Wilhelm Jan Ansorge

Wilhelm Jan Ansorge (born July 14th 1944) is a German-Czech scientist, born in Czechoslovakia. He developed novel Scientific Instrumentation and Software, enabling major advances in analyzing genomes, genes and proteins in cellular and molecular biology, as well as in medical fields. His laboratory pioneered multidisciplinary developments of automated technology and techniques in **:** Sequencing and Analysis of genomes, first complete Human Genome Chip Array (and the International standard protocol for microarrays MIAME), devices for synthesis and analysis of DNA and proteins, Automated Systems for Microinjection and Image Analysis in Single Cells, Fast Screening of Monoclonal Antibodies, Electro-transfection of cells. He investigated magnetic properties of materials, worked in design of semiconductor devices, and of superconducting magnets.

After dissertation and 2 years as Assistant Professor at the Faculty of **Mathematics and Physics,** Charles University Prague, he joined for 4 years **Texas Instruments**, Dallas, USA (Development of semiconductor technology). Then he worked 6 years at **CERN**, (www.cern.ch), the Particle Physics Research Centre in Geneva, in development of superconducting magnets for accelerators. Thereafter he joined for 25 years the **EMBL**, European Molecular Biology Laboratory in Heidelberg (www.embl.de), as the Head of Genomics Technology Department. At EMBL he developed the **fluorescence DNA sequencer (1986), the first functional automated system** capable to sequence reliably large genomic DNA. The **feasibility** of sequencing the **Human Genome** with this automated technology was **demonstrated** by his team on **human HPRT (60kb) gene locus (Genomics, 1990)**. In the work was for the first time applied the **paired-end sequencing** strategy, developed in the team for the project. This method is now a standard in genome sequencing**.** In 1991 he presented a High throughput planar fluorescence **technique for DNA Sequencing by Synthesis without gels,** similar to those used in high throughput Next Generation DNA Sequencing systems.

Technology developments were made commercially available and applied in biological and medical fields. In 1996, Ansorge was one of the three founders of Lion Biosciences, a **Biotech company** listed in 2000 on **Nasdaq**.

Currently, he is a visiting scientist at **EPFL**-**ETH Lausanne**, serving on several European Scientific Advisory Boards, evaluating scientific projects and institutions, with continued interest in innovative analysis techniques for genomics and medicine.

Wilhelm Ansorge co- authored over 250 publications, some included in Teaching material by universities worldwide (e.g. Next Generation DNA Sequencing review (I) in 2009, its updated version (II) in 2016), and 5 books on **Molecular Diagnostics, Genomics**, **Microarrays** techniques, **DNA Sequencing** and Analysis.
He applied for and was granted over 30 **patents in genomics and technology**, with license agreements and commercial products by leading European companies.
He presented research results of his group in about 100 international conferences.

Education

Faculty of Mathematics and Physics, Charles University of Prague.
Dissertation Thesis subject : Magnetic Properties of Uranium Compounds at Cryogenic Temperatures (1968).

Career

Assistant professor at the Charles University

In this position he continued for 2 years the work on Magnetic properties of Uranium Compounds at Cryogenic Temperatures, and published discoveries of ferromagnetism and anti-ferromagnetism in several compounds **(1968-1971).**

Texas Instruments Inc. in Dallas, Texas

Then he joined Texas Instruments, USA, and worked for 4 years in development and improvements of novel Semiconductor technologies (e.g. high precision Regulation Servo-systems, Darlington Control circuitry), with applications in various fields, and detailed in company's technical reports.

CERN, European Particle Physics Research Organisation, Geneva.

After Texas Instruments, he spent almost 6 years at CERN, European Particle Physics Research organisation in Geneva, in the team developing Superconducting magnets technology planned later for LHC Large Hadron Collider accelerator. The work involved specification of parameters, design of the system cooling the magnet structure to cryogenic temperatures, current leads with minimum heat losses, magnet sectors ensuring the desired field quality and precision, selection of materials, their magnetic and mechanical properties, as well as testing performance of magnet prototypes. First application was in "low-beta" intersection in accelerator's rings, for focusing of the particle beams to increase the collision rate of particles circulating in opposite directions. Publications and CERN reports **(1973-1979).**

EMBL, European Molecular Biology Laboratory, Heidelberg

Wilhelm Ansorge then joined for 25 years the newly established EMBL institute, founded by the Director Sir John Kendrew. He started as a group leader in the department of Leo de Meyer, a visionary leader in development of advanced scientific devices for Molecular Biology and Life Sciences. Ansorge and his group worked in development of Genomic Technology for Biology and Medical fields, introducing interdisciplinary research to the institute.
When Lennart Philipson became the Director of EMBL, a new Department of Genomic Technology and Biochemical Instrumentation was established, with Ansorge as coordinator. To his group on Genome Technology and Single Cell Techniques, and to Protein and Peptide group (leader Rainer Frank), he added and introduced to EMBL new fields of Mass spectrometry (with a new group leader Mathias Mann), and Nucleic Acid Chemistry (group leader Brian Sproat).
While at EMBL, Ansorge received many international **research and development grants**, coordinating most of them.
His work, publications, conference presentation, patents and Teaching Courses are described in **EMBL Research Reports 1979-2004, and in Publications list below.**

Some of the innovative Developments in Ansorge's group at EMBL were :

- **Next Generation DNA sequencing system WITHOUT GEL.**
In **1991** Ansorge filed one of the first patent applications for DNA sequencing without gels **(**Review in **Next Gen DNA Seq (I), 2009, 2010).** This fluorescence technique established high throughput planar technology for DNA Sequencing by Synthesis, similar to those used at present in commercial high throughput Next Generation Sequencing systems. A patent application by another laboratory, focusing on biochemical labelling in a similar technique, was submitted several years later.

- The EMBL **DNA fluorescence sequencer**. It was **the first functional automated system** capable to sequence reliably large genomic DNA (published in **1986,** reads 1100 bp, licensed to LKB, Pharmacia, and Amersham companies). Among the applications was sequencing of the **complete (60kb) human HPRT gene locus.** This work **demonstrated the feasibility to carry out the Human Genome Project** with automated sequencing system. For the first time was applied the **paired-end** sequencing strategy increasing **accuracy**, developed in the group for the project**.** This technique is now the standard in genome sequencing **(Genomics, 1990).**

- Initial planning and preparative meetings for the Human Genome Project. Ansorge team was involved contributing demonstration work, technology and robotics systems, helping in the decision about the feasibility of the project. (**Wolf Trap conference 1989, Daily Telegraph Magazine report August 1991, Science in May 1992, Bermuda Genome Meeting 1996).**

- Fully automated Sequencing technique and **Robotics systems** for DNA template preparation and sequencing reactions **(1987),** computer systems for data acquisition and programs for sequence analysis. Biochemicals and various DNA polymerases were tested for optimum sequence resolution **(1988).**

- **DOUBLEX** technique for **Simultaneous sequencing** on **both DNA strands** in one reaction, with **two dyes**. This method improves read accuracy and doubles the sequence throughput **(1995, 1996)**.

- Internal Labelling Sequencing technique. Instead of fluorescently labelled primers (more expensive to produce), fluorescently labelled nucleotides were incorporated for labelling of fragments to be sequenced **(1995, 1996).**

- Technique using **only one label, one tube reaction, in one lane or a capillary**. Sequence is deduced from different signal intensities for each base **(1989, 1990).**

- Maxam-Gilbert chemical degradation sequencing protocol on solid support, developed by the team for automated fluorescence sequencers **(1988).**

- First use of SAGE (Serial Analysis of Gene Expression technique, based on DNA Sequencing) for **Evaluation of Gene expression in Yeast (1999).**

- Nanopore DNA Sequencing with potential for long sequence reads. In 2011 Ansorge proposed using DNA polymerases as the motor for moving DNA through

the nanopore, which helps in the control of its speed, and improves the accuracy of base sequence determination **(Next Gen DNA Seq (II), 2016).**

- **Genome Projects** with the EMBL Sequencing System **(1986 – 2004) :**
  - **HPRT** gene locus (60kb) with Thomas Caskey Baylor College **(Genomics 1990).** as feasibility test for Human Genome project **(J. Sulston, book on HGP, 2004).**
  - Sequencing **of Genomes : Human, Yeast** (largest part of genome in Europe), **Mouse, Arabidopsis, Anopheles, (1990-2006).**
  - **Archaebacterium** Desulfurococcus mobilis, thermophile, 74% G-C pairs **(1987).**
  - **Catalogue of Human Genes and Proteins**: Coding Human cDNAs **(2001).**
  - **The Genexpress IMAGE** knowledge base of the human transcriptome **(1999).**

- **Clinical Biology and Medicine Laboratory work**

The commercial versions of the EMBL sequencer (ALF, ALFexpress, ALFred by LKB, Pharmacia, Amersham) were used in **analysis of mutations** in laboratories worldwide, with high accuracy, long reads over 1000 bases, sensitivity and reliability. Sequencing of DNA fragments for projects in Biology, Clinics **(1989-2004).**

- **Automated Microinjection in Single Cells,** with control of miniscule (femtoliters) injected sample volumes (**1982, 1988, 1991, 1998)**, licensed to Eppendorf and Zeiss. Applied widely in collaborative projects, e.g. cell cycle, development biology, STEM cells, gene expression, as indicated in the List of Publication below **(1982-2005)**.

- **Imaging System for Evaluation of Gene Expression** in **Single Cells**, collaborative projects listed in Publications below **(1991, 1993, 1988-2004)**.

- The first apparatus for **Electroporation of cells (1984, 1995)**, allowing simultaneous electro-transfection of thousands of cells (devices were used in some European Institutes, e.g. Cesar Milstein MRC, Pierre Chambon Strasbourg). Know-how transferred to Bio-Rad Co, and licensed to Eppendorf.

- **Flow Cytometry** of cells and organelles, also with **magnetic beads** (**1988, 2000**).

- **DNA Microarray technique developments, standardisation at EMBL :**
  - First complete **Human DNA Microarray (press release EMBL, Dec. 2002).** Applied to STEM cells, Evolution Biology, Tumour Angiogenesis **(2000-10).**
  - **Yeast**, **Mouse, Anopheles, Iron metabolisms** arrays produced **(2000-2006).**
  - International **standard MIAME protocol** for cataloguing of Microarray experiment results in **databases** (**Nature Genet, 2001**).

- High throughput production of **Monoclonal Antibodies,** and Fast and sensitive screening with **Antigen Microarrays (2005)**, licensed commercially**.**

- **Innovations in Gel Separation and Band Detection Techniques :**
  - Development of **Ultrathin gels (0.1 mm),** DNA, Protein applications **(1980).**
  - Straightening and removal of band pattern distortions (the **Smiling Effect**) in gel electrophoresis, by the thermally stabilized gels technique **(1980, 1981). (**EMBL license to LKB, Pharmacia companies, as Macrophor system**).**
  - **Wedge gels** with improved band resolution and reading length by **modification of the electrical field** along gel achieved by Gradient in Gel Thickness **(1984).**

- High density **Simultaneous loading of 200 sample** lanes on gel **(1997).**
- Fast, sensitive **Silver Staining band** detection techniques **(1982, 1985).**
- **Neuronal program (artificial intelligence)** for band pattern analysis **(1998).**

Development projects in other groups of Ansorge's department at EMBL :

- **Novel Nano-electrospray Mass Spectrosopy,** determination of **peptide sequence** from DNA sequence, in the group of Mathias Mann, Mathias Wilms,
- Various chemical **modifications of DNA and RNA** in the group of Brian Sproat,
- Construction of **DNA Synthesiser** by groups of W. Ansorge and Brian Sproat,
- **Protein chemistry**, **Peptide Synthesiser** group of Rainer Frank.

Department's Genomics and Proteomics Facility

In1986 the groups from the department founded a service facility at EMBL, helping scientists from the institute and external centers with techniques in :
DNA, RNA, Peptide sequencing and synthesis. Robotics system for DNA sample preparation. Microinjection, Imaging and analysis of Single Cells, Cell cultures. Mass spectrometry. Microarrays preparation, result analysis. Flow Cytometry. Separation of Cells and Organelles, magnetic beads. Fast Screening of Monoclonal Antibodies.
In 1996 an EU grant was written and applied for funding as European Facility.

AWARDS and HONOURS

- In **1999** Wilhelm Ansorge was elected **EMBO member**, for innovations and advancements in interdisciplinary development of instruments for biology and medicine (Automated DNA sequencers, Automated Microinjection in Single Cells, Using Single Cell as a Laboratory, First complete Human Genome Microarray, Automation and Robotics handling processes, innovations in Biochemical DNA sample preparations).

- Member **in FEBS, HUGO, HUPO** organisations.

- In **1992** - the **Golden Medal for Science** from the Charles University, Prague, **for the development of the automated fluorescent DNA sequencing,** demonstrating feasibility of Human Genome Project.

- In **1992** - the **Honorary Doctor**, Charles University, Prague, for development of techniques advancing genome research and molecular medicine.

- In **1993 - granted the first European Chair**, sponsored by European Union, selected by an international committee chaired by Lord Dahrendorf, Oxford.

- In **2009** - elected a foreign member, Council of the **Czech Academy of Sciences.**

GRANTS and TEACHING ACTIVITIES
In the years **1985-2004** he applied for and received about **30 scientific grants** from EU, EMBO and FEBS, majority of them as the grant coordinator.

Between **1987- 2008**, over **60 EMBO, EMBL, FEBS COURSES** were organized by Ansorge group, at EMBL, in Europe, China and Japan.

1. **PUBLICATIONS LIST** :
https://www.researchgate.net/profile/Wilhelm_Ansorge2/publications

2. **LINK for BOOKS** :
https://www.amazon.co.uk/Books-Wilhelm-Ansorge/s?ie=UTF8&page=1&rh=n%3A266239%2Cp_27%3AWilhelm%20Ansorge

3. **PARTIAL LIST OF PATENTS AND APPLICATIONS** (JUSTIA) :
USPTO patent applications submitted by and patents granted to **Wilhelm Ansorge**.
Wilhelm Ansorge Inventions, Patents and Patent Applications - Justia ...
https://patents.justia.com/inventor/wilhelm-ansorge