Love Surface Wave Biosensors

(From Earthquakes to Biosensors)

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Poland in Europe

Fig.1. Poland has 7 Neighbors in Central Europe

Polish Academy of Sciences

69 Institutes, 8700 Scientists (Researchers)

Institute of Fundamental Technological Research:

300 employees, 200 Researchers

Main domains of research: Advanced Materials
Ultrasonics,
Biotechnology
Mechanics
Applied Mathematics

Laboratory of Acoustoelectronics:

- Surface wave sensors with Love and Bleustein-Gulyaev surface waves
- High pressure characterization of liquids using Love and BG waves
- Mathematical modeling and numerical analysis
- Computerized instrumentation

Philosophy (Message) of the Presentation:

Show paramount importance of multidisciplinary research in biosensor technology

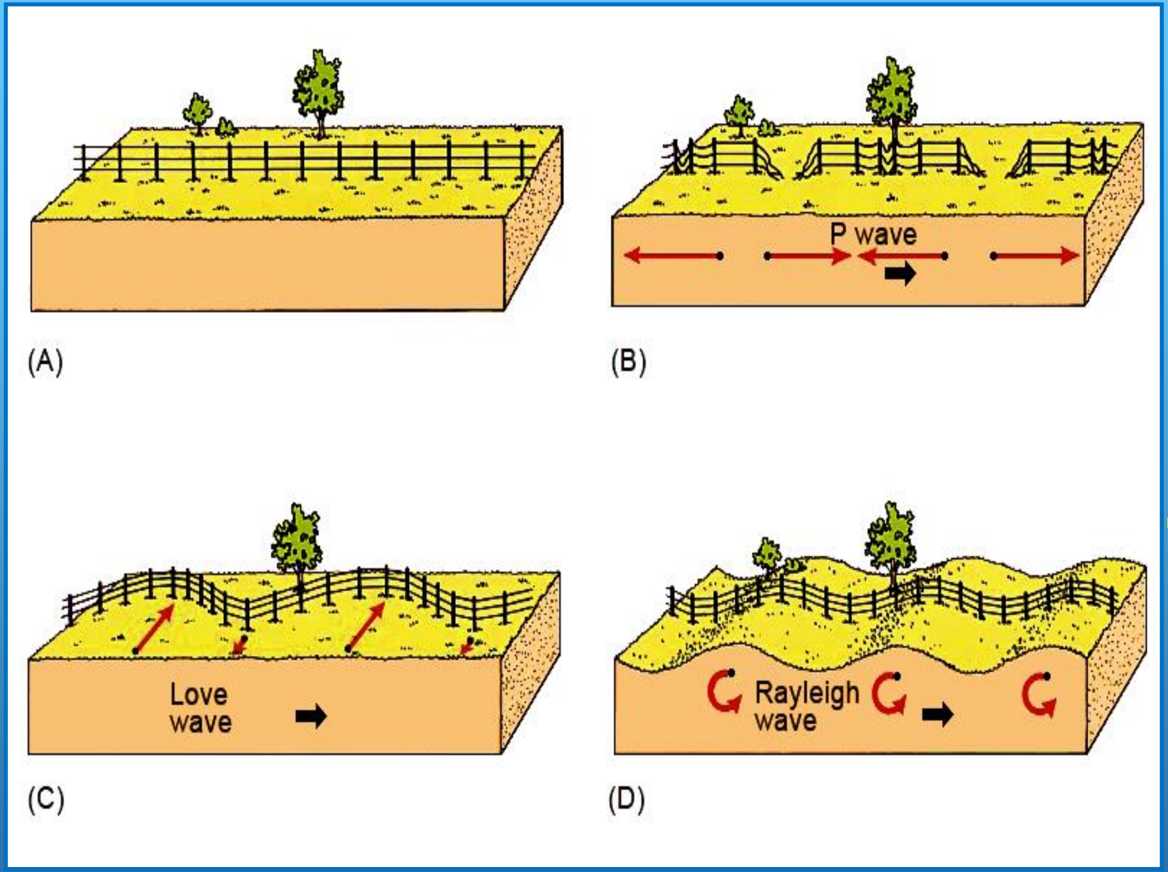
Outline of the Presentation

A)
- 1) From Earthquakes to Biosensors (Acoustic Love surface waves)
- 2) General Concept of Biosensor
- 3) Chronology of the development of the Love wave Biosensors
- 4) Physical Model of the Love wave Biosensor
- 5) Mathematical model of the Love wave Biosensor
- 6) Complex Dispersion Equation
- 7) Examples of Portable and Wireless Love Wave Biosensors

B)
- 8) Natural Biosensors in Human Body (Cochlea)

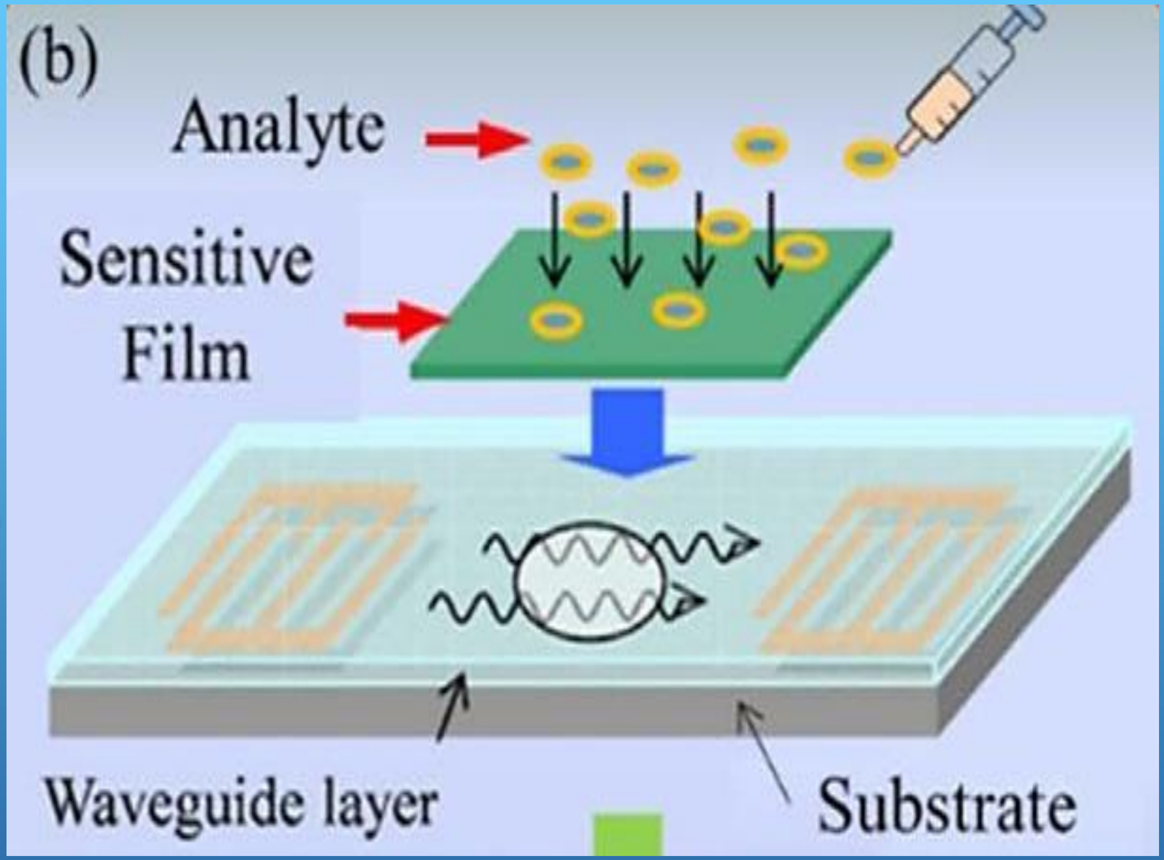
C)
- 9) High-Pressure Applications of Love Wave Sensors

Part A: From Earthquakes to Biosensors



?

Fig.3.



Seismic Waves

Love Wave Biosensor

Earthquakes. TIT in Tokyo

How to use Love waves
in Biosensors?

Twisted Railroad Tracks

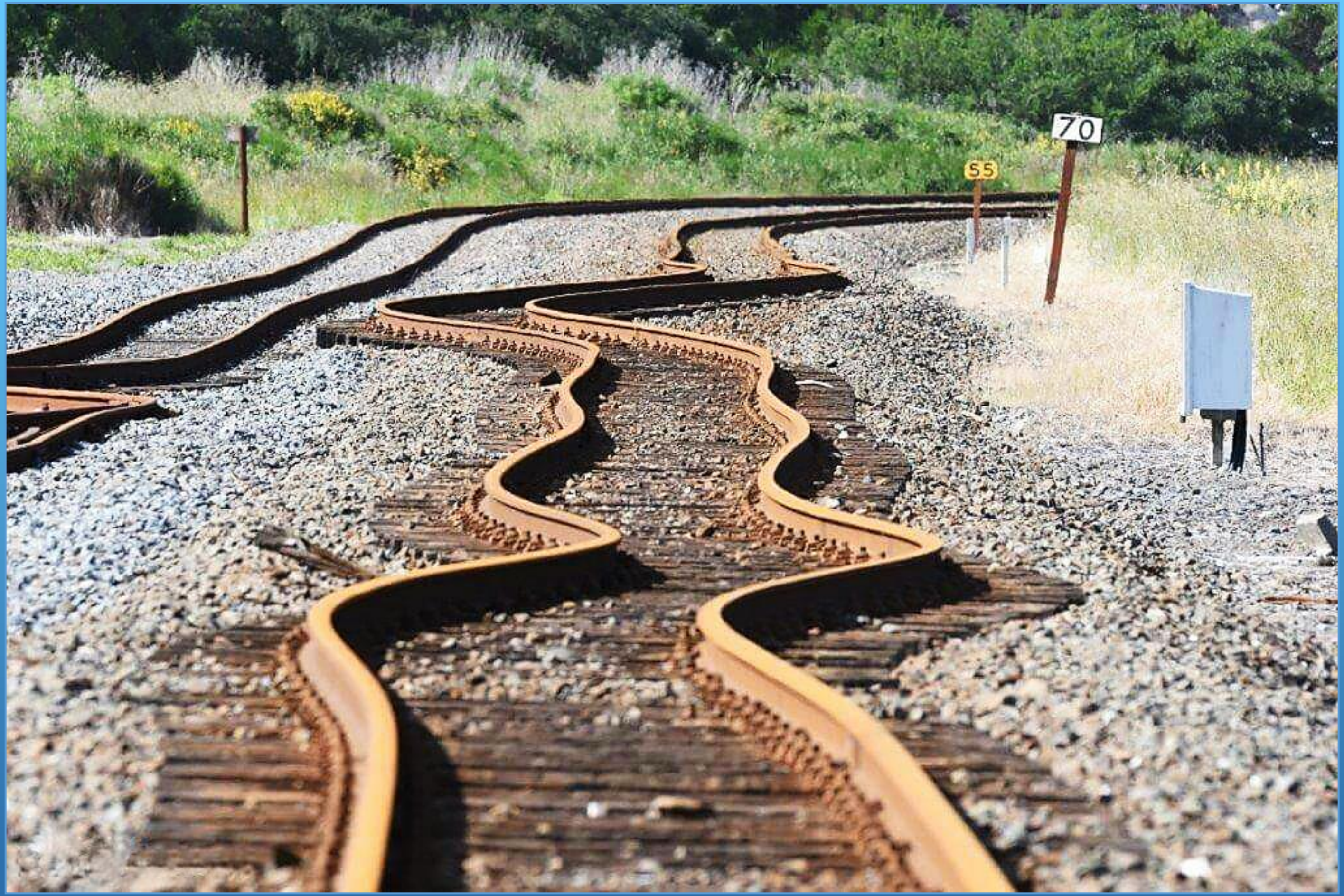
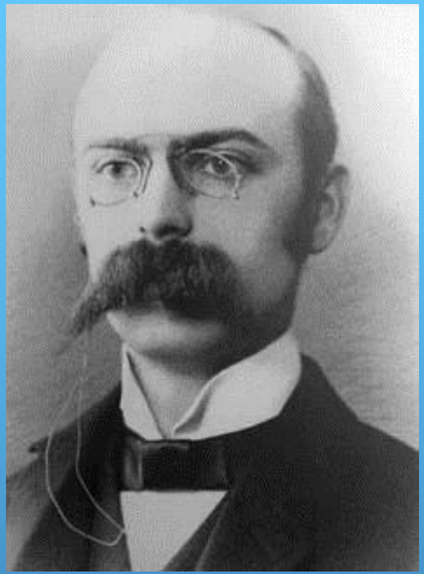


Fig.4. Example of structural damages due to SH displacement of Love surface waves

Fig.5.



Augustus, Edward, Hough Love - 1911

General Concept of Biosensor

- Analyte
- Sensing Layer
- Transducer
- Output Signal is electrical

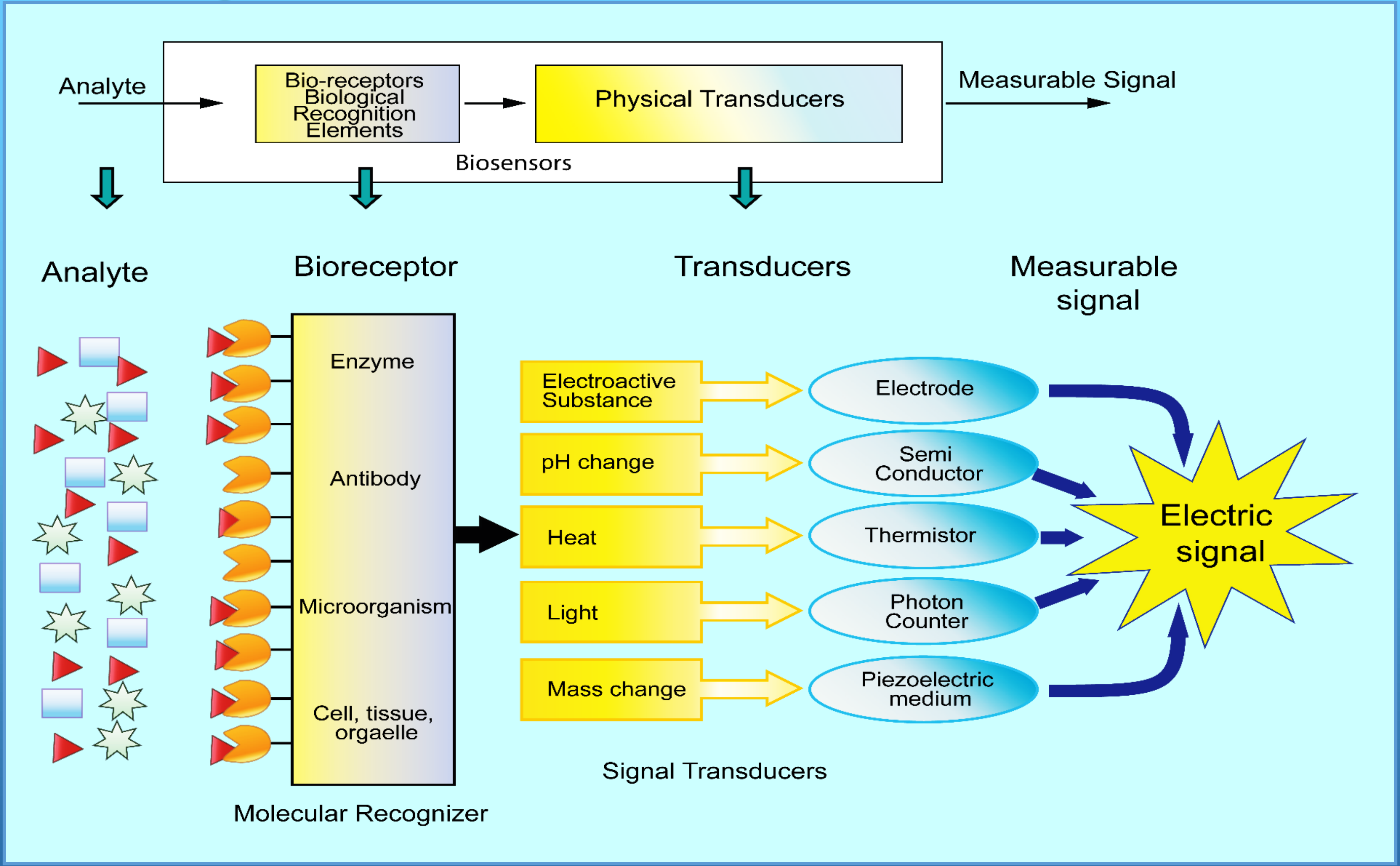


Fig.6.

- Sensor should operate in a liquid environment: (nasal swabs, whole blood, serum, urine, saliva) } (!!!)

Design of Love Surface Wave Biosensors is a Complex, Multidisciplinary Task !!!

R&D domains involved:

1. Physics:	wave motion, waveguides
2. Mechanics:	theory of elasticity, viscoelasticity
3. Mathematics:	differential equations, complex numbers
4. Electromagnetism:	piezoelectricity, IDT transducers
5. Electronics:	integrated circuits
6. Circuit Theory:	resonator and delay line configurations
7. Signal Processing:	digital filtering, FFT, Cross-correlation
8. Numerical Methods:	nonlinear equations, optimization procedures
9. Computer Programming:	C++, Fortran, (Matlab)
10. Chemistry:	surface bonding agents
11. Biology:	analyte selection and DNA
12. Medicine:	data interpretation and feedback

Desired Characteristics (Features) of Love Wave Sensors

- a) electrically responsive: the ability for automation (computerization) of measurements
- b) possibility of amplification (high sensitivity)
- c) short measurement time
- d) transmission of measurement results at considerable distances
- e) no moving parts
- f) miniaturization
- g) portability
- h) cost effectiveness

Why it was so Difficult to Develop a Biosensor Based on Viscosity Measurements?

Answer: Deficiencies of the Existing Methods and Sensors:

1) Conventional mechanical sensors (rotating cylinders) were of monstrous dimensions and completely unfit
2) Developed in 1950 ultrasonic sensors, with bulk SH waves, were inherently of very low sensitivity

Breakthrough:

3) Employment of SH surface waves proposed by P. Kielczynski in 1981 and further developments in the Laboratory of Acoustoelectronics (1981-1989)
4) Question: Why Love waves?
5) Answer: Love waves are SH surface waves
Acoustic energy is concentrated near the surface; high sensitivity

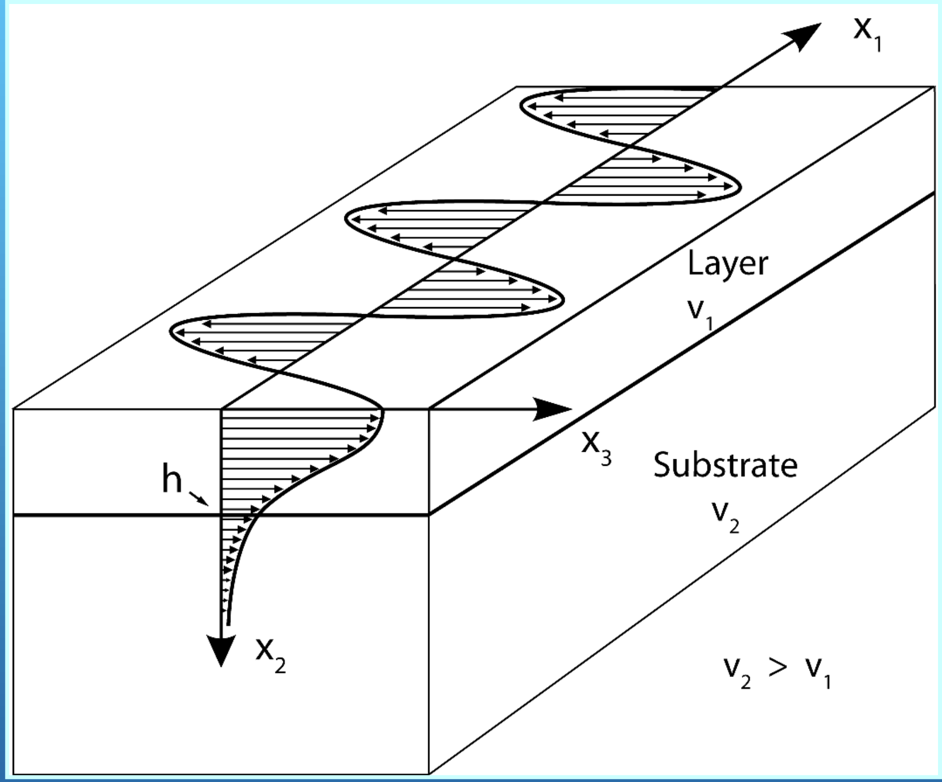


Fig.7. Mechanical displacement of the Love wave

First Publications on Love Wave Biosensors

Exactly 70 years after A.E.H. Love (1911)

1) P. Kielczynski and R. Plowiec, Polish Patent (1981)
2) P. Kielczynski, W. Pajewski, European Mechanics Colloquium (1987), (Nottingham, Great Britain)
3) P. Kielczynski, W. Pajewski, IEEE Ultrasonic Symposium (1988), (Chicago, USA)
4) P. Kielczynski, R. Plowiec, Journal of the Acoustical Society of America (1989)

In the above papers we have developed theoretical and practical basis of ultrasonic sensors, such as:

a) biosensors b) chemosensors and c) physical sensors

First publications in USA appeared 3 years later:

5) G. Kovacs et al., IEEE Ultrasonic Symposium (1992)

Determination of the shear impedance of viscoelastic liquids using Love and Bleustein–Gulyaev surface waves

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(Received 3 May 1988; accepted for publication 22 February 1989)

This paper presents a new method, using shear *SH* (shear horizontal) surface waves in solids, to determine the rheological parameters of viscoelastic liquids. Appropriate analytical formulas have been derived for Love and Bleustein–Gulyaev surface waves. The sensitivity of the proposed method is compared to that of the classical Mason method employing *SH* bulk waves. The measuring range of the proposed and classical methods is discussed in detail. Preliminary measurements are performed for typical mineral oil. The measured quantities agree very well with those obtained theoretically. The proposed method can be a few orders of magnitude more sensitive than the bulk wave method.

PACS numbers: 43.20.Ye, 43.35.Mr

INTRODUCTION

The determination of the viscosity of liquids is of great importance in investigating the internal structure of liquids as well as in controlling industrial processes employing oils, resins, or biological mixtures. Information about the viscosity of some organic liquids in the human body, such as blood or saliva, can be very useful in the medical diagnosis of certain diseases.

Using ultrasonic methods, one can determine the real R and imaginary X part of the shear impedance Z_l of the viscoelastic liquid. Ultrasonic methods are incomparable for frequencies above ~ 100 kHz. Shear bulk waves are highly damped in a viscoelastic liquid; i.e., their amplitude decreases e time after the fraction of the wavelength. Moreover, in the case of a Newtonian liquid, when $R \approx X$, the wavenumber of the *SH* (shear horizontal) bulk wave is pure imaginary. In this situation, the wave is then the nonpropagating mode. Therefore, the existing ultrasonic methods were reflectance methods, i.e., the shear impedance of the liquid was determined from phase $\Delta\theta$ and modulus r of the *SH* bulk wave reflected at the solid–liquid interface.[1] The considered methods were comparative; i.e., the results of two measurements were taken into account, the first for a free probe and the second for a probe loaded with the investigated liquid. Due to the big difference between the shear impedance of the liquid Z_l and the solid Z_q, the bulk wave method is of low sensitivity, e.g., for the probe of AT quartz $Z_q = 8.8 \times 10^6$ N s/m^3 loaded with H_2O one has $r = 0.997\,593$ and $\Delta\theta = 0.000\,241$ rad (Ref. 2), for frequency $f = 40$ MHz, and temperature $t_a = 25\,^\circ$C. These quantities are equivalent, respectively, to 0.0208 dB and 0.138° for one reflection of the *SH* bulk wave and, of course, are too small to be measured. For the 50th echo of the wave, the amplitude and phase changes are equal to 1 dB and 6.9°. To obtain an error of measurements lower than 10%, the amplitude and phase should be measured with an accuracy of 0.1 dB and 0.69° (for 40 MHz). These are rather strong requirements for electronic equipment. Moreover, the parallel faces of the probe should be polished with optical accuracy. Concluding, one can say that the classical bulk wave method is of low sensitivity *per se*. Therefore, a very precise electronic unit is required.

On the other hand, surface acoustic waves (SAW) propagating in solids are strongly dependent on the boundary condition on the surface of propagation: in particular, on the properties of an adjacent medium—liquid or gas, for instance.

SAW can be classified into two general groups: Rayleigh type waves and *SH* waves. The former waves have at least two components of vibration, i.e., longitudinal (L) and vertical transverse (*SV*), which cannot be separated. By contrast, *SH* surface waves possess only one *SH* component of vibrations. Therefore, they can be used to determine the shear parameters of an adjacent fluid. There are two well-defined types of *SH* surface waves; Love waves[3] and Bleustein–Gulyaev[4] waves. The former can propagate in layered subsurface structures and the latter can exist in some piezoelectric materials having at least a twofold axis of symmetry. Due to the characteristic dimension, i.e., thickness of the surface layer, surface waves of the Love type are always dispersive and exhibit a multimode structure. On the other hand, surface waves of the Bleustein–Gulyaev (B–G) type are nondispersive; this can be of some advantage during impulse measurements.

The other types of *SH* surface waves, such as surface skimming bulk waves (SSBW) or surface transverse waves (STW) are not taken into account in this paper.

Inspired by the facts presented above, the authors have proposed the application of *SH* surface waves propagating in solids to determine the rheological parameters of the adjacent viscoelastic liquid.[5]

It is interesting to note that surface waves of the Rayleigh type were employed to determine the acoustic impedance of nonviscous liquids for longitudinal waves.[6]

The fundamental principles of the proposed *SH* surface wave method are described in Sec. I. The appropriate analytical formulas are derived in Sec. II. Experimental procedures for measuring R and X are given in Sec. III. The parameters of the classical and the proposed methods are

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Physical Model of Love Wave Sensor

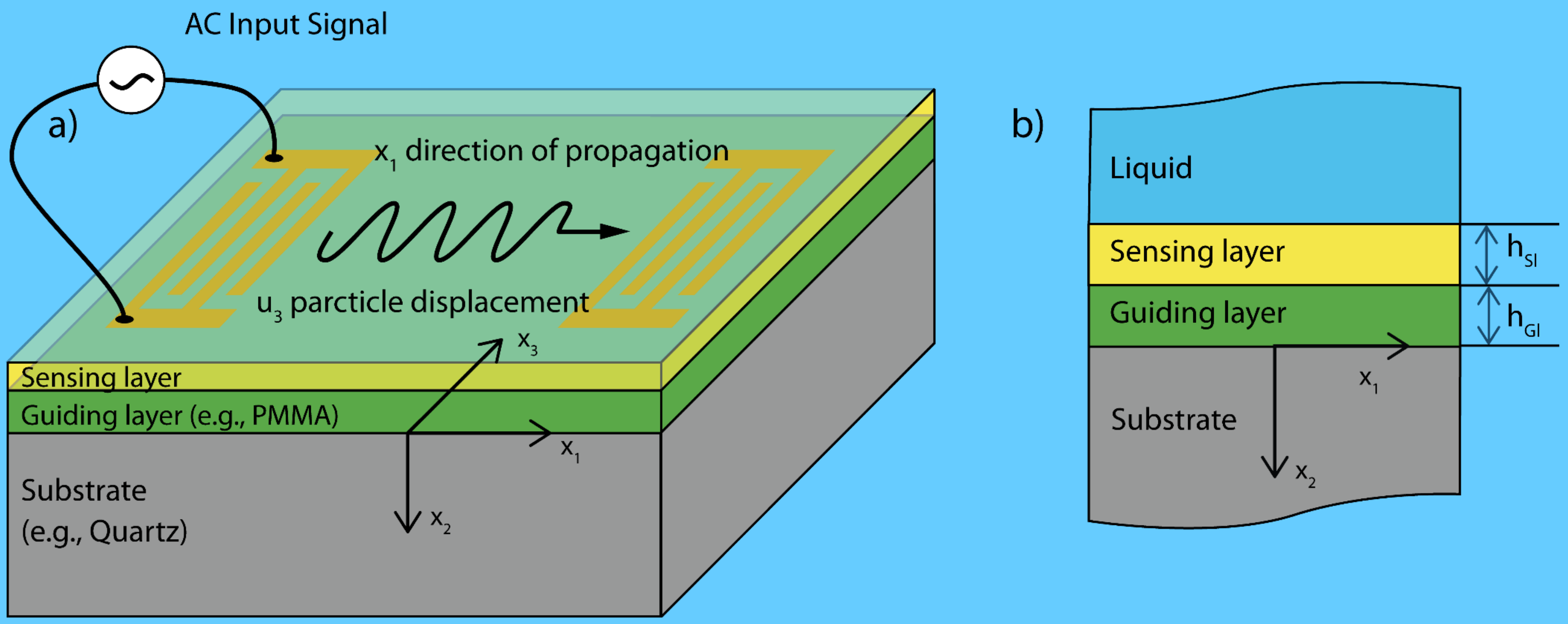


Fig.9

a) Typical dimensions - 1 x 5 x 20 mm
b) Circuit configuration - resonator or delay line
c) Frequency range - 50 - 500 MHz
d) Wavelength range - 10 - 100 μm

Mathematical Model of the Love Wave Sensor (Basic Equations)

$$\boxed{u_3(x_1, x_2, t) = f(x_2)\cdot exp[j(\beta x_1 - \omega t)]}$$

- Equations of motion:

  Newton's second law (principle) of motion

  u_3 = mechanical displacement of the Love wave

In the liquid (Newtonian)

$$\frac{\partial v_3}{\partial t} - \frac{\eta}{\rho_l}\left(\frac{\partial^2}{\partial \boldsymbol{x}_1^2} + \frac{\partial^2}{\partial x_2^2}\right) v_3 = 0 \qquad (1)$$

In the layer h_{sl}=0

$$\frac{1}{v_1^2}\frac{\partial^2 u_3}{\partial t^2} = \left(\frac{\partial^2}{\partial \boldsymbol{x}_1^2} + \frac{\partial^2}{\partial x_2^2}\right) u_3 \qquad (2)$$

In the substrate

$$\frac{1}{v_2^2}\frac{\partial^2 u_3}{\partial t^2} = \left(\frac{\partial^2}{\partial x_1^2} + \frac{\partial^2}{\partial x_2^2}\right) u_3 \qquad (3)$$

- Boundary conditions:

- 1) $(\text{shear stress})_{\text{Liq}} = (\text{shear stress})_{\text{Lay}}$ (upper surface)
- 2) $(\text{mech. displ.})_{\text{Lay}} = (\text{mech. displ.})_{\text{Sub}}$ (upper surface)
- 3) $(\text{shear stress})_{\text{Liq}} = (\text{shear stress})_{\text{Lay}}$ (interface)
- 4) $(\text{mech. displ.})_{\text{Lay}} = (\text{mech. displ.})_{\text{Sub}}$ (interface)
- 5) $(\text{mech. displ.})_{\text{Sub}} = 0$ (Infinite depth)

Mathematical Model of the Love Wave Sensor Sturm-Liouville Problem

- Mathematics is a Queen of Sciences

$$\frac{d}{dx_2}\left(c_{44}(x)\frac{df(x_2)}{dx_2}\right) + \rho\omega^2 f(x_2) = \beta^2 c_{44}(x_2)\, f(x_2) \qquad (4)$$

$$\frac{df(0)}{dx_2} = 0 \qquad\qquad f(\infty) = 0 \qquad (5)$$

- Sturm-Liouville Problem (4-5) for eigenvalues and eigenvectors:
- β^2 = eigenvalue – determines the phase velocity of the Love wave ($\beta = \omega/v_P$ - wave number)
- $f(x_2)$ = eigenvector – determines the distribution of the mechanical displacement with depth
- Analogous equations describe the motion of quantum particles in a potential well (Schrodinger equation), and planar optical waveguides

Complex Dispersion Equation for Love Waves

$$\sin(qD) \cdot \{(\mu_1)^2 \cdot q^2 + \mu_2 \cdot b \cdot \lambda_1 \cdot j\omega\eta\} - \cos(qD) \cdot \{\mu_1 \cdot \mu_2 \cdot b \cdot q - \mu_1 \cdot q \cdot \lambda_1 \cdot j\omega\eta\} = 0 \quad (6)$$

- Quantities q, b and λ_1 in Eq.6 are complex: (P. Kielczynski et al., 2012)

- This is an implicit function of (β, ω) i.e., $F(\beta, \omega) = 0$ (7)

$$Re\, F(\beta, \omega) = 0 \quad (8)$$

$$Im\, F(\beta, \omega) = 0 \quad (9)$$

$$\Rightarrow (v_P, \alpha)$$

- v_P = phase velocity of the Love wave
- α = attenuation of the Love wave
- This is a mathematical model of the sensor (Eq.6)

Attenuation and Phase Velocity of Love Surface Waves Versus Concentration of the Analyte

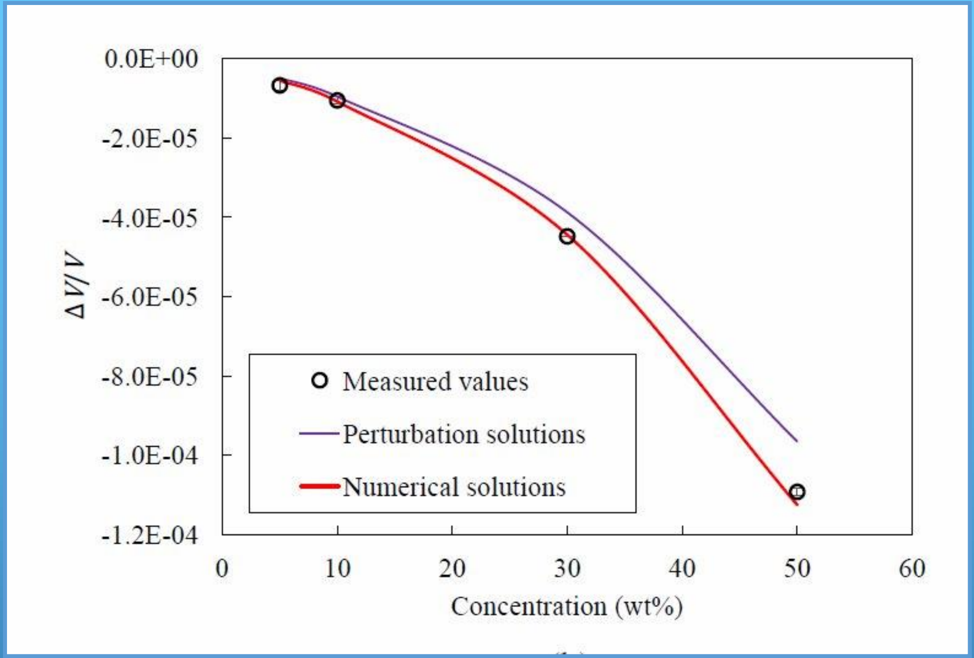


Fig. 10 Changes in phase velocity versus analyte concentration (glycerol in water)

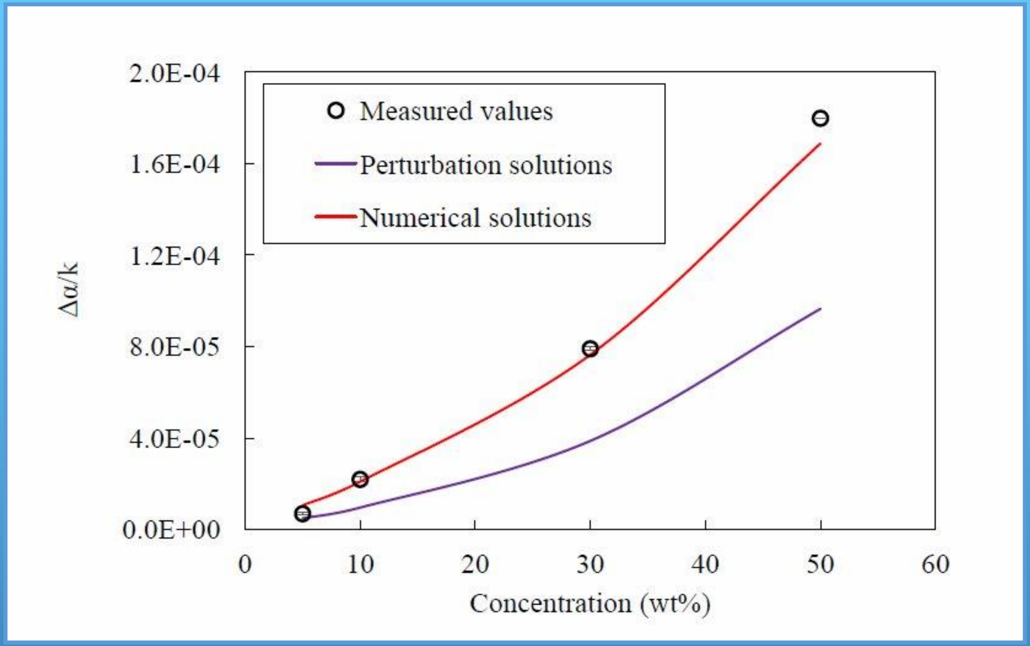


Fig. 11 Changes in attenuation versus analyte concentration (glycerol in water)

Dependence of the dispersion curves on the analyte parameters can be evaluated:

1) analytically $v_P = v_P(C, \rho, \eta)$; $\alpha = \alpha(C, \rho, \eta)$
2) numerically and
3) experimentally

Laboratory Design of Love Wave Biosensor

- 36°Y-90°X piezoelectric quartz substrate
- 250 MHz centre frequency IDT
- 92 nm gold layer
- 9 mm, distance between IDTs

1. Input and output signals are electrical Analog Signals (in Nature) Digital Signals (in Electronics).

2. Piezoelectric effect

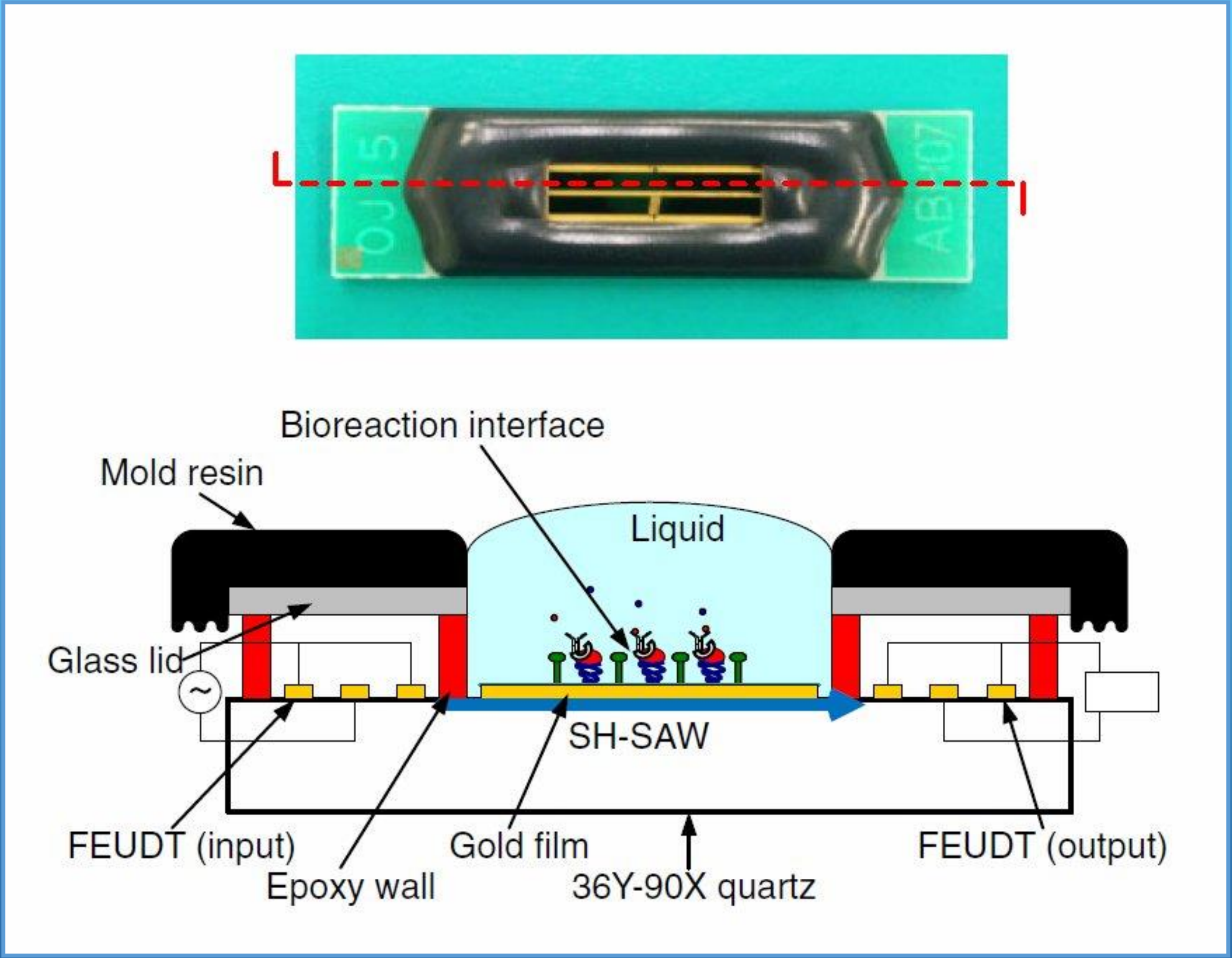
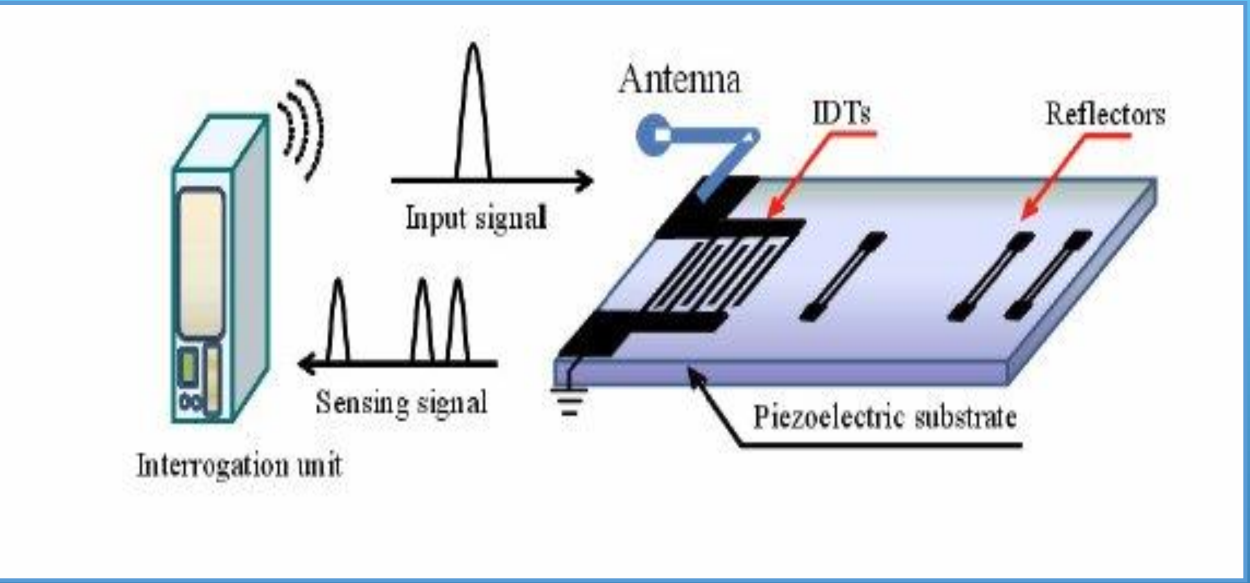


Fig.12. Cross section and top view of a Love wave biosensor

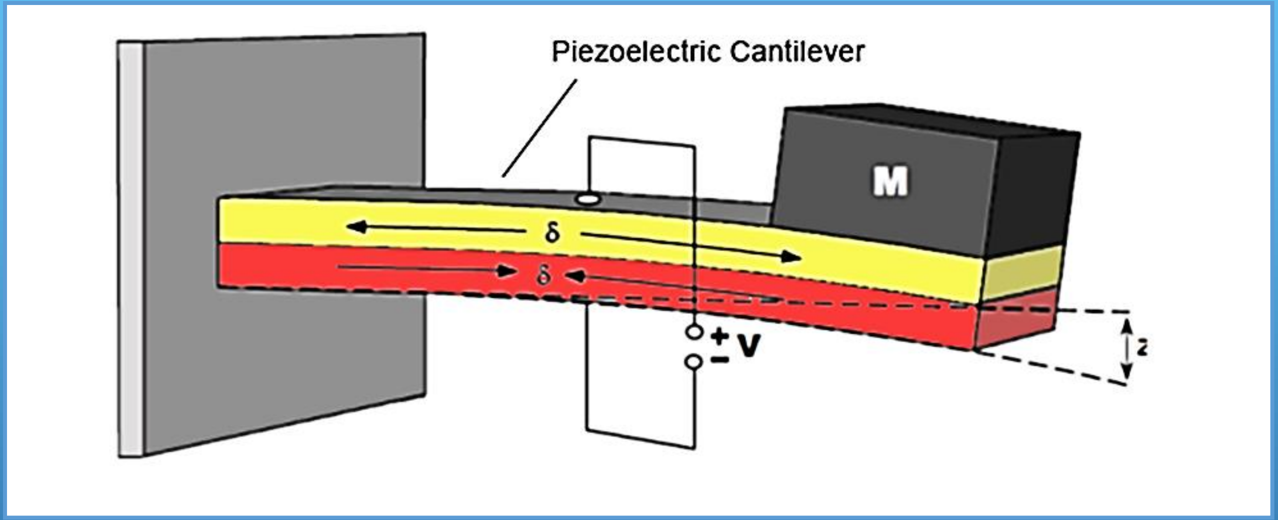
Analytes Measured with Love Wave Biosensors

- Size and shape of DNA
- Detection of cocaine
- Detection of toxic heavy metals in liquids
- Pesticides and metabolite detection in fruit juices
- Real-time detection of hepatatis B
- Virus and bacteria detection in liquids
- Detection of chemical warfare agent simulants
- Real-time detection of antigen-antibody interactions in liquids (immunosensor)
- Diagnostic tests for Flu
- Diagnostic tests for Chlamydia

Wireless Bioelectronic Sensors with Love Surface Waves



Wireless communication



Energy Harvesting - Self powered sensors

Fig.13 Modern Concepts

Prototype of a Portable Diagnostic Kit with Love Surface Wave Immunosensor for a Personal Home Healthcare Use

Fig.14

a) Disposable sensor unit
b) Hand-held electronic reader
c) Wireless connectivity to the smart-phone
d) User-friendly diagnosis

Advantages of Love Surface Wave Biosensors

a) electrical input/output: ability of computerized measurements
b) high sensitivity and low Threshold of Detection (TOD)
c) high linearity and dynamic range
d) no moving parts
e) stable operation: long inter calibration time
f) wireless connectivity, possibility for energy harvesting
g) miniature and portable
h) short measurement time
i) temperature compensation
j) HF (AC) driving signal, high accuracy of phase (time difference) measurements

Future Developments and Perspectives for Love Wave Biosensors

New Analytical Methods:

1) Inverse problems (higher accuracy),

   Minimization of the Objective Function Φ: $\min \ \Phi(\text{analyte, waveguides, experiment}, \omega)$

   proposition in:

   P. Kiełczyński et al., Inverse procedure for simultaneous evaluation of viscosity and density of Newtonian liquids from dispersion curves of Love waves, Journal of Applied Physics, 116 (2014) 044902

2) Optimization methods in Banach space (Functional Analysis)

New Hardware Innovations:

1) Multilayer (N>10) LSW waveguides (wideband characteristics)
2) Higher operating frequencies 2-5 GHz (higher sensitivity)
3) Metamaterials and phononic crystals (miniaturization)

Part B: Extraordinary Parameters of the Human Ear (Cochlea) – Natural Biosensors

No man-made device can even approach the extraordinary parameters of the Cochlea

1) Huge dynamic range (120 dB)
2) Ultra low power consumption (14 μW)
3) Very high frequency selectivity (2 Hz)
4) Extremely low threshold of detection (TOD = 10^{-18} W) close to the thermal noise in air

Nature is always more clever than Humans (PK)

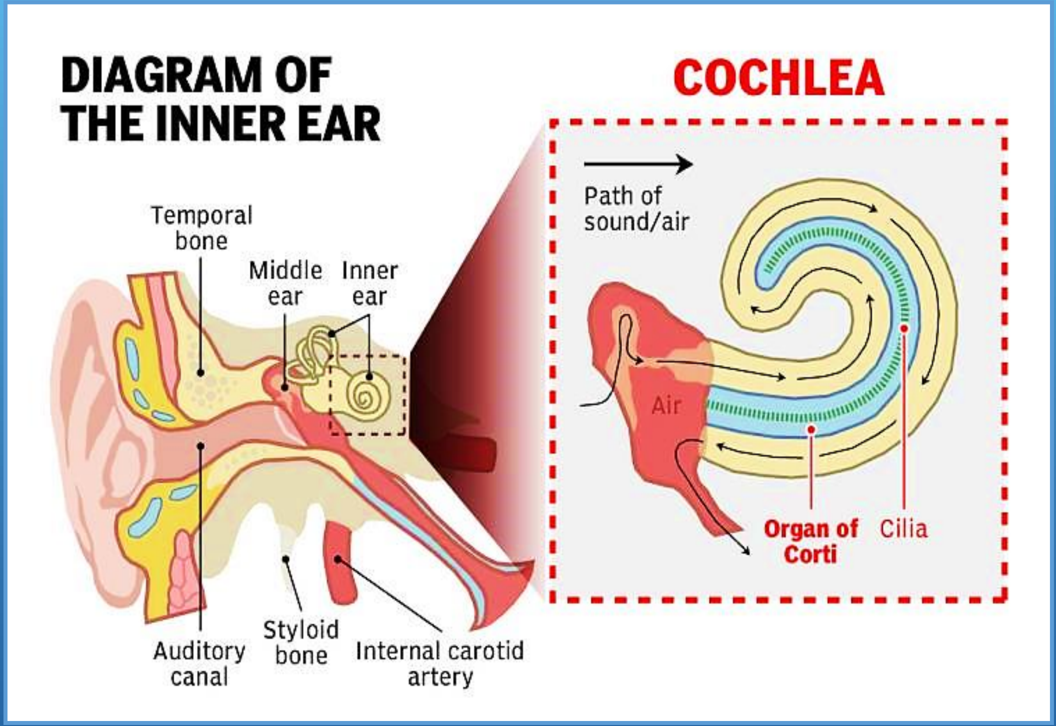


Fig.15. Cross-section of the Human hearing organ

Flow of Ionic Currents (K^+ Cations) in a Closed Circuit in the Human Inner Ear (Cochlea)

- Current of K^+ cations (not electron current)
- OHC – Outer Hair Cells
- DC Voltage Source

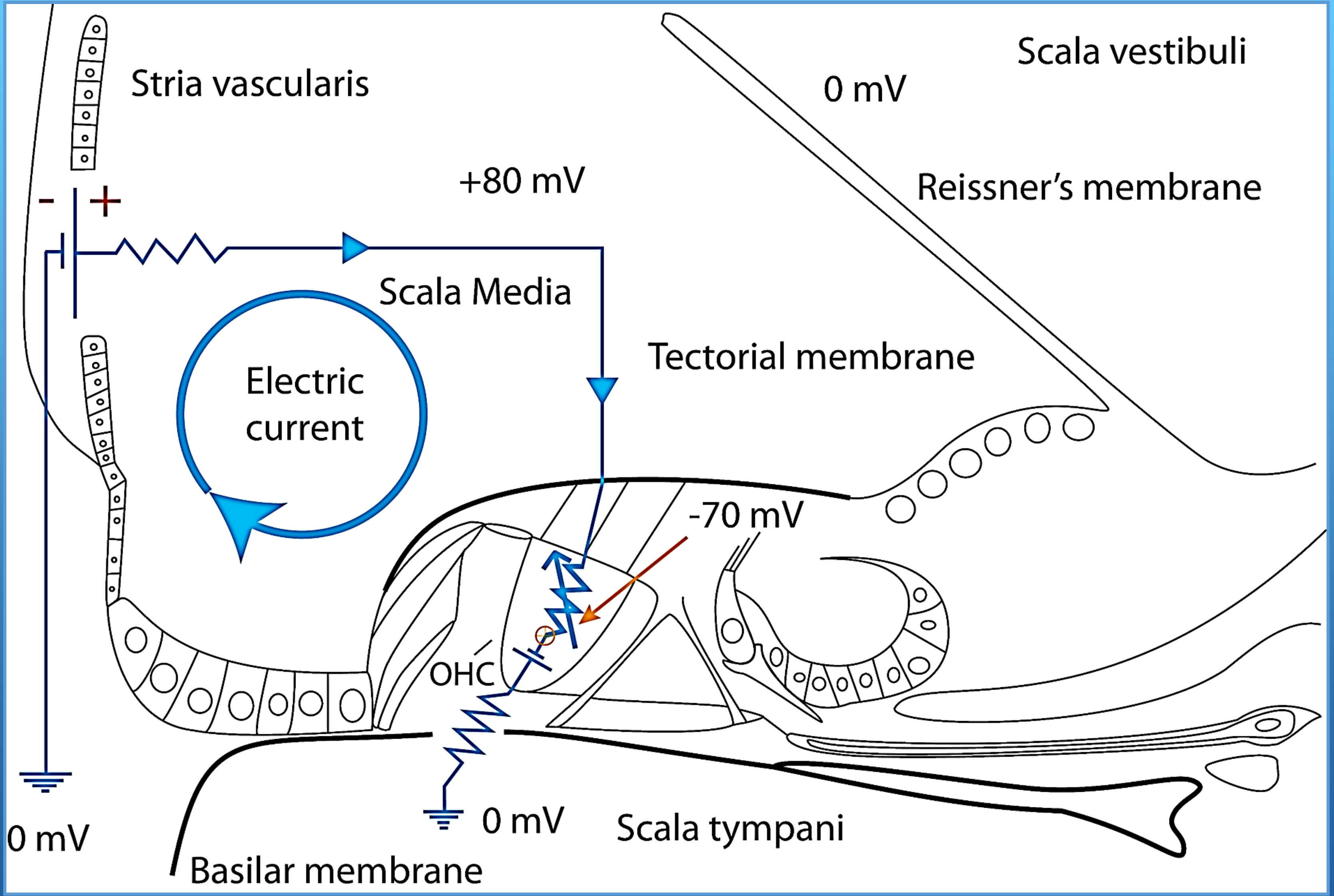


Fig.16. Cross-section of the Cochlea

Biological Electromechanical Transistors
Transistor Effect in the Cochlea

- What is a transistor?
- A device (valve) that controls the flow of power from the source of potential energy to the loading resistance

Ionic channels

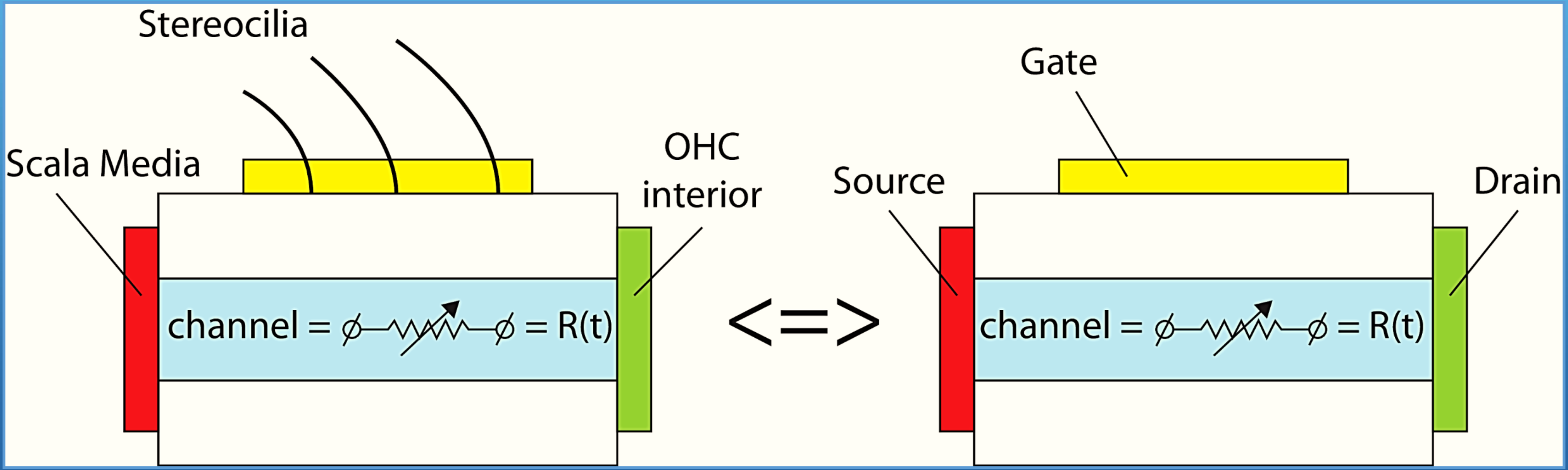


Fig.17. Physical models of the proposed electromechanical transistor and the classical field effect transistor. (P. Kielczynski – 2014).

Selectivity of the Parametric Amplifier in the Cochlea via a Nonlinear Capacitance

- Negative resistance (conductance) represents an active element supplying an external energy into the system
- It is amazing (although expected) that in the human body all laws of the classical electrical circuit theory do apply, i.e.,
- Ohm's Law
- Kirchhoff's Current Law
- Kirchhoff's Voltage Law
- Direct and Inverse Piezoelectric Effect

Part C: Very High Pressure Love Wave Sensors (Green Technologies)

1) At the bottom of the Japan trench:
   (9 km deep) p = 90 MPa = 0.09 GPa

2) Weight of two elephants per 1 cm^2:
   p = 1 GPa (1000 MPa)

3) On the bottom of the Marianas Trench:
   p = 110 MPa = 0.11 GPa

4) Diesel engine: p = 300 MPa
   (Common Rail)

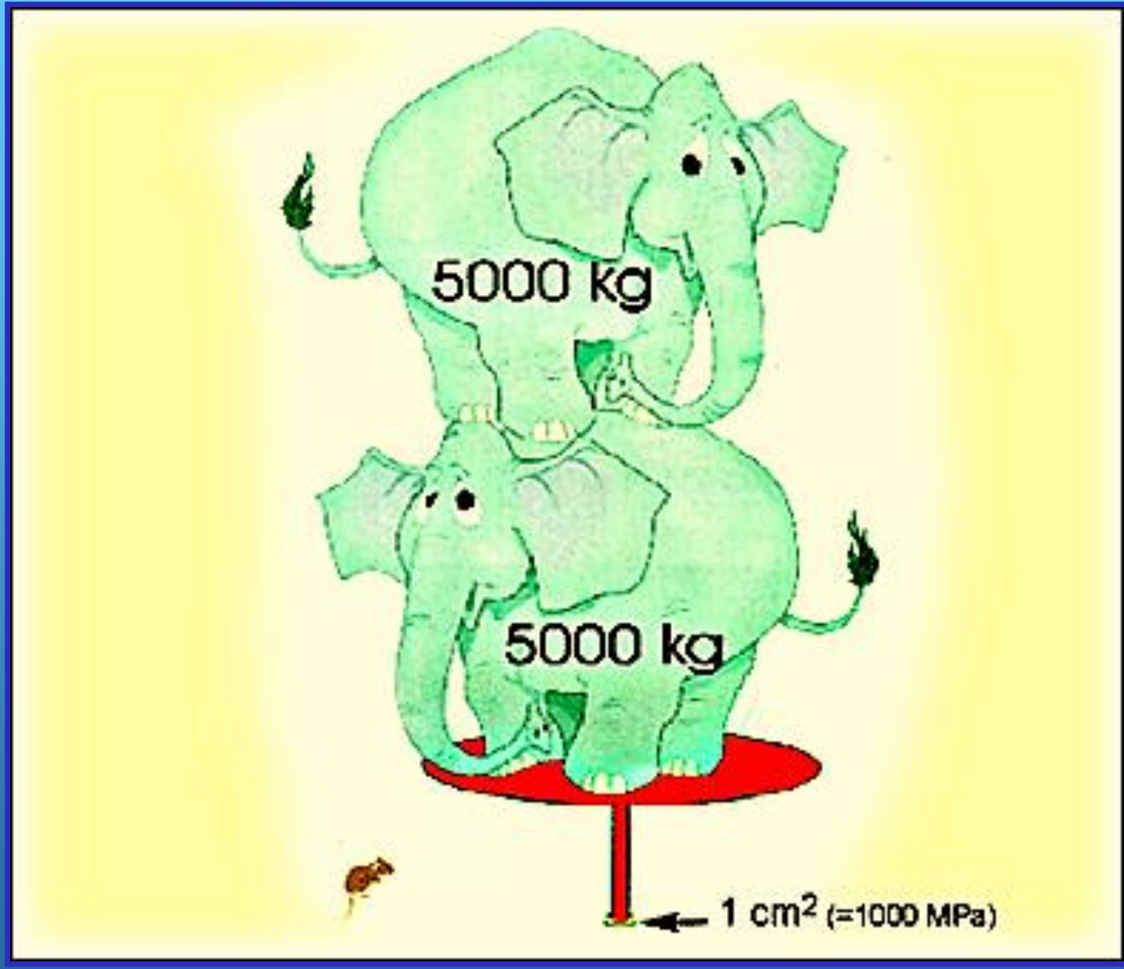


Fig.18 Pressure exerted by two elephants

Measurements of Liquid Viscosity at Very High Pressures with Love Wave Sensors

Fig.19. High pressure Love wave waveguide

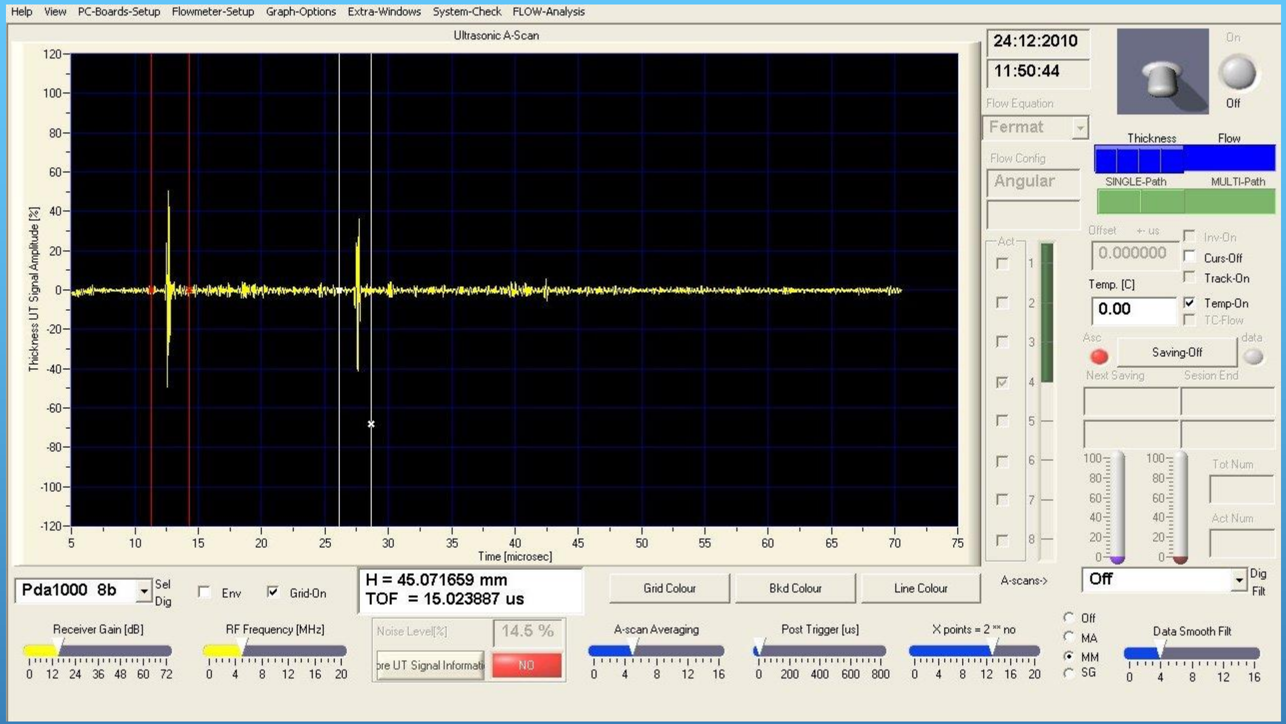


Fig.20. Love wave impulses

New method: P. Kielczynski et al., Review of Scientific Intruments, 79, 026109, (2008)

Conventional mechanical methods are entirely useless at high pressures

Importance of High Pressure Investigations

1) Oceanographic research.
2) Deep sea research
3) In environmental protection

   Green Technology

4) In biofuels (cold-start problems)
5) In food conservation and processing
6) Zig-zags (Phase transitions)

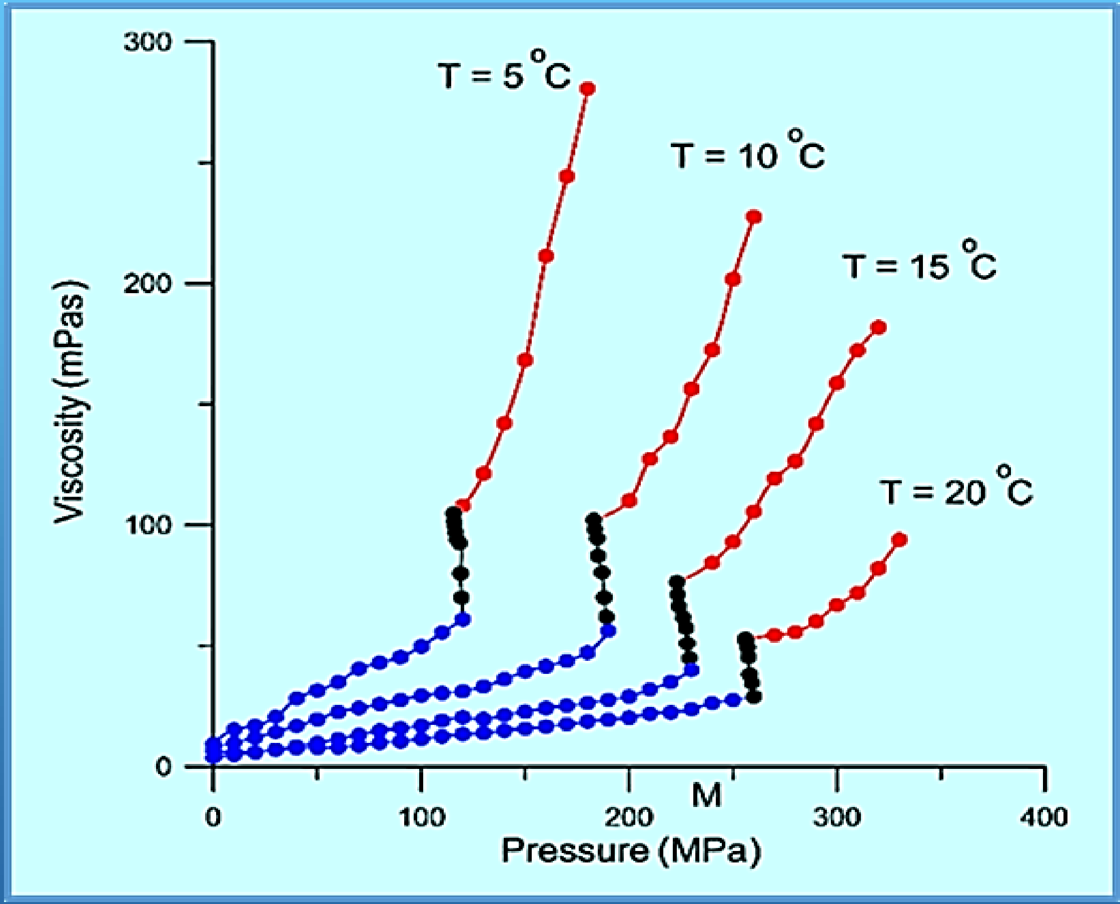


Fig. 21. Viscosity of the rapeseed methyl esters (RME) sample measured as a function of pressure p. (P. Kielczynski et al., 2017).

General Conclusions of the Presentation

1) Sensor development requires complex multidisciplinary research
2) Biosensors employing Love surface waves have great potential in clinical diagnostics applications
3) Sensors employing Love surface waves and B-G surface waves are unique at high pressure measurements of phase transitions in liquids
4) High pressure phase transitions measured with Love and B-G surface waves are of crucial importance in the emerging new green technologies (biofuels) and modern food processing industry
5) Extraordinary properties of the human auditory organ, such as the Cochlea, are very far from understanding and require further extensive research

Chopin Monument in Lazienki Park in Warsaw , Poland

Fig. 22. Portrait of Frederic Chopin
Polish Composer (1810 – 1849)

Fig. 23. Similar monument is located in Hamamatsu , Japan
(near the Railway Station)