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GAS SENSORS AND ARTIFICIAL OLFACTION INSTRUMENTS - RESEARCHES AND APPLICATION AT UNIVERSITY OF LATVIA

MF Medicīnas fakultāte

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Function in the Action (External Expert)

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Contribution from:

- **Institute of Solid State Physics, University of Latvia:** Dr. L. Grinberga, Dr. J. Hodakovska, Dr. J. Kleperis, Dr. V. Ogorodniks;

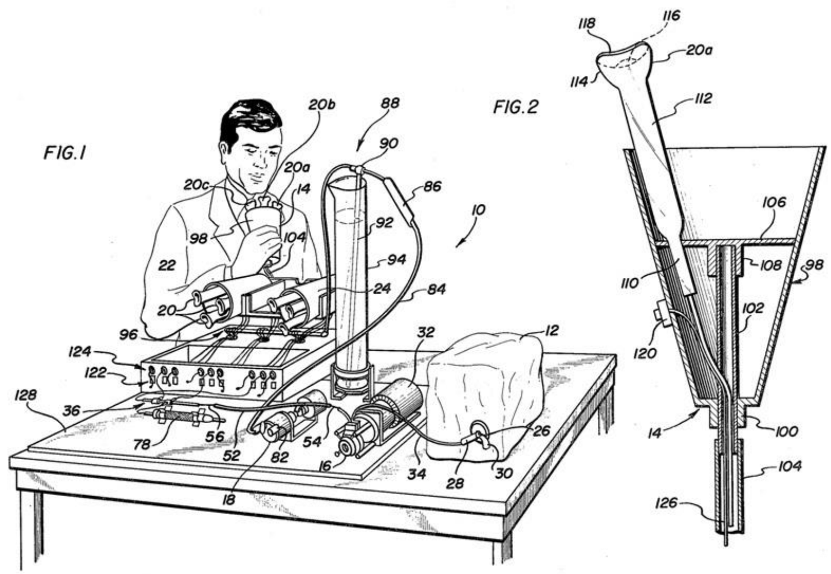
- **Faculty of Medicine, University of Latvia:** Prof. I. Taivans, Dr. M. Bukovskis, Dr. N. Jurka

MF Medicīnas fakultāte

From history

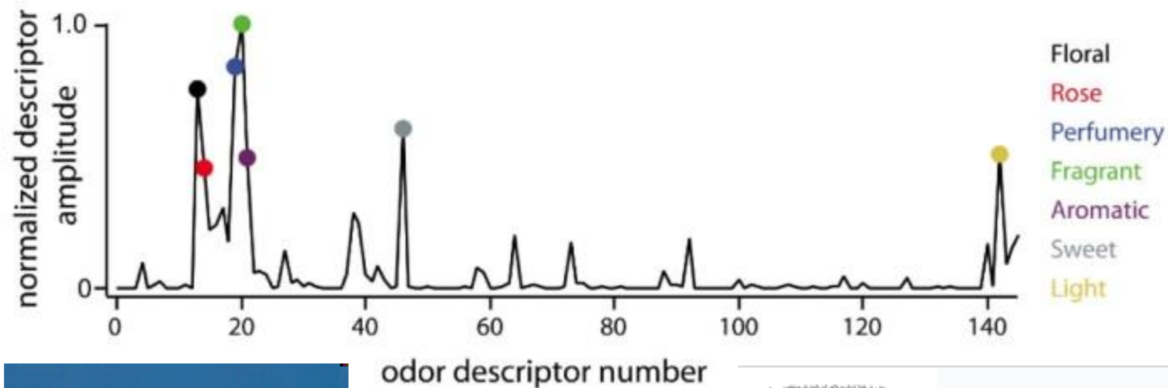
Andrew Dravnieks (1912-1986), famous Latvian Chemist received his Master's degree in chemical engineering from the University of Latvia in Riga, and a Doctor degree in physical chemistry from Illinois Institute of Technology when he immigrated to USA (1944). Andrey Dravnieks developed original techniques for collecting, concentrating and trapping odorous atmospheres and for analyzing them, developed widely used nowadays olfaction method, consisting from sniffing panellists and diluted odours.

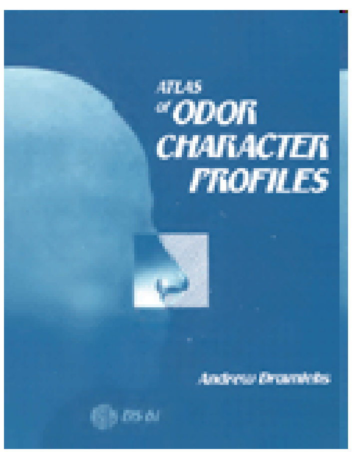
Figure from U.S. Patent 3,902,851 (1975), "Method of detecting odors and apparatus therefore," by Andrew Dravnieks).



From history

Andrew Dravnieks together with his friend Paul Laffort (France) were the first using discriminant analysis in processing the data from panelists and gas chromatograms of odorants, and his greatest work at the end of life was ASTM Data Atlas of odour character profiles.





ELSEVIER

Journal of Theoretical Biology

Volume 38, Issue 2, February 1973, Pages 335–345

An approach to a physico-chemical model of olfactory stimulation in vertebrates by single compounds ☆

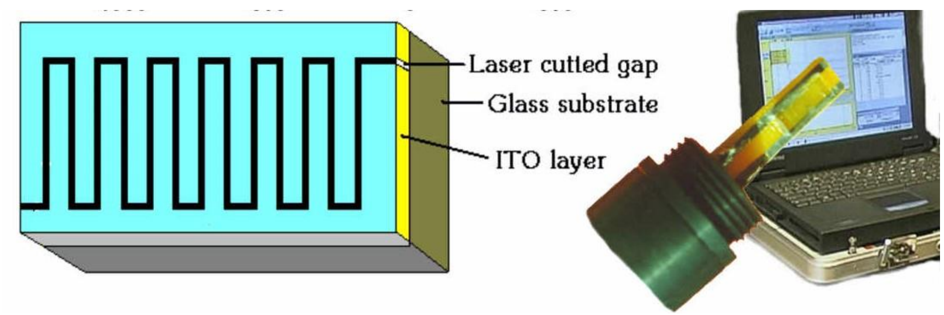
Paul Laffort

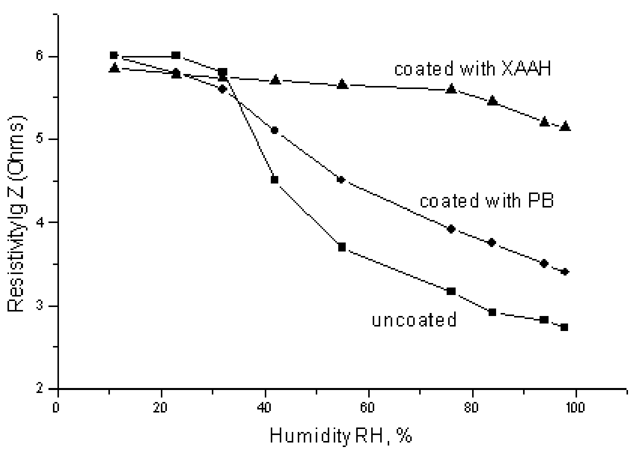
Andrew Dravnieks

Research of Gas Sensing Materials at ISSP UL

Different gas sensing materials and sensors were elaborated and researched at ISSP UL during 1980-1990ies:

Humidity sensor:





Electrochemical: hydrogen sensor (Pd/WO_3/Sb hydroxide/H_xWO_3); ammonia sensor (β-alumina exchanged with NH_3 ions;

Metal oxide sensors (alcohol, ozone etc)

Electrochemical hydrogen sensor. Лагздонс Ю.Л., Лусис А.Р., Клеперис Я.Я., Баярс Г.Э., Электрохимический сенсор водорода; Авт. Свид. СССР, н. 1440179 от 29 сентября 1987 года.

Kleperis J., Bajars G., Vaivars G., Kranevskis A., Lusis A. Gaseous sensors based on solid proton conductors. - Sensors and Actuators. V. 32, (1992) p. 476-479;

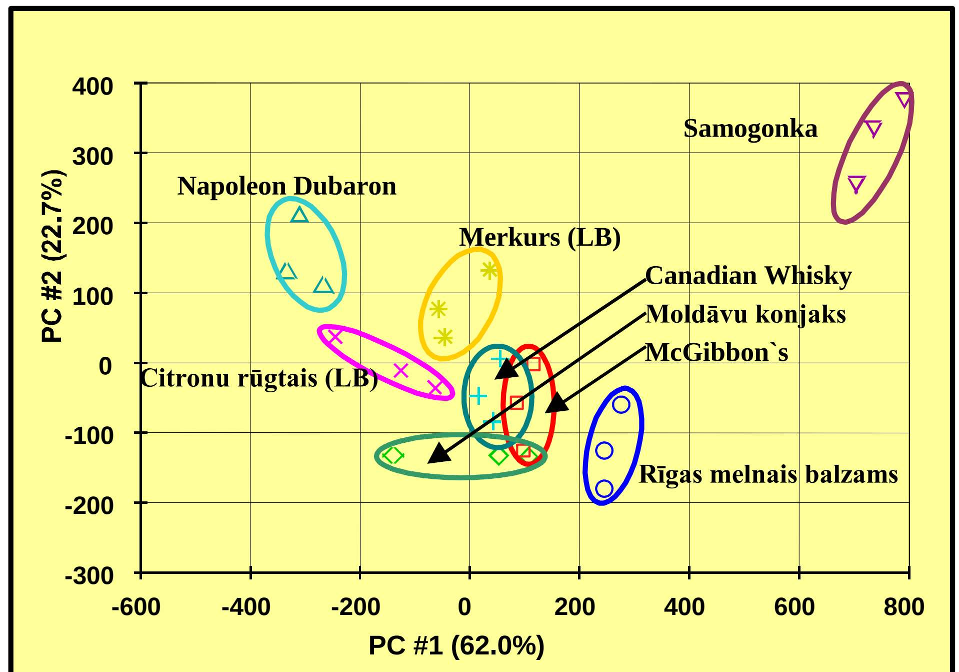
J.Kleperis, A.Lusis. Hydrogen transfer problems at metal/proton electrolyte interfaces. Z. fur Physik. Chemie 181 (1993) p. 321-328;

J.Kleperis, M.Kundzins, G.Vitins, V.Eglitis, G.Vaivars and A.Lusis, Gas-sensitive gap formation by laser ablation in In2O3 layer: application as humidity sensor. Sensors and Actuators B 28 (1995) 135-138

First Artifical Olfaction Instruments in LV

Interest in artificial olfaction instruments started from 1994 when cooperation was established with Linköping University (Prof. Ingemar Lundström, Dr. Anita Lloyd-Spetz).

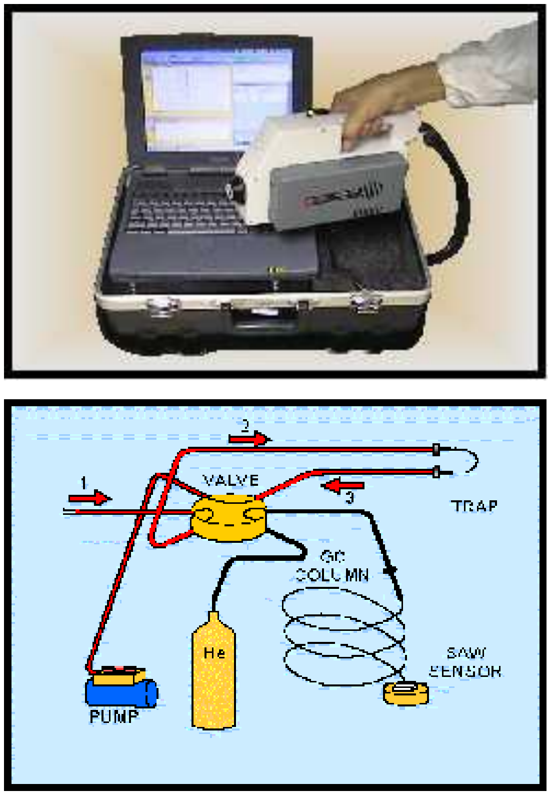
As instrument the electronic nose at ISSP UL appeared in 1997, from "Nordic Sensors AB" (Sweden), containing 14 gas sensors - 10 MOSFETs with different gas sensing electrodes (Pt, Pd, Ir and their alloys) and temperature gradient from 115 and 150 °C, and 4 high-temperature semiconductor oxide resistive sensors (TGS-813; 800; 881; 825).

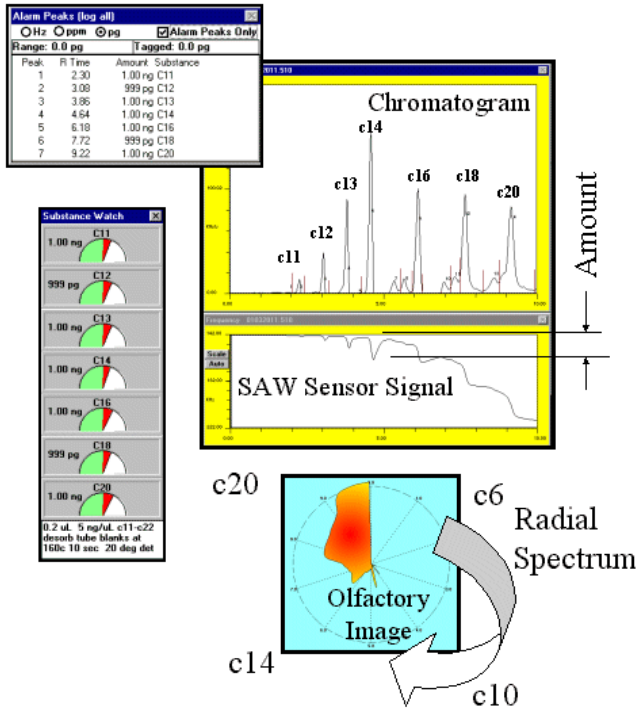


J. Kleperis, L. Grinberga, A. Lusis, Electronic nose: what it is and application examples. Latvian Journal of Physics and Technical Sciences, No.5, (2001), p. 57-66.

First Artifical Olfaction Instruments in LV

Different applications were tested together with second instrument: z-Nose (Electronic Sensor Technology, USA) – portable gas chromatograph coupled with extremely sensitive surface acoustic waves sensor.

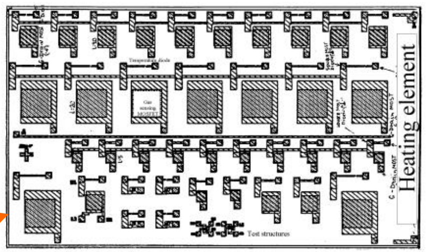


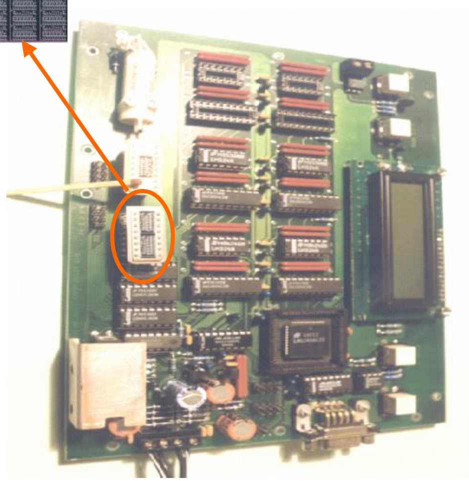


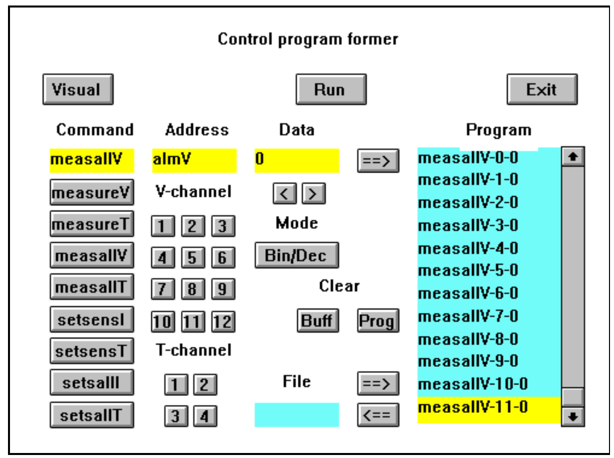
L. Grinberga and J. Kleperis, Fast Gas Chromatograph for determination of alcohols and benzene in the air and fuel; International conference EcoBalt'2003, Riga, 2003, pp 44-45.

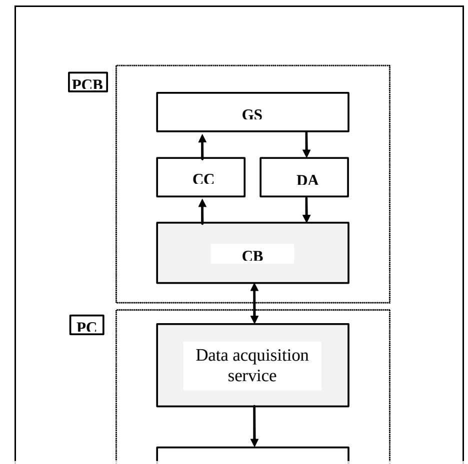
First Artifical Olfaction Instruments in LV

Together with Prof. Pēteris Misāns from Riga Technical University micro-system prototype for the mobile artificial sensing instruments was constructed, using HW/SW co-design as tool to create it. Microcontroller (Texas Instrument 3705x) was used as control module to deliver gas, control of sensor array and perform data acquisition.









[P.Misans, G.Dzilums, J.Shirs, “The Hardware for Artificial Nose”. In Proc. Baltic Electronics Conference ‘96, Tallin, October 7-11, 1996, pp. 425-428.

P.Misans, , J.Shirs, “The Software for Artificial Nose”. Baltic Electronics Conference ‘96, Tallin, October 7-11, 1996, pp. 343-346.

J.Kleperis, P.Misans, J.Shirs, G.Dzilums, J.Zubkans, V.Eglitis, A.Lusis, "An electronic nose developed as single module analyse system". In book: Digest of Technical Papers: The 11th International Conference Eurosensors XI. Warsaw, Poland, September 21-24, 1997. Vol. 3, p. 150-153.

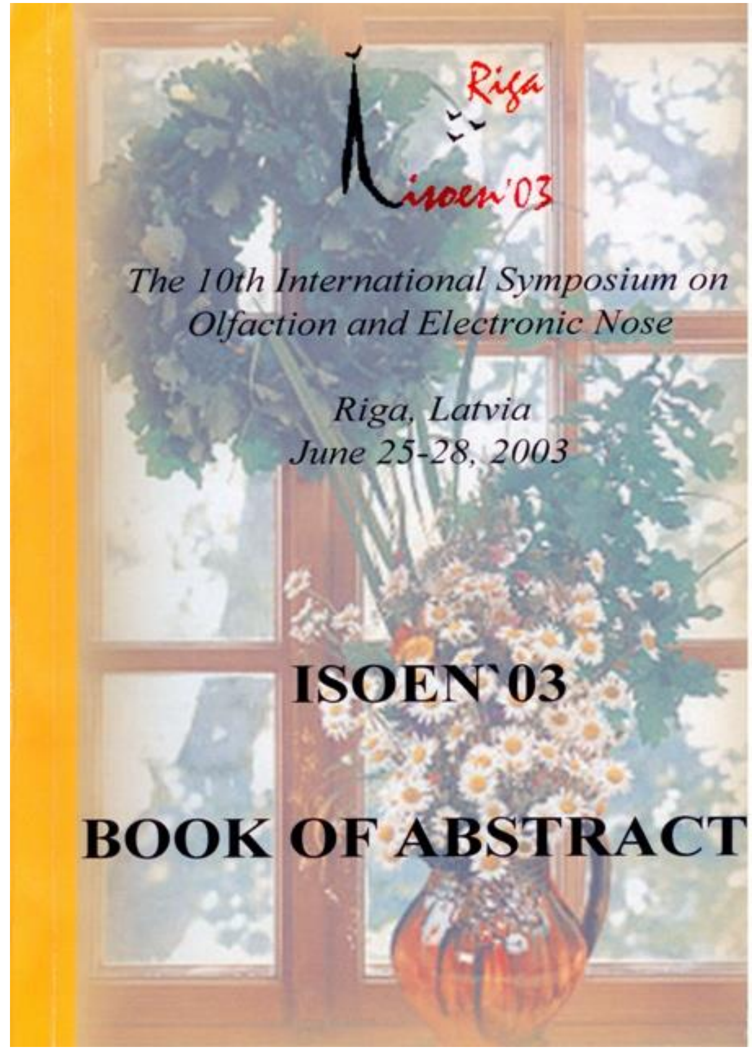
P.Misans , J.Kleperis, J.Zubkans, V.Eglitis, A.Lusis, I.Osmanis ,"The MATLAB-based Software for Data Acquisition and Control of Artificial Nose". In Proc. Nordic MATLAB Conference '97, Stockholm, Sweden, October 27-28, 1997, pp. 141-145.

10th ISOEN`03 in Latvia

The 10th International Symposium on Olfaction and Electronic Nose, ISOEN'03 was organized in Riga (Latvia), at University of Latvia, in June 25-28, 2003.

93 participants from 22 countries visited Riga to discuss main results in sensor and sensor array technologies, e-nose miniaturisation, odour description in electronic files and unified description language formation, e-nose applications in different fields, making emphasis on product adulteration and environment pollution control.

J. Kleperis, L. Grinberga, A. Lusis, P. Misans, Quick authenticity testing of food and goods. Is it real with e/z – nose? In book: Proceedings of ISOEN 2002, Ed. A.D`Amico, C. Di Natale, Rome, 2003, p. 89-94, 2003.



E-Nose in Life Science also Latvia

Later we had an interest in the use of e-nose for human health status monitoring, and research began with the athletes who were prepared for the Olympic Games.

The first idea was to find in breath lactic acid, which is indicative of muscle fatigue pregnant.

E-Nose in Life Science also Latvia

Cooperation started with the Faculty of Medicine at University of Latvia to study early diagnostics possibilities for pulmonary diseases. It is very important, because:

American Cancer Society. Cancer Facts & Figures 2012:

Lung cancer causes 1.3 million deaths annually, more than the next three most common cancers (colon, breast and prostate) combined

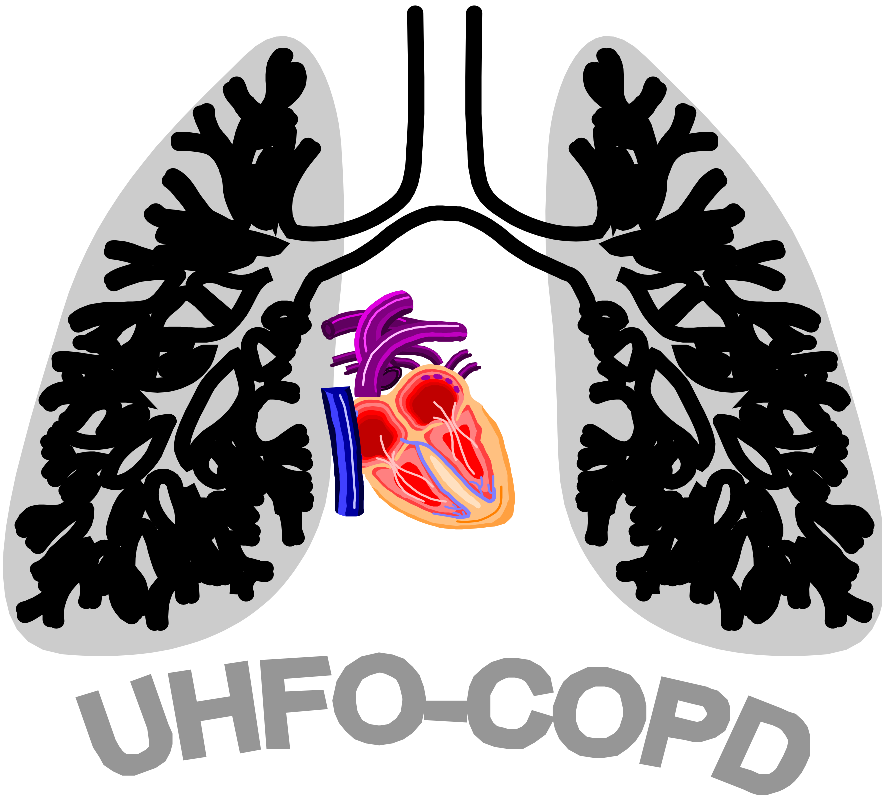
For NSCLC, the proportion with metastatic disease (stage IV) in Europe range from 47% - 55%

About 78% of NSCLC and 94% of SCLC cases are diagnosed in stage III or IV even ir Europe and Canada

58 - 73% of patients with stage I lung cancer survive for 5 years, for distant tumors the 5-year survival rate is only 3.5 %

E-Nose in Medical Faculty, UL

Collecting samples of exhaled breath from people at a high risk of lung cancer could be a cheap and non-invasive method of diagnosing the disease.



Lung cancer sniffer dogs
CBC News Aug 17, 2011

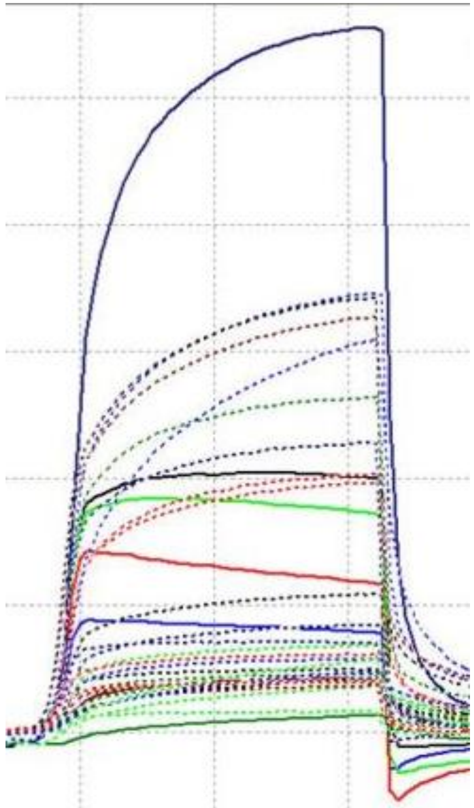
Gordon SM et al. Clin Chem 1985
Machado et al. AJRCCM 2005
Chen X et al. Cancer 2007

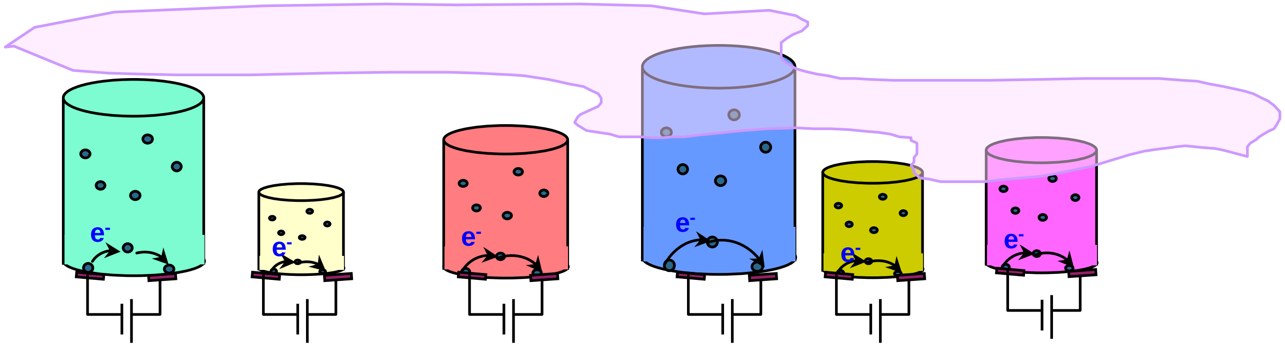
E-Nose in Medical Faculty, UL

Electronic nose sensor device Cyranose 320 (Smith's Detection Ltd, USA)

Functional principles of electronic nose

- VOC's induce change of the sensor volume and electric resistance;
- A unique response curve combination, contains information allowing discrimination of different samples





E-Nose in Medical Faculty, UL

Researchers collected and analyzed exhaled breath samples from 1232 lung cancer patients, patients with different lung diseases and healthy volunteers.

The aim of our study was

1) to develop optimal diagnostic algorithm by multi factorial logistic regression analysis (MLRA) bacward stepwise method;

2) and test its diagnostic potential for exhaled breath analysis by eNOSE in patients with lung cancer.

Method of sampling of the exhaled air was next:

Inspiration of VOC-filtered air by tidal breathing for 5 minutes, through T-shaped two-way non-rebreathing valve (Hans Rudolph Inc., Shawnee, USA);

Inhalation to total lung capacity and full exhalation with approximate flow rate 0.25 – 0.5 L/s into a polyethylene terephthalate plastic bag;

Analysis by electronic nose device (Cyranose 320, Smith Detection, USA) within 5 minutes after breath sample collection.

E-Nose in Medical Faculty, UL

Methods

Statistical analysis

Continuous predictors: relative maximum (R_{max}), area under curve ($\sum_{0\text{-}60''}$) and tg $\alpha_{0\text{-}60''}$ for each curve of 32 sensors, age, soaking history (pack-years) and ambient temperature tº C at the moment of measurement

Optimal detector parameter combination and mathematical model for discrimination of lung cancer was computed by multi factorial logistic regression analysis (MLRA) backward step-wise method in smokers, ex-smokers and non-smokers

Calculation of the probability of lung cancer:

Logistic regression equation

$$Y = \frac{e^{b_0 + b_1 \bullet x_1 + \ldots + b_n \bullet x_n}}{1 + e^{b_0 + b_1 \bullet x_1 + \ldots + b_n \bullet x_n}}$$

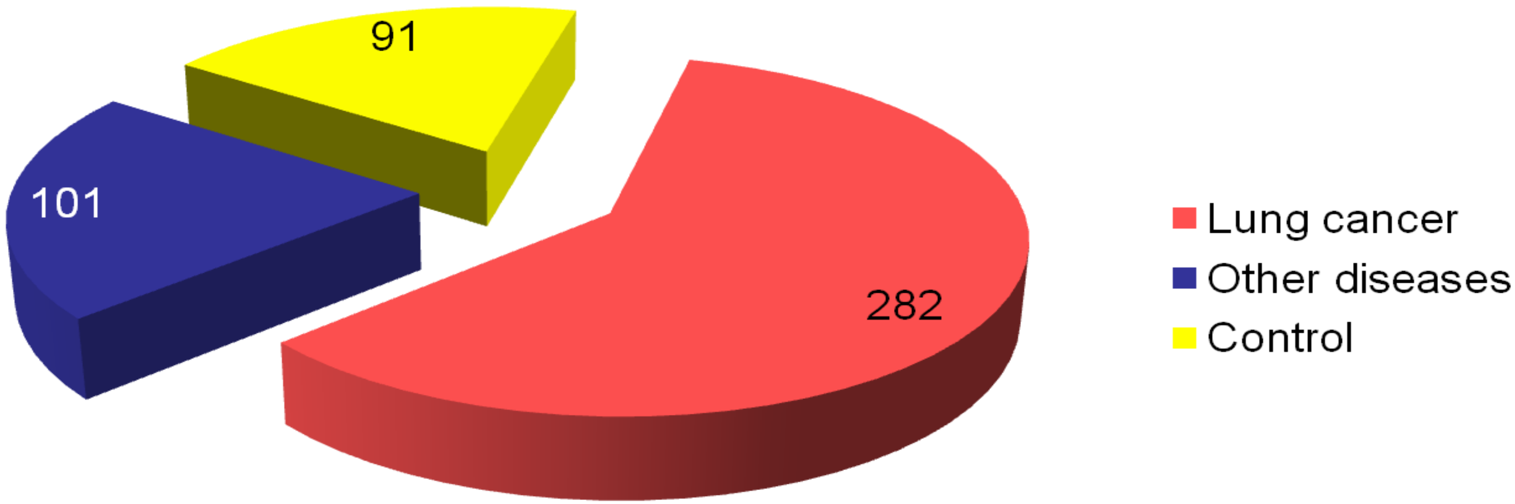
Y – probability of lung cancer
cancer if Y≥ 0.5
no cancer if Y<0.5
b_0 – free coefficient
b_1…..b_n hyperplane slope for variables
x_1…..x_n – variables
e – natural logarithmic base 2,7182818...

- Sensitivity, specificity, positive (PPV) and negative predictive value (NPV) of the algorithms in the training sample of each group was calculated.

E-Nose in Medical Faculty, UL

Results

Morphologically confirmed lung cancer
Other diseases: COPD, pneumonia, tbc, PATE, benign tumors etc.
Control – healthy volunteers, post-inflammatory pneumofibrosis



n=474	Total	Cancer	No cancer
Smokers	210	138	73
Ex-smokers	135	96	39
Non-smokers	129	49	80

E-Nose in Medical Faculty, UL

Results

Non-smokers (n=129)	Cancer	No cancer		
Cancer	48	1	94.12	PPV
No cancer	3	77	98.72	NPV
	97.96	96.25		
	Sensitivity	Specificity		

Ex-smokers (n=135)	Cancer	No cancer		
Cancer	93	3	95.88	PPV
No cancer	4	35	92.11	NPV
	96.88	89.74		
	Sensitivity	Specificity		

Smokers (n=210)	Cancer	No cancer		
Cancer	136	1	98.55	PPV
No cancer	2	71	98.61	NPV
	99.27	97.26		
	Sensitivity	Specificity		

E-Nose in Medical Faculty, UL

Summary

Development of new diagnostic algorithm taking into account exhaled breath analysis data in combination with lung cancer risk factors allowed to predict correctly lung cancer diagnosis with sensitivity up to 99.3% and specificity up to 97.3% in training group, and 86.0% and 87.0% respectively in the test group.

Authors have shown that it is possible to use breath tests to correctly identify lung cancer with a high sensitivity rate.

The results of our study take us one step further to understanding this important new technology.

V. Ogorodnik, J.Kleperis, I.Taivans, N.Jurka, M.Bukovskis, Electronic nose for identification of lung diseases. // Latvian Journal of Physics and Technical sciences, No.6, 2008, p. 60-67;

Maris Bukovskis, Gunta Strazda, Normunds Jurka, Uldis Kopeika, Ainis Pirtnieks, Liga Balode, Jevgenija Aprinceva, Inara Kantane and Immanuels Taivans. Detection of early stage lung cancer by electronic nose. European Respiratory Journal, September 1, 2013 vol. 42 no. Suppl 57 P2888

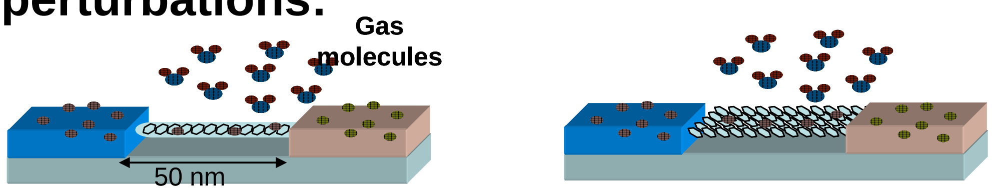
Tail - End

Research of Gas Sensors at ISSP continues:

Blue luminescence of hexagonal boron nitride (hBN) is studied - it was found that the intensity of the 400 nm luminescence in hBN depends on oxygen content in ambient atmosphere surrounding the sample. It allows conclusion that the material defects responsible for the 400 nm luminescence are located at or near material surface. This feature allows propose hBN as a material applicable for oxygen sensors.

V. Korsaks, B. Berzina, L. Trinklere. Influence of air, oxygen, nitrogen and argon gases on 400 nm luminescence in hexagonal boron nitride. Latvian journal of physics and technical science 49 (2012) 57-62

Fundamental electromagnetic properties of carbon nanotubes (CNTs) and graphene nanoribbons (GNRs) with the essential concentration of ‘dangling bonds’ as well as point defects and functionalized atomic groups of various concentrations are very sensitive to local external perturbations:



Shunin Yu.N., Zhukovskii Yu.F., Burlutskaya N.Yu., Gopejenko V.I., Bellucci S. (2012) simulation of fundamental properties of CNT- and GNR-metal interconnects for development of new nanosensor systems in: Nanodevices And Nanomaterials For Ecological Security Series: Nato Science for Peace Series B - Physics and Biophysics, Springer Verlag, 2012, 237-262

and that's not all...

Thank you for attention!

Acknowledgements: Authors (L.G., J.K., V.O.) acknowledge Latvian Science Council for financial support, and M.B. and N.J. acknowledge ERDF project 2.1.1.1 project "Development of lung cancer diagnostic methods and software prototype using expiratory air analysis with artificial olfactory sensor" (2011-2013) for support.