look to a special mechano-sensor: the PIEZO-channels

Ardem Patapoutian was awarded 2021 the Nobel prize in Medicine for establishing PIEZO channels *as a sensory system of internal organs via receptors for pressure and vibration in all vessels and the skin,* David Julius was awarded for TRPV1- channels as receptors for heat and cold. "*TRPV1 and PIEZO channels provide a completely new basis for sensing mechanical forces and vibration, heat and cold." Quote page 1 [48]. […] "The work by the two laureates* *has unlocked one of the secrets of nature by explaining the molecular basis for sensing heat, cold and mechanical force, which is fundamental for our ability to feel, interpret and interact with our internal and external environment."*

PIEZO ion channels in general mediate the *conversion of mechanical forces into electrical signals* and are conserved structures in *all* multicellular organisms, also plants**,** therefore important for all living entities from plants, bacteria up to mammals**.** In line with their significance**,** they are *in the focus of actual PIEZO research*.

PIEZO proteins form *homotrimer structures* with a central ion-conducting pore and three peripheral large mechano-sensitive propeller-shaped wings. See schematic graphic in FIG 7. *When Ca^{2+} permeable PIEZO-I* channels are activated by physical force on the cell membrane, they flatten the wings in an opening movement and reveal the entrance to a central pore, using a *unique lever mechanism* [24]. The Na^{2+}/Ca^{2+} channel is activated and triggers a signal transduction via a Ca^{2+} influx, Rode et al. 2017 [49], therefore *PIEZO-I is responsible for flow-sensitive, non-inactivating, non-selective cationic channels which depolarize the membrane potential.* In a remarkable research progress, authors like Fang [24] characterized PIEZO- I and- II channels in their protein structure, biological functionality and their possibly biophysical significance and used new techniques such as the *cryo-electron-microscopy*, comparative studies with a mouse model (*mPIEZO*) and e.g., the comparison with known PIEZO channel gene mutations. These are for example the autosomal dominant xerocystosis, the autosomal recessive congenital lymphatic dysplasia, the autosomal recessive syndrome of muscular atrophy with perinatal respiratory distress. In FIG 7 there is a schematic presentation of a PIEZO-I channel in an A closed and B open position.

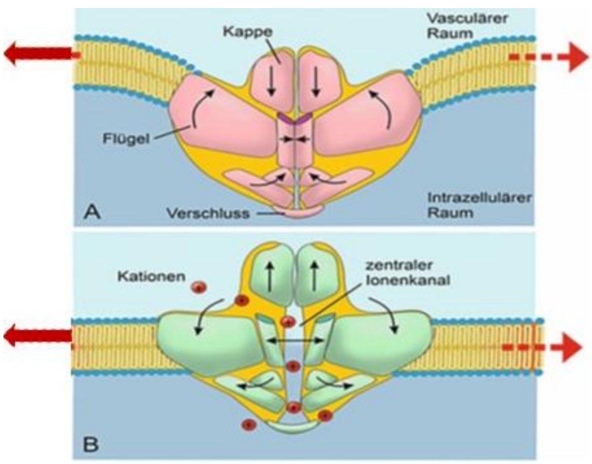

FIG 7 Schematic representation of a PIEZO 1 channel in a closed A and B open position. Graphic Bellut-Staeck

In eukaryotic cells, a plurality of ion channels is involved in *mechanotransduction* pathways. An overview is given in [24] in Tab. 9**.** Some do not occur as conserved structures in mammals, but in invertebrates. Some of them, *transient receptor potential channels in particular (TRP*) are not only sensible to forces, but also to chemicals, temperature, osmolarity and heat [24]. Quote page 1 [24]: "*Furthermore, most MS candidates, the TRP channel in particular, are activated not only by mechanical stimuli by but also by chemicals, temperature, osmolarity, and heat (> 27–34 °C).*" An additional voltage dependence is described from Sachs, Gottlieb and Moroni [50,51].

3.4.1. Expression of PIEZO- I and -II in multiple tissues

As a result of actual PIEZO-channel research, the following body regions and organs are apparently particularly characterized by *mechanotransduction processes* via PIEZO-I channels such as the *cardiovascular system*, the neuronal *development*, the gastrointestinal *tract*, the lung *endothelium* and the *urinary tract,* (FIG 8). PIEZO-II channels dominate in the somatosensory via Dorsal Root Ganglion, articular cartilage, balance, proprioception and pain. [24]. FIG 8 demonstrates an overview of the occurrence of PIEZO-I channels and II channels in different organs.

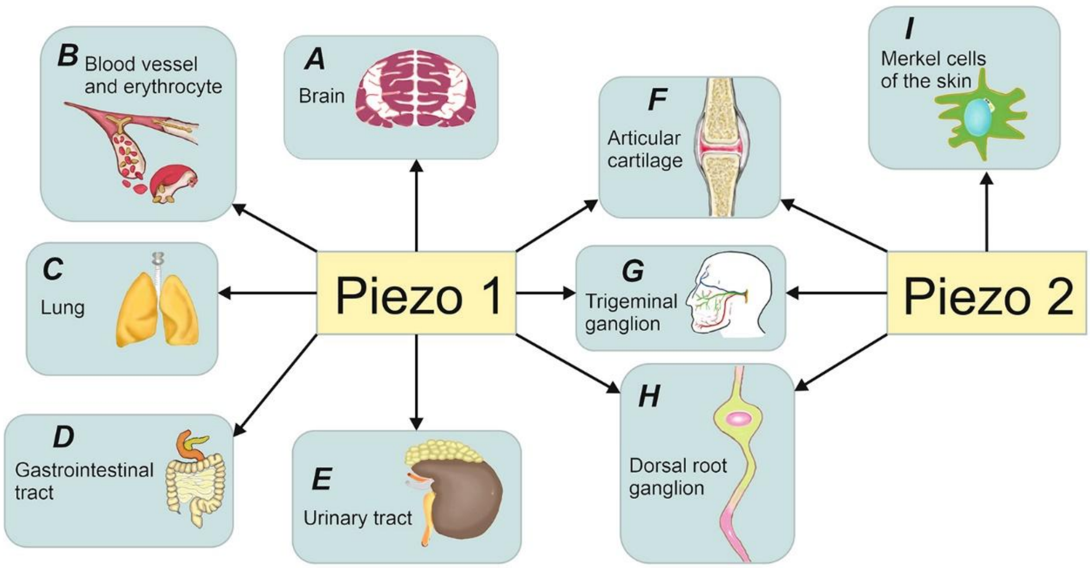

FIG. 8 After Fang+ et al. [24] Schematic overview: Expression and function of Piezo channels Multiple tissues and cells express Piezo channels. a–e demonstrates the vital role of the Piezo1 channel in the CNS, blood vessels, erythrocytes, lungs, gastrointestinal tract and urinary tract. f–h illustrates the expression of both the Piezo1 channel and Piezo2 channel in articular cartilage, trigeminal ganglia, and dorsal root ganglia. i shows that the Piezo2 channel is expressed in Merkel cells, which are involved in sensing light touch

The c*ardiovascular system*: The regulation *of vascular tone, blood pressure and adequate provision of NO,* takes place in the classical *laminar shear stress reaction***.** The PIEZO-I channel is activated and releases adenosine triphosphate (*ATP)*. The phosphorylation of endothelial *NO-synthetase* leads to NO-production and adequate vasodilation [24,38]. PIEZO-I channels also play an important role in erythrocyte homeostasis in regulating its volume and plasticity [24]. Erythrocytes themselves release *ATP* via own PIEZO-I channels. Different manifestations of the dominant hereditary disease *xerocystosi*s are incompatible with life**.** PIEZO-I senses whole body's physical activity to reset *cardiovascular homeostasis* and enhance performance by a *dichotomic* reaction of the endothelial cell in the mesenteric tract as answer to physical stress [49,5].

A new aspect in Fang's work is the involvement of PIEZO channels in the *baroreceptor reflex*. *B*oth PIEZO -I and -II channels are highly expressed in the *nodose-petrosal-jugular-ganglion complex*. Physiologically a *beat-to-beat* regulation of the blood pressure takes place. According to Fang, the knockout of both PIEZO-I and -II channels led to a fully impairment of the baroreceptor reflex [24], FIG 8. Hailin Liu et al. (2022) [52] confirm the correlation between uncontrolled overstimulation of PIEZO-I channels, usually in connection with increased tissue pressure and the development from an acute to a chronic inflammation situation. This applies, for example, to *cardiac fibrosis. In a feedback loop*, myocardial fibrosis leads to *increased atrial pressure* and *overstretching of the heart muscle* via stimulation of PIEZO-I, which in turn leads to increased Ca^{2+} -influx, *promotion of inflammation* and *proliferation of fibroblasts* with increasing fibrosis.

PIEZO- I and its role *in the endothelium of lung*: Due to an increased hydrostatic and alveolar pressure, the lung endothelium as well as alveolar cells are physiologically and artificially – in mechanical ventilation— exposed to an increased mechanical stress. There is a high expression with PIEZO-I channels in the lung´s endothelium. Proven is that mechanical stress like a mechanical ventilation is activating PIEZO-*I* and leading to an increased Ca^{2+} influx that subsequently is followed by an *apoptosis* of the alveolar cell. Conversely, mechanical stimulation of Piezo-I channels in alveolar type I cells triggers *ATP* release and paracrine stimulation of surfactant secretion that maintain lung function. According to [52], in chronic lung diseases, the increase in tissue pressure causes positive feedback on PIEZO-I channels, which exacerbates the process via pro-inflammatory pathways and via fibrosis. According to these authors, overstimulation of PIEZO-I channels which is leading to excessive surfactant formation, also tends to have negative effects on the outcome.

Organ systems with a high number of PIEZO channels outside the cardiovascular system and lung:

The PIEZO- I channel and its role *in **nervous system***: The discovery of PIEZO-I channels in structures of the *central nervous system (CNS)* led to research in their biophysical functions. According to Fang, the result is the transmission of mechanical forces from the environment of *the extracellular matrix (ECM)* into information that results in many processes such as cell *division, migration, morphogenesis, vesicular transport, gene expression and fluid homeostasis*. In *CNS* PIEZO-I was detected in myelinated axonal pathways (more than in demyelinated) of the mouse brain, including *corpus callosum and cerebellar* arbor vitae [24]. PIEZO channels apparently play an important role in the *neuronal development* such as the differentiation of neural stem cells into *neurons, astrocytes **or** oligodendrocytes*. Here a particular sensitivity to external forces is described. Ca^{2+}-influx, following triggered PIEZO-channels, directed the choice of neuronal stem cell towards a *neuronal phenotype*, while inhibition or knockdown of Piezo1 suppressed *neurogenesis* and enhanced *astrogenesis,* Quote Fang [24] page 12: "[…]" "*Is the Piezo1 channel also involved in astrocyte-neuron interactions that are key for the maintenance and regulation of neuronal function? An elegant study by Blumenthal et al. showed that pharmacological inhibition of Piezo1 abolished neuronal sensitivity to nanoroughness, a mechanical signal resulting from neighbouring cells and ECM molecules, and sequentially promoted the decoupling of neurons from astrocytes, thus providing evidence for the role of Piezo1 in neuron–astrocyte interactions. This information provides a clue for answering this question.*" According Liu et al., local increase of stiffness in the brain with a high mechanical sensivity of neurons and astrocytes, can lead in a positive loop to *further stiffness*. Connections with Alzheimer's disease are under discussion. Deeper insight in the original article.

PIEZO-I and –II channels in the ***gastrointestinal (GI) tract*:** According to Fang, chromaffin epithelial cells are enriched in humans and e.g., mouse GI tract and produce serotonin in response to mechanical forces within milliseconds. In the submucosa, multifunctional mechano-sensors in enteric neurons have been identified. The function of the PIEZO channels, found in enteric neurons of humans and mice still needs to be investigated in more detail in [24].

PIEZO-channels in *the **urinary tract***: According to Fang, piezo-I channels are expressed in the overall urinary tract, including epithelial cells, interstitial cells, and smooth and striated muscle cells. The ability to sense intraluminal pressure and changes in the flow, is a crucial precondition for a proper function. A deeper insight in the original article [24].

In the cartilage, PIEZO -I and-II are apparently partly responsible for the inflammatory processes caused by increased pressure, for example as a result of osteoarthritis.

3.4.2. Mechanotransduction in plants

To demonstrate the extraordinary important role of mechanotransduction, here a chapter to plants. Like animals, plants are *living organisms* with life cycles and vital reactions to environmental stressors. In plants we find corresponding structures such as a *cytoskeleton, mechano-sensors* and *mechanotransduction pathways*. Plants, along with animals and fungi, have a cell nucleus as eukaryotes, unlike prokaryotes. A rigid cell wall surrounds the living cell substance (protoplast) with the cytoplasm and the cell nucleus. We can find structures comparable to those of animals, such as *organelles*, *mitochondria*, *endoplasmic reticulum* and *Golgi apparatus*, *ribosomes*, *actin filaments and microtubules.* [53}. The difference in plants are especially the *plasmids*, sites of *photosynthesis* and the *vacuoles*. Comparable to animals are the structure and function elements from the six basic components elements H, C, O, N, Ph, S. Correspondingly to animals, four different molecules (glucose, proteins, lipids and phospholipids) and their compositions are the main components. In plants, energy is released by hydrolysis, energy (same amount) is introduced by condensation mechanisms. Similar to animals, *actin filaments* form a complex network with *intermediary filaments* and *microtubules* in the *cytoplasm* [54}. According to [54], plants are „prestressed structures" from shape-derived stress. Due to this fact, it is more difficult to recognize the functional processes in mechanosensory perception in plants. The intrinsic and external mechanical stress cannot be differentiated so easily. The epidermis of plant aerial organs is under *tension*, while inner tissues are under *compression*. As in animals, the *cytoskeleton* is also a central principle of the plant cell's response to mechanical stress. A*ctin* seems to orient along maximal tensile stress; internal turgor pressure is the engine for the growth. The most famous genes are called the TOUCH (TCH) genes, being induced within minutes after touch [54].

About 20 different mechanosensitive channels are described in plants.

An overview to different mechano-sensors in living things is given in FIG 9.

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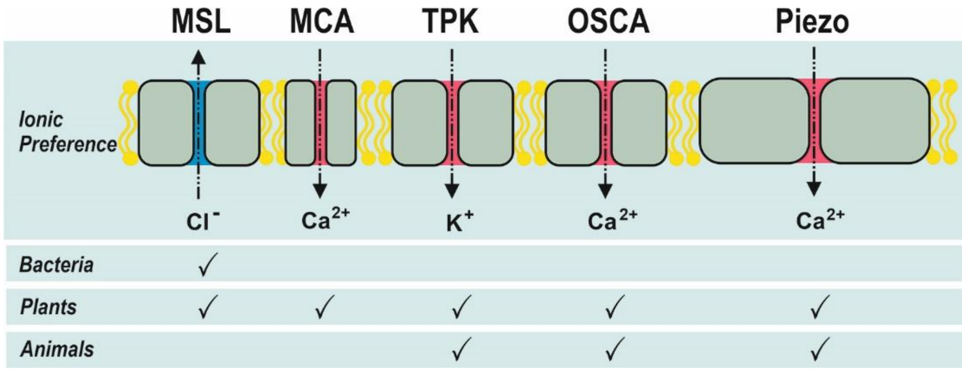

FIG. 9 Overview of different mechano-sensors after [54]. The presence of homologs in bacterial, plant, and/or animal genomes is indicated with a checkmark. The predominant ion flux is shown for each channel, but for simplicity no directionality nor specificity is shown. Shortened original description

Similar to the animal kingdom, mechanosensitive ion channels in plants are opened by lateral membrane tension and Ca^{2+} -Influx in context with mechanical stimuli. The perception of pollen tube growth, hypo- or hyperosmotic stress, gravity, vibration and touch or pathogenic invasion, is assigned to the function of mechanosensitive ion channels. Drought stress increases osmolarity. A trichome is an example for the trigger hair of a *Venus flytrap*. Its deformation leads to an increase in *apoplastic* (outside cytoplasma) pH and cytosolic Ca2+ oscillations in the cells [54]. When plants are under environmental *abiotic or biotic* stress, they reduce growth not only passively, but also actively as defence. This is achieved through stress-triggered cell signalling [55]. When there is an excess of light energy, the electron transfer in photosynthesis is significantly reduced, as a stress response. Similar to the reaction in the animal world, stress *leads to increased oxidative stress* (*ROS*), $H_2 0_2$ and other oxygen radicals and impairs the functions of the plant [55].

Plants respond to stress. They can release fleeting chemicals to protect themselves and also others from herbivores, e.g., so called VOC`s [56], but plants can also *"cry"*. The authors [56], 2023 examined the communication of plants with their outside world via *airborne ultrasound* that could be measured and recorded in a distance of 3-5 meters. This in turn requires a kind of "hearing ability". Plants can demonstrably respond to sound, inter alia, with a change in expressing specific genes. By training machine learning models, it was even possible to differ the emitted sound in its significance and thus to assign to *drought stress or injury*. Other organisms such as moths, are able to hear ultrasound, in this way could possibly communicate, also other plants. More insight in the theme bioacoustics and limitations of the study [23].

A study conducted between 2000 and 2022 on the reduction of *plant biomass production* (PBP) within a 10 km radius of each individual wind turbine shows that infrasound could be a significant stress factor for the entire environment. The study bases on an evaluation of 2404 wind farms with 108,361 turbines and shows significant consequences for the impact on plant growth [57]. The study analysed 10 PBP indicators such as the normalized differential vegetation index (NDVI), enhanced vegetation index (EVI), percentage of tree cover (PTC), percentage of non-tree vegetation cover (PNTV) and percentage of non-vegetation cover. A buffer zone of 10 kilometers was examined. The results show a significant negative impact on PBP, even if the extent of this impact varies depending on the indicator, respectively. The greatest negative impact can be observed in the summer and fall months and in relation to landscapes that are more flat than hilly. Furthermore, the negative impact increased for three years and persisted. The greatest negative effect e.g., *EVI* could be found between one and seven km with a maximum in 2 kilometers. An Example: "*The negative impact of wind farms on EVI is significant within 1 km to 8 km, with a peak at 2 km and a maximum decrease of − 0.0088 (P < 0.001; 95% CI − 0.0128 to − 0.0047)*". Quote in results [57] The authors consider the negative impacts on biodiversity to be *considerable*.

4. Noise and Sound

Pressure is force acting on a surface (N/ m^2) and measured in Pascal (Pa). Power per m^2(watts) is the *power density*. Sound, infrasound and ultrasound propagate as longitudinal waves in *all viscoelastic materials*, i.e., the pressure changes oscillate in the direction of propagation. It is an *energy transfer*. *Audible sound* is in the range from about *20 hertz (Hz) to 20 kilohertz (kHz), infrasound* is below 20 Hz and *ultrasound* above *20 kHz. Sound* differs physically in frequency and thus in wavelength. The wavelength (L) is in relation to the frequency (f) and to the speed of sound (V) in the respective medium. In general: The lower the frequency, the greater the wavelength, the lower the damping, the greater the flexural capacity of the sound. For example, sound propagation in air with a wave length of 0,1 Hz is about 3,4 km, that of 1000 Hz is about 34 mm. *Infrasound* is much less attenuated by propagation through the atmosphere as well as through roofs and walls than the *audio spectrum*. It propagates in all viscoelastic mediums, therefore also organisms. *Infrasound* is generated by heavily moving masses as well as by *resonance phenomena and vibrations*. Its exposure can be *occupational such as from the aviation industry or residential* such as from heat pumps, combined heat and power plants and as increasing factor from industrial wind turbines (IWT*`s*). *It* can be emitted from *natural* (e.g., earthquakes) or *technical sources* (cars, airplanes) or residential emitters. The sound differs in frequency, sound pressure, time/effect profile (impulsiveness) and duration, which is crucial for *the information* it has and the organism's ability to *compensate and to recover*.

4.1. Properties of infrasound emissions from IWT`s

IWT`s are a particularly far-reaching environmental factor [58]. Every time a rotor blade passes the tower, air masses of high-pressure differences are emitted, which propagate as *infrasound*. These pulses lead to several integer multiples of the determined fundamental frequency, the so-called ´harmonics´. Harmonics occur with any waveform that *deviates* from a sinusoidal wave. Since infrasound does not propagate linearly from the source, higher values can often be measured at greater distances than near the source due to reflections [59]. Due to the increasing number and size of IWTs, complaints from local residents are therefore on the rise, especially after the so-called repowering (the replacement of an IWT with a greater one) [60]. The reason is suspected of being in the increasingly lower frequency due to the increasing length of the rotor. The larger the rotor, the lower the emitted frequency. Infrasound of IWT's is meanwhile with big parts in the range of 0.2 to 8 Hz according to the authors in [61,62,63]. The infrasound emissions are impulsive in the effect/time profile according to Roos, Vahl [62] and Vanderkooy [63], as shown in FIG 10. This is an important factor for the relevance of information when comparing reactions to impulsive signals or consistent signals [44.45].

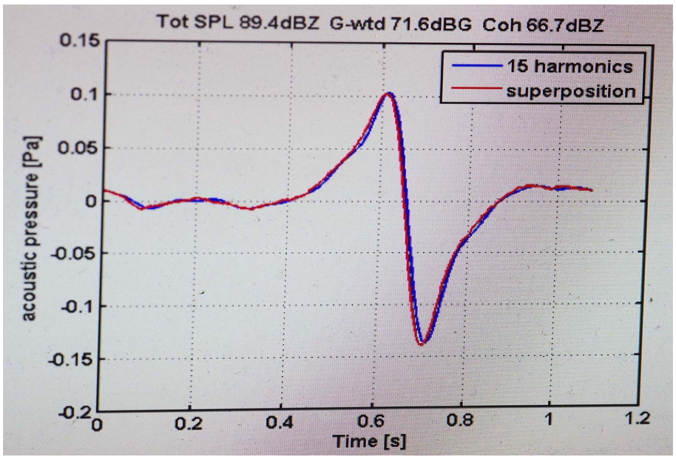

Figure 10 [63]: An infrasonic pulse extracted from the emission of a wind turbine. The fluctuations of sound pressure measurable near a wind installation usually contain noise, *i.e.,* irregular sound events of different origin. Noise removal is possible by averaging the sound pressure over a large number of mast-blade passages (here 4100), which reveals their common element (red line). The red peak thus visualized from the time sequence coincides

with the blue peak, which shows the fundamental pulse as reconstituted in the frequency domain from 15 (very sharp) harmonic lines by Fourier analysis. The result is the coherent fundamental peak of this turbine of 0.9 Hz frequency, accordant to 1.08 seconds required per blade passage. The extracted infrasonic pulse of a wind turbine shows the relation between sound pressure (P) and time (s). Original source [63]**.** corresponding to Figure 7 in Vanderkooy[1] J, Mann[2], R Measuring Wind Turbine Coherent Infrasound Department of Physics and Astronomy 1, Department of Computer Science 2 University of Waterloo, Waterloo, ON, Canada, N2L3G1 jv@uwaterloo.ca, mannr@uwaterloo.ca Date posted: 2 October, 2014. With permission.

Particularly in indoor spaces of buildings, interferences of airborne sound pressure and *structure-borne sound are possible*, which can lead also to relevant amplifications or attenuations of the total impacting sound [64]. The recording of the measured values must be done with suitable sound pressure levels [SPL], unweighted as shown in FIG 11.

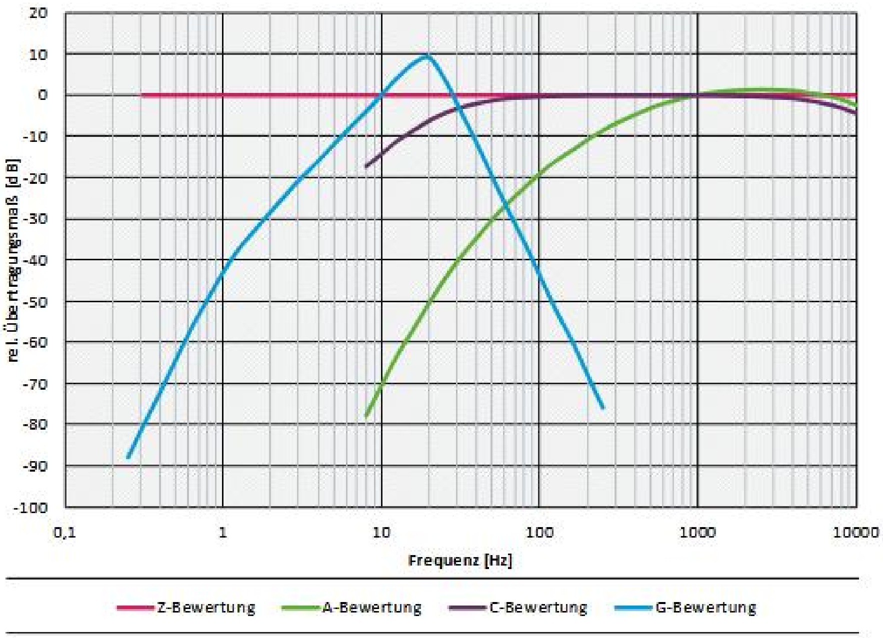

FIG 11: Typical frequency weighting curves in dBA, dBC, dBG and dBZ. Original source: Eulitz C., Zobel P., Ost L., Möhler U., Schröder M. (2020) Ermittlung und Bewertung tieffrequenter Geräusche in der Umgebung von Wohnbebauung, TEXTE 134/2020 [65]

As result in FIG 11 only the unweighted curve dBZ (red), can actually images infrasound. The G rating extends far into the infrasonic range, but with a significant loss of real sound pressure values.

The A- rating, which is suitable for evaluating audible sound, and the C- rating only extend to just below 10 Hz. The difference between the A- and C- ratings when more than 20 dB, can only indicate the presence of infrasound, not assess it.

The spectrum in FIG 12 shows that the main frequencies emissions from a IWT are below 8 Hz.

Remarks: According to the UBA (Environmental Protection Agency), the frequencies in the 30 Hz range cannot originate from the rotor blades, as the frequency difference is significantly different. It is assumed that these frequencies originate from the gearbox present in this wind turbine.

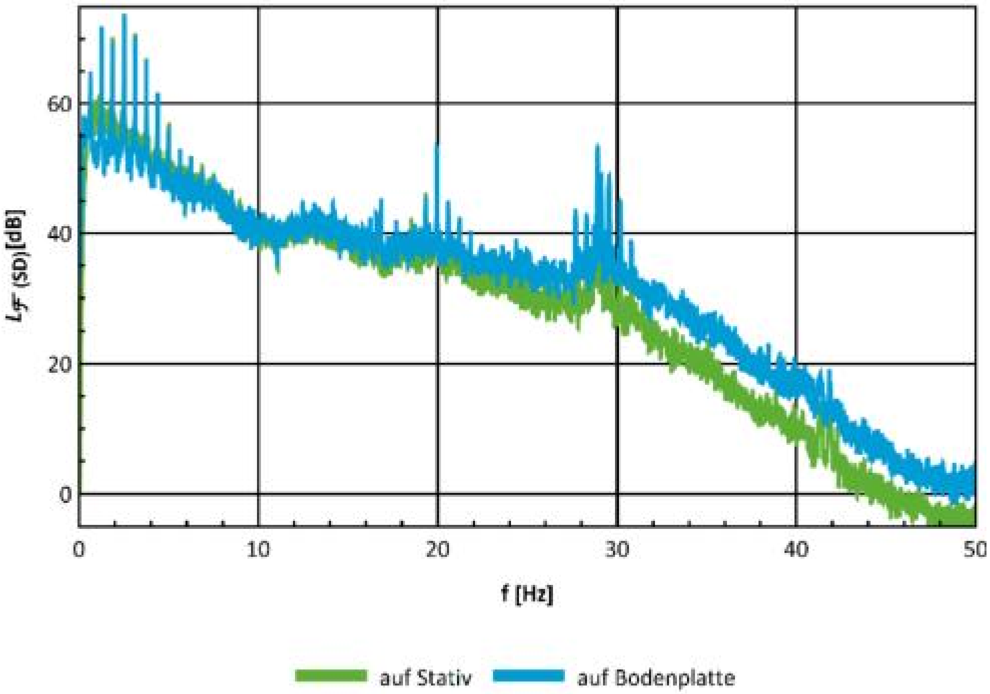

FIG 12: The following spectra are taken from: Texte 70/2022 (in English) Final Report, Federal Environment Agency, UBA Image 39: [66] Page 73

4.2. Information of an infrasound signal arises from all its qualities

Every cell interacts with its environment by exchanging *tiny quanta of energy* [59]. According to Persinger [59], it has been known for some time that living organisms vibrate in a range of mainly 6-12 Hz with amplitudes of 1-5 µm, and about 50 µm when muscles are tensed, and thus emit *sound* as a result of the fusion of all activated muscular subunits. During sleep, the amplitudes are reduced. In addition to natural sources, the environment is increasingly confronted with human-made sound waves in different frequencies, also increasing *infrasound*. At the current heights of the IWT`s above 250 meters and high rotation speed, the emitted frequencies are in a similar range to one's own body vibrations. It is known that resonances, which arise in spatial and temporal similar patterns, can lead to a significant instability of the *overall system* even with minimal stimuli.

Quote Persinger [59] page 503: “*Pure sine waves or simple time-varying patterns are found less frequently in the environment than complex acoustic and electromagnetic patterns that have the potential to mediate information between the environment and cells at very low levels of intensities. Relying on only the average intensity overtime for these sources (such as infrasound) as indicators of their importance is about as useful as only measuring the loudness of a conversation to discern its syntactic content and meaningfulness* “. Thereby the effects of impact do not require awareness [83].

Black box IWT: IWT`s with heights of 250m+ reach meanwhile verifiable a ground frequency of about 0,25 Hz. The frequency between 0,2 and 4 Hz corresponds to the slow delta waves of the brain during sleep; this could disrupt the synchronized *release of hormones and proteins* involved in repair mechanisms and disturb the homeostasis [59] inclusive the production of *serotonin* and *noradrenaline* of the brain stem. This could mean greater sensitivity during night-time sleep. According to Persinger frequencies below 10 Hz have *a high biological significance*.

Music also consists of a fundamental tone, which is overlaid with other tones in integer multiples of the fundamental frequency. As with music, the totality of information is not determined by a single characteristic, but by the interaction of all characteristics. These tones are called overtones or harmonics. Music can activate neural circuits that reach specific areas for emotions and reward. This leads to an instant improvement of the microcirculation [71,4]. An example according to Persinger of the variability of an information content: under slightly different circumstances, mundane stimuli can lead to a “disaster”. According to Persinger, Murugan et al. (2013) [67] demonstrated that planarians - a type of aquatic flatworm- exposed to a specific field pattern of sound for a few hours per day, dissolved within two hours. The decisive factor was the effect over time. They dissolved when a different temporally structured field was applied on day five, but not after the first day.

4.3. Hydroacoustic

In the sea, sound propagates at 1480 m/s, which is about 4.3 times faster than in air. The pressure increases with depth; therefore, the speed of sound increases with the depth. However, it also increases with salinity and temperature. In the low-frequency range, water sound waves can be perceived over any uninterrupted stretch of water on earth. In an infinite space at a constant speed of sound, sound intensity decreases with the square of the distance ($1/r^2$) and sound pressure decreases with the linear distance ($1/r$). According to Lurton,[68] in the northern hemisphere, the background noise below the surface of the sea is now permanently characterized by a diffuse noise from ships in frequencies between 100 and 300 Hz. More insight in the complex thematic, measured quantities and reference levels in the original article.

The authors [68] examined acoustic differences between deep and *shallow waters*, which is important in regard to the location of offshore turbines (verifiable *offshore installations are anchored in the ground, from about 21 meters water depth up to about 120 meters water depth)*. It is important to note that only sound sources between *50 Hz and 50 KHz* - not the infrasound range- *were included in this study*. Quote in Chapter 6 in Katsnelson B, Petnikov [69]*: „An extremely important part of shallow water acoustics is the study of long-range, low-frequency reverberation. In particular, one is studying acoustic wave backscattering by medium inhomogeneities, which are generally separated by a distance of a few to several tens of kilometres from a sound source and receiver. […] This reverberation, along with its main role as an undesired noise signal, can also play the role of an additional source of environmental information "*. When infrasonic sound waves are continuously emitted from *offshore wind turbines*, they will be likewise carried continuously to the next land mass in a constant repetition. So far, no studies have been conducted that look at the effects of inaudible noise in deep frequencies *on marine ecosystems*. The special hydroacoustic properties not only threaten the orientation of whales and their communication, but also their *vital functions.*

5. The Hypothesis

5.1 The paradigm shift

Effect and conscious perception must be considered completely independently of each other. [24,59,83]**.** The biological significance of information depends on *numerous factors*. All cells exchange information and oscillate. All organisms have a crucial level of perception via mechano-sensors. Mechanotransduction is one of the essential foundations for *maintaining structure, function and communication*. For this reason, external forces are able to cause a disruption of vital functions due to certain properties.

5.2. The Hypothesis in Detail

- Noise, when it affects organisms, is under *certain conditions in frequency, sound pressure, effect/time profile and duration* able*,* to lead to irregular information's on the mechano-sensor level.
- The consequences of irregular information's at the endothelial mechano-sensor level of the PIEZO channels are e.g., an inadequate NO release with an increase in oxidative and oscillatory stress as well as a lack of energy due to a disruption of the autochthonous vascular regulation.

In chronic impact this will lead to a loss of endothelial integrity with all consequences.

- With decreasing frequency, there is an increasing transmission of irregular information. This means increasing harm with decreasing frequency.
- Functional and later on structural disorders are particularly conceivable in all organ systems.
- Plants have comparable mechanisms and can therefore also be affected in essential functions by irregular information.
- Once the homeostasis of tissue pressure is disturbed in various organs, there is an additional risk of aggravation and self-reinforcement due to overstimulation of PIEZO channels everywhere they are located.
- The possible consequences might be severe, In particular for embryological, cardiovascular and neurological functions.

5.3. The Hypothesis Is based on the Evidence for

- ➢ Noise is a mechanical force, therefore subject to physical laws
- ➢ Mechano-transduction has a key role in the transmission of maintenance of structure, function and information in all living beings
- ➢ The information of a sound event arises from its complex qualities
- ➢ Low frequencies demonstrate increased conductivity in conductive structures such as actin fibres and microtubules
- ➢ An impulsive signal is more likely to be answered than a uniform signal
- ➢ The cardiovascular system is controlled and adjusted beat-to-beat
- ➢ Vital developments in the morphogenesis of the embryo are particularly susceptible to interferences not only for chemical substances or radiation, but also for external forces
- ➢ Overstimulation of PIEZO channels leads to gene expression with inflammatory mediators and thus intervene in processes of mutual reinforcement

- The low frequencies emitted by IWT`s lie within a frequency spectrum comparable to that of an animal organism, which means that there is a risk of resonance effects
- The effect of a stressor is independent of its conscious perception.

5.4. Evaluation of the Hypothesis

5.4.1. Positive Support for Evidence

Mechanotransduction which is responsible for many vital regulatory processes, has been scientifically proven [1,2,24,44,45]. Several international studies have shown that the transmission of *infrasound* is associated with verifiable stress reactions: infrasound interacts with cell metabolism and leads to perivascular fibrosis in *Infrasound induces coronary perivascular fibrosis in rats* according to Lousinha [70]. Similar findings are presented in [25,72,73]. Empiric data in experimental studies show clear indications that exposure to infrasound leads to a *ROS increase* [18,19,74]. Also, the study of Chaban et al. *indicates positive evidence by decreasing myocardial contractility of heart under Infrasound [75*] and the direct cell effect is shown in *the Effect of infrasound on the growth of colorectal carcinoma in mice* [76]. There is evidence for a direct cell and membrane effect in the review of Roos and Vahl [62]. A positive evaluation is also the *metanalysis* from Dumbrille et al. [60]: This evaluation results in the causality of *adverse health effects (ADH´s)* and the stressor in *all* "*Bradford Hill criteria*". Reported adverse effects on animals revealed not only stress reactions but also negative effects on *fertility, development, and reproduction* [76]. Positive evidence for the frequent occurrence of atrial fibrillation is presented in the "*nurse cohort study*" [78]. increased diastolic intracellular Ca^{2+} plus levels under infrasound [18,24,62]. A case study reports on a family in Ljungbyholm, southern Sweden, with a chicken farm. From 2009 to 2020, the normal hatch rate *after 21* days of incubation was at least 95*%*. After 12 turbines of 4.5 MW were commissioned at a distance of 950 metres, egg mortality was 100%. A direct link was established between the distance of the eggs to be hatched and the wind farm; noted by the Swedish authorities and published in a veterinary medicine journal 2024 {79]. Further positive support for evidence results from the re-evaluation of the pathohistological images from Alvez-Pereira and Branco [80,81] who examined the long-term effects of occupational exposure to infrasound and vibration in the context of the aircraft industry, known as *vibroacoustic syndrome. The pathohistological findings in FIG 13, FIG 14 and 15 confirm the effects of infrasound on cells and membranes.*

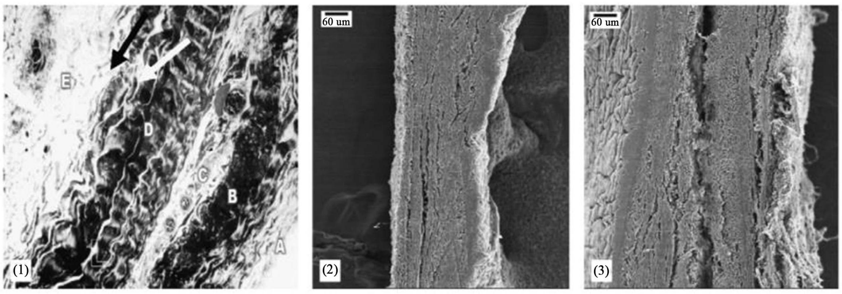

Figure 13. *Original description*: Light microscopy (100×)—VAD patient pericardium, with pericardial sac on right. Five (instead of the normal three) layers are identifiable: (A) mesothelial, (B) internal fibrosa, (C) loose tissue, (D) external fibrosa, and (E) epipericardium. The loose tissue is rich in vessels. No inflammatory cellularity was identified in any of the five layers. In both fibrous layers, wavy collagen bundles are visible, however the wave length of fibres in layer B (internal fibrosa) is smaller than that in layer D (external fibrosa). Taking together the increased amount of collagen bundles, in wavy, accordion-like arrangements, with different orientations in relation to each other, and with more than one elastic fibre accompanying the bundles at seemingly perpendicular angles (seen through electron microscopy, not shown), seems to suggest a pneumatic-like structure, designed to absorb abnormally large external forces. Similarly, this functional arrangement also explains why there is no diastolic dysfunction, despite the thickened pericardial walls. (2) SEM of non-VAD patient pericardium. Normal three layers are visible: mesothelium (white arrow), fibrosa (black arrow) and epipericardium. (3) SEM of VAD patient pericardium. Fibrosa has split into two halves (arrows) that sandwich a newly formed layer of loose tissue (L). [..]Remarks: ultrastructure micrographs, obtained with scanning (SEM) and transmission (TEM) electron microscopy. Pericardial wall in exposed and non-exposed persons 1) exposed (Light microscopy) 2) non-exposed (SEM) and 3) exposed (SEM)Alves-Pereira M., Branco C. (2007) Vibroacoustic disease: biological effects of infrasound and low-frequency noise explained by mechanotransduction cellular signalling http://www.sciencedirect.com/science/article/pii/S0079610706000927. [80] Page 11 FIG 2. With permission.

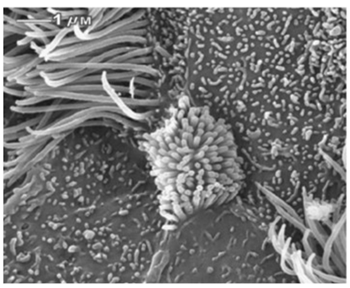

FIG 14 *Original description* (SEM) Non-exposed bronchial epithelium. The BC in the centre of the image exhibits a tuft of microvilli that are individually identifiable, uniformly distributed, and sprouting upward into the airway. Surrounding the BC are SC with microvilli of different sizes. Tufts of cilia featuring vesicles are also visible. No sheared, shaggy or wilted cilia are visible SEM). No oedema is present. *BC* (*brush cells*), *SC* (*Secretory cells*). Rat bronchial epithelium, exposed to 2160 h of continuous IFLN. With permission

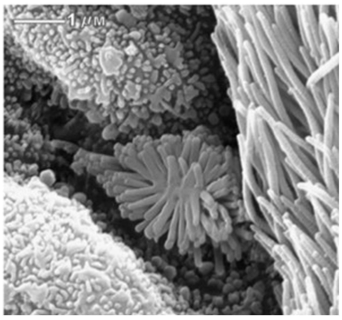

FIG 15 *Original description* (SEM) Rat bronchial epithelium exposed to 2160 h of continuous ILFN. A *BC* is in the centre of the image. Its *microvilli* are not sprouting upward and, instead, have fused, forming a central indentation that seems to be spreading outward. The prominent *SC* that surrounds the *BC* are swollen forming deep valleys at the intercellular junctions. SC microvilli are very irregular. Ciliary vesicles are visible. *Ultrastructure micrographs, obtained with scanning* (*SEM*) *and transmission* (*TEM electron microscopy*. *BC* (*brush cells*), *SC* (*Secretory cells*). Rat bronchial epithelium, exposed to 2160 h of continuous IFLN. With permission.

A positive support for evidence is the state of scientific knowledge in PIEZO research, which has made significant progress in elucidating *mechanotransduction`s processes* in various organ systems (24, 52). Mechanotransduction regulates essential functions such as cell *division, migration, morphogenesis, vesicular transport, gene expression and fluid homeostasis*. Both the symptoms such as increased cardiovascular symptoms, blood pressure, cardiac arrhythmias, pericardial thickening can be conclusively explained for the first time. Systematically higher MI incidences, *not case fatalities,* in rural environment, are the result of myocardial-infarction-related mortality in Germany 2024 [82]. Data collection took place between 2012-2018 nationwide for all MI incidences and case fatalities.

The study from Weichenberger et al. 2017 shows the unconscious regarding and processing of infrasound beyond the acoustic perception threshold in certain brain structures [83].

Several current studies show comparable areas of influence that speak in favour of the infrasound factor as stressor. What the studies have in common is the affected radius of minimum 10 kilometers, also in the study [57].

1) The considerable decline in plant biomass production in all indicators of the current study [57] on over 100,000 IWT shows clear positive evidence for a negative influence of installed IWT`s on plant growth. Other factors such as changes in local surface temperature or moisture content add up to the effect of infrasound, but can be differentiated by the sphere of influence of infrasound, which always remains in the same radius [57].

2) A recent study (2023) shows a significant decline (63%) in the population of seabirds a) with loons within a 10-kilometre radius after the installation of new offshore wind turbines [84] and b) with kittiwakes: 46 offshore wind turbines also had a significant impact on the kittiwake (Rissa tridactyla), used in the current study showing a 45% decline in the observed area during the breeding season [85].

3) The Impact of Wind Farms on Suicide, Eric Zou, October (2017) [86].

5.4.2. Possibly Negative Support for Evidence

In [42] there is a small sample size, but the results are based on a careful study design and consistent results. Several studies about the possible *adverse health effects* (ADH`s) of infrasound on its environment show contradictory results or do not show any effects when using infrasound. On closer inspection, the study designs and/or the used criteria, prove therefore to be unsuitable for their purpose. Investigations either used invalid frequency weightings such as dBA, were conducted *after* the impact *or* cannot reflect the influence on mechanotransduction processes because impact and measurement did not take place at the same. One example therefore is [87].

Regarding the question of the validity of computer-aided statements, we refer to Mazzag [44,45] for a detailed statement and our comment [5] regarding to this.

The current PIEZO research and vasomotion research is an ongoing process. The authors themselves point out corresponding limitations and partially contradictory results that require further research.

6. Established Methods to Assess and Visualize Microcirculatory Processes

The microcirculation can be visualized *in vivo* on new born babies via the skin, and on adults via the oral mucosa [2,14]. Appropriate techniques are video microscopy techniques such as *side stream dark field* (*SDF)* imaging [14]. A further visualization of vasomotion *in vivo* has become possible [15]. The *microcirculation* in the context of diseases can be visualized and quantified immediately after exposure to the stressor, as well as in its absence. Parameters that are be specifically observed, include:

- *The intact vasomotion in the first order*
- *An instantaneously changing in vasomotion under a defined stressor effect*
- *The functional blood vessel density (FVD) (mm/mm2)*
- *The red blood cell flow velocity* (*RBCV*)
- *The number of perfused capillaries* (*N/A*) (*n/mm*^{2})
- *The capillary vessel diameter* (*DM*)
- *The glycocalyx thickness in nm* (*conceivable for further research projects*)

7. Proposed Research Avenues and Questions Regarding Target

- Direct experimental verification of endothelial mechanotransduction in on/off setting under impact with different low frequencies and different sound pressure
- Clarification of the issue, which sound pressure is required at a certain frequency to obtain a transfer response? Based on this: Below which frequency does a *particular danger for all living organisms exist (we call it a threshold frequency)*?
- What role do resonance effects play?
- Evaluation of pathohistological effects after longer exposition and increased markers for inflammation in the blood of mammals

8. Discussion

The information of a sound depends on its complex pattern, as well as its temporal occurrence. Low frequencies encounter particularly high conductivity in organic structures, which may be a reason why low frequencies below 10 Hz *have a particularly high information content*. Research results show an increasing transmission of infrasound through *actin filaments and microtubules* depending on the *depth of its frequency*, even to cell nuclei. It remains to be demonstrated that the transduction, as already calculated, leads to an increase in irregular information as the frequency decreases. This would mean an increasing incompatibility with foundations of life.

Many studies have already confirmed the stress effects of low frequencies and interactions with cellular structures and membranes.

The conversion into *partial irregular information* and a possible *overstimulation of PIEZO channel is a further logical and compelling step*. Since the frequencies of conventional IWTs are in a comparable range to the body's own frequencies, harmful resonance effects cannot be ruled out, in particular, interferences with the body's own hormone and protein production during sleep.

Much research is still needed to clarify the significance of *mechanotransduction`s processes* in individual organ regions, however the ongoing PIEZO channel research demonstrates already a high sensitivity to uncontrolled external forces esp. during embryogenesis, in the growing organism as a whole, in the cardiovascular system and in the neurological system according to its equipment with PIEZO channels.

It is state of the art that inadequate NO supply leads to an increase in *oxidative and oscillatory* stress which is an important prerequisite for the *loss of endothelial integrity* and consequently for all endothelial functions with consequences such as blood pressure increase, inflammation, arteriosclerosis, myocardium fibrosis, cardiac arrhythmia, myocardial infarction, stroke, infertility, immune deficiency and possibly cancer.

Over-additive effects must be taken into account, e.g., the possibility of an impact with alkylating substances and the already reduced resilience of the redox system under increased oxidative stress.

The shift in the inflammatory balance towards fibrosis in the event of increased tissue pressure and overstimulation by PIEZO channels in the direction of myocardial or pulmonary fibrosis, therefore takes on new significance in connection with mechanotransduction`s processes.

9. Conclusion

An organism can be viewed *both mechanically and energetically*. *Every atom vibrates*. Communication takes place through the *exchange of energy and forces*, which forms the basis for the *maintenance of structure and function* both within an organism and within a biosphere. The principle of undisturbed *mechanotransduction* is a fundamental prerequisite for all life functions.

The possibility of infrasonic frequencies being transmitted to mechano-sensor levels, is highly evident.

Depending on the individual's ability to compensate, exposure to a chronic stressor such as impulsive and periodic infrasound must lead to an exhaustion which manifests first in functional disorders of the substrate and oxygen supply, later on in an increasing loss of endothelial functions. New knowledge in a clinical context can contribute to behavioural changes e.g., awareness of high sensitivity to external forces, especially in the first trimester of pregnancy during *vasculogenesis* where a random event can have significant effects according to the stochastic principle. Another example is the risk of a workplace with vibrations and low frequencies that could aggravate cardiovascular diseases. Recent studies indicate that *humans, animals and plants* within a radius of *at least* 10 kilometers can be harmed by far reaching emissions through IWT techniques.

Since all organisms are equipped with mechanosensory systems, a further increase in far-reaching low frequencies in open-air and open-water situations is likely to pose a major *threat to biodiversity* as *a whole*. Marine ecosystems and also whales and dolphins are particularly vulnerable to low-frequency emissions from offshore installations due to the specific properties of hydroacoustic. It must be assumed that insects, bees and other pollinators are also affected which would mean a potential threat to a further fundamental basis of life. Urgent questions arise, such as the connection between the increase of cardiovascular diseases and neurological disorders, the decline of fertility, the decline in insect and bee populations and the plant biomass reduction in the affected surroundings. The common denominator is with high evidence *malfunctioning mechanotransduction`s process.* Appropriate preventive measures should be taken now, as stressors are currently present in the home environment well as open-air and open-water situation before all scientific questions are clarified. Sensitive groups must be the benchmark.

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11. Disclaimer

For the author there are no conflicts of interests. The author would like to clarify that: Alternative forms of renewable energy are considered as worthful additions at suitable locations. The data reported herein have been scrutinized under one, and only one agenda, that of pure scientific inquiry. There are no commercial, financial or professional agreements.

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