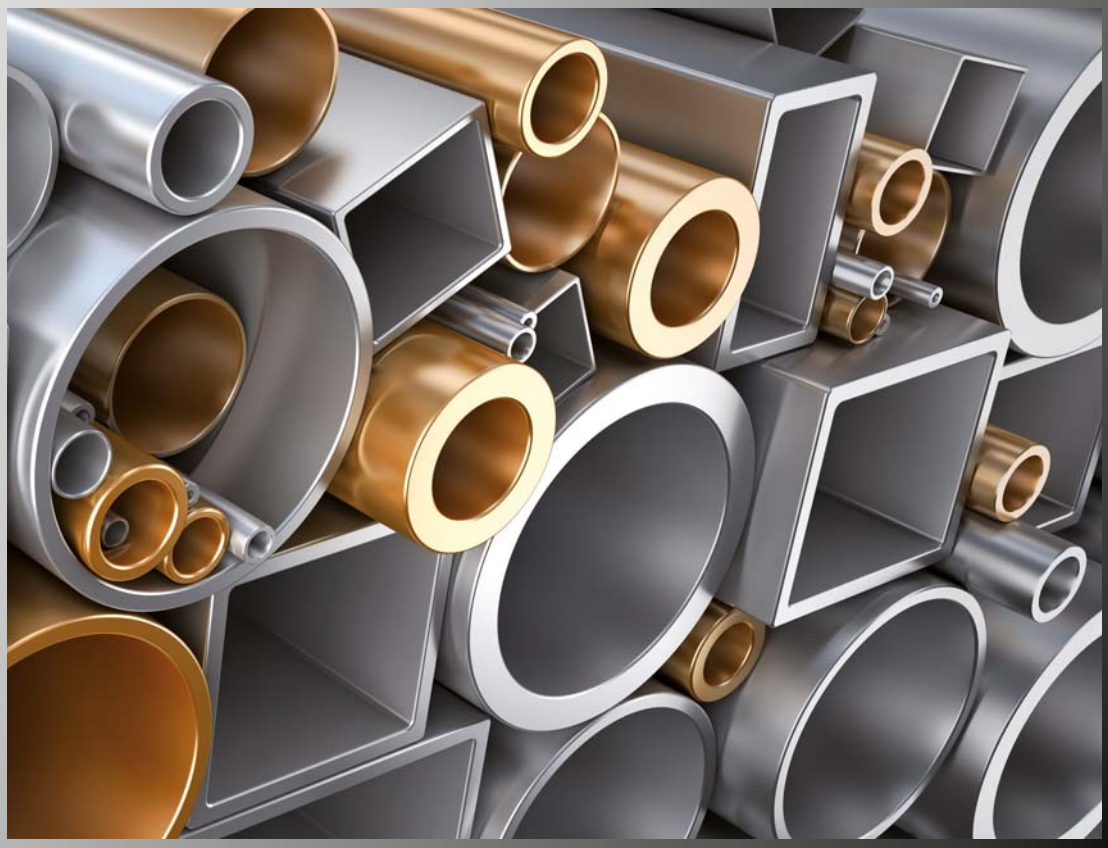
Wendelsbergs beräkningskemi

2019



New Research Field:

Modelling for Steel Industry

Welcome to Wendelsbergs beräkningskemi

At the consultancy and research company Wendelsbergs beräkningskemi we work with computational and predictive science. Using mathematical modelling, especially within chemistry, chemical engineering, physics and materials science, we assist companies with building knowledge, and predicting and designing physical and chemical behaviour. Often our projects lead to simulation software for use by our clients.

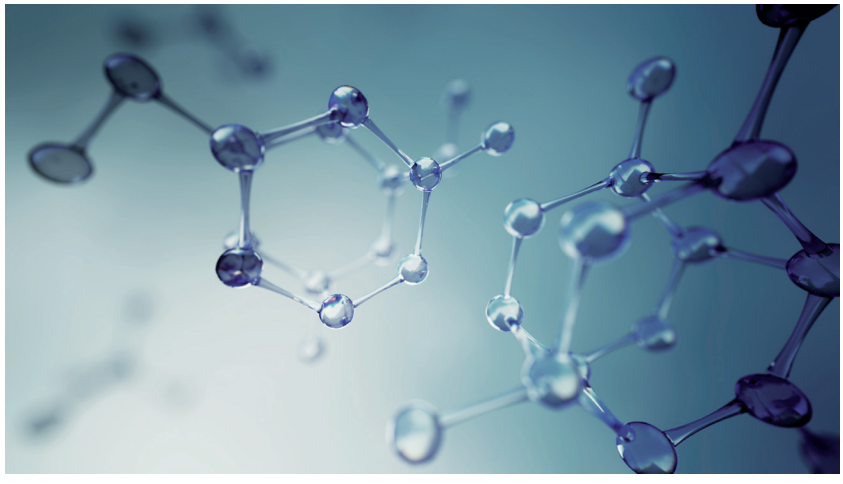
Our research fields cover for instance pharmaceutics, concentrated solar power technology, vehicle technology, steel technology, polymer technology, nanoparticle technology, electrochemistry and heat transport.

Our new leaflet is here, the first one since 2015. We have been busy modelling!
And publishing a new web site. Welcome to www.wendelsbergskemi.se!

Jan Westergren
CEO Wendelsbergs beräkningskemi AB

What we do

Using modelling together with experiments is a good recipe to improve scientific and technological knowledge. With our expertise in physical and theoretical chemistry and experience of various modelling and simulation techniques we want to contribute to our customers' knowledge and modelling capability.



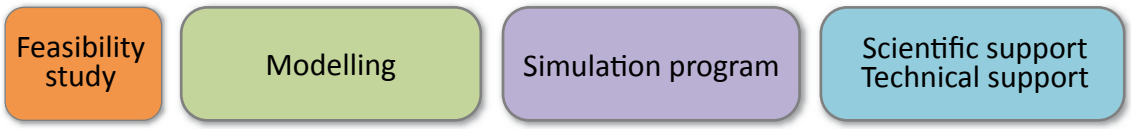
Research Consultants

Our belief is that research and deeper understanding are important pieces when developing and designing new products or processes. The scientists at Wendelsbergs beräkningskemi have a long experience of contributing to research and development for companies in for instance chemical and materials industry.

Your company may already have a big research staff with a need of additional scientists – we are happy to assist you with our knowledge in science and mathematical modelling. Your company may lack research staff – we are happy to be your research staff. Projects may be long or short and customers may be located close to us or world wide – we are happy to add to your research.

Our research is mainly within chemistry, chemical engineering, physics and materials science. Our knowledge in physical chemistry and molecular physics we use for understanding for instance chemical mechanisms and processes on a deep level. The understanding is converted into a mathematical model and simulation programs describing the mechanism and process.

Work packages



A normal project starts with a feasibility study. Wendelsbergs beräkningskemi, sometimes in collaboration with the customer, makes a preliminary investigation of the issue. As a result, a proposal for a research project is presented.

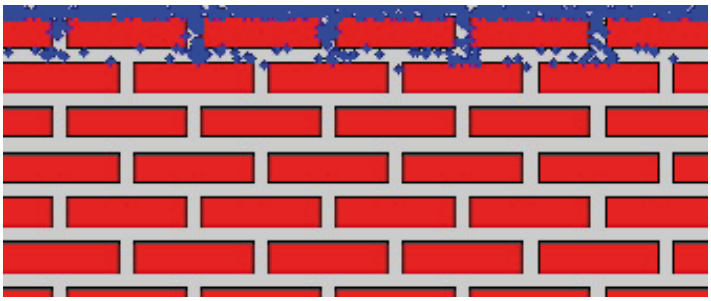
In the next part, the modelling, the mechanism or process is studied in more detail. What are important physics and chemistry and what can be neglected? When important details have been extracted, they are converted into mathematics.

The emerged mathematical model is then often implemented as a simulation program. From simulations, vital information and understanding are obtained.

After finalization of the research project we of course offer further scientific support and technical support.

Mathematical Model & Simulation Software

Our mathematical models describe static and dynamic properties of systems of matter. An example of such a system would be drug molecules that should diffuse through the skin. The skin is imagined as layers of corneocytes embedded in lipid. The drug molecules can only move in the lipid matrix where they diffuse from the high outside concentration to low concentration beneath stratum corneum. A mathematical model describes the transport of molecules using the Fick's diffusion equation with constraints that the corneocytes are forbidden volumes.



Simulation of diffusion of drug molecules
(blue dots) through skin (stratum corneum).

In our research, by the combination of scientific knowledge in the form of equations, a model is formed. The solutions to the equations are often corresponding to experimental results. The modeller's first task is to select details and equations significant to describe the system. The second task is to solve the equations or to simulate the system.

In most cases, the equations cannot be solved analytically but numerical methods must be used. A simulation is a numerical method used to calculate how for instance a system of molecules evolves with time where the translation of the molecules is determined from the mathematical model. A simulation of the diffusion of drug molecules through stratum corneum may be designed as random walk of molecular dots where the random steps are generated from Fick's law.

A model may be at various levels of detail. The properties of a material or of a chemical process depend in the end on atomic and molecular properties. Sometimes it is actually reasonable to design a model on this level of description. In a molecular simulation, each atom is described individually and the forces between atoms are expressed as functions of distances between atoms and angles between molecular bonds. A box of molecules may be simulated by for instance Molecular Dynamics Simulation or Monte Carlo Simulation.

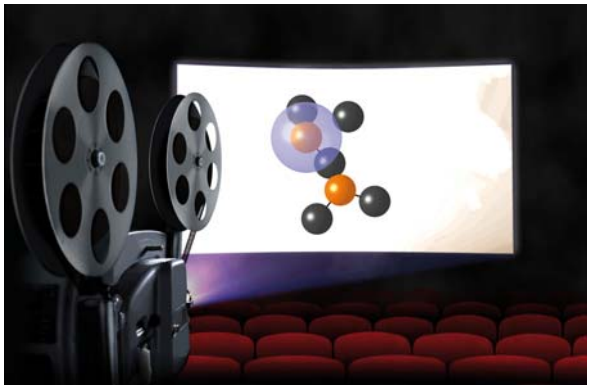
Sometimes a process of interest may be better described by macroscopic properties. Diffusion is such an examples. A model including diffusion normally leads to a Partial Differential Equation (PDE). According to Fick's law, the flux of matter is proportional to the gradient in concentration. In the case of diffusion through the stratum corneum, Random Walk Simulation was our method of choice. In other cases, Fick's law is solved by the numerical Finite Element Method where the diffusivity is one input parameter. The solution yields the transport rate. Models for diffusion may for instance be used for calculating the permeability of membranes and thin films. Heat conduction due to a non-uniform distribution of temperature is analogous to diffusion. Heat transfer from a hot particle in an air steam is preferably described by the continuous heat equation.

When reaction mechanisms are explored for a chemical reaction, the activation barriers need to be determined as they give the rate constant. In this case, quantum chemistry is the method of choice. This kind of modelling is on a scale involving electrons.

Our research often aims for developing a mathematical model of a physical/chemical mechanism, process or property. There are many options for how to write the subsequent simulation program. Sometimes we write new code in languages like fortran or python. Sometimes we make programs within some modelling environment like matlab or Comsol Multiphysics. We have a long experience of making the programs with user-friendly interfaces.

A simulation program can be used for various reasons. Unknown mechanisms can be explored by simulations. But often simulations are used together with experimental work. If simulations and experiments agree, the foundation of the proposed mechanisms is made stronger. If disagreeing, an incitement for further search of mechanisms is triggered. One of the simulation programs developed by Wendelsbergs beräkningskemi together with the pharmaceutical company AstraZeneca is GI-Sim/LungSim. In this program, the path of drug molecules from mouth to intestine (or lung) to blood to degradation is simulated.

Literature Study



Before starting a research project within a scientific area it is always a good idea to search literature for the state-of-the-art knowledge. In particular if the new scientific or technological area is not yet well established within the company. Wendelsbergs beräkningskemi offers to search literature to extract the latest findings and discussions. Our experience of reading scientific and mathematical texts is useful for investigating literature.

The gained understanding is then presented in a comprehensive way. As we know that text full of equations may be hard and time-consuming to read, we make an effort to explain science both with and without equations, yet without omitting details.

The results will be presented in reports, animations and seminars. A literature study is often part of a feasibility study but may also be a stand-alone project.

Science Courses

Do you want your personnel to learn more about physical chemistry and theoretical chemistry? Wendelsbergs beräkningskemi offers tailor-made courses in various areas.

Diffusion	Permeability	Autoxidation
Solubility	Simulation techniques	Relating simulations and experiments

World Wide Wendelsbergs beräkningskemi

Wendelsbergs beräkningskemi has already worked for customers in Scandinavia, Europe, Asia and North America. We are happy to take on projects for customers, wherever they are on the globe. By telephone and internet meetings as well as face-to-face we will have a close contact with you.

Industrial Areas

Wendelsbergs beräkningskemi has been active in many different industrial areas. Four examples of our industrial areas are pharmaceutical industries, concentrated solar power technology, vehicle technology and steel technology.

To exemplify, our client the pharmaceutical company AstraZeneca, has been at the forefront when it comes to using modelling and simulations in research and development. The pharmaceutical industry has interest in many chemistry and biology areas. Chemical understanding for manufacturing of formulations (tablets, solutions, etc) is one area. How drugs are dissolved in intestine and then absorbed another.

Wendelsbergs beräkningskemi has been active in many different aspects of pharmaceutics. Nanoparticle dynamics, degradation chemistry, drug solubility, polymer science, diffusion and intestinal and lung absorption are examples of that.

Recognition

In the AstraZeneca IMED Biotech Unit review, Wendelsbergs beräkningskemi was mentioned under A selection of key collaborations in 2017 for pharmaceutical sciences.

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> **Wendelsbergs beräkningskemi, Sweden**
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> This collaboration will develop next-generation modeling tools for drug absorption through oral and inhaled administration of small molecules and lipid nanoparticles.

A selection of key collaborations in 2017

1. **North West Centre for Advanced Drug Delivery, University of Manchester, UK**

The North West Centre for Advanced Drug Delivery (NoWCADD) is a translational science centre based at the University of Manchester's Division of Pharmacy and Optometry, and is funded through a collaboration with AstraZeneca's Pharmaceutical Sciences and Pharmaceutical Technology and Development departments. NoWCADD aims to transform emerging drug delivery science into valuable medicines for treating serious and life-threatening conditions. It seeks to identify talented students, and stimulate their interest in early career pharmaceutical science roles in industry, create collaborative research and development programmes with research groups in Manchester, and across the global scientific community. Initial projects have focussed on scalable and reproducible methods of manufacturing nanomedicines, using novel microfluid technology and delivery systems to improve intracellular delivery. In addition, AstraZeneca is the industrial champion on the Engineering and Physical Sciences Research Council (EPSRC) Program Grant "2D Health", awarded to Professor Kostas Kostarelos for the research theme investigating graphene oxide as a delivery system in cancer immunotherapy.

2. **FoRmulaEx Chalmers University of Technology, University of Gothenburg, Karolinska Institute, Sweden**

The industrial research centre will design new lipid nanoparticle formulations that gain inspiration from nature's use of extracellular vesicles and exosomes to transport nucleotides such as RNA.

Critical molecular and cellular factors for successful uptake and efficiancy will be explained and this collaboration which aims to develop innovative drug vehicle concepts that are efficacious and safe for clinical use.

3. **Inform 2020, Molecules to Manufacture: Formulation and process engineering of inhaled particle therapies University of Hertfordshire, University of Leeds, University of Bath, University of Cambridge and University of Manchester, UK**

The INFORM 2020 consortium will deliver a multidisciplinary research programme that aims to expand the scientific understanding of the properties, formulation options and critical manufacturing process parameters needed to accelerate development pipelines. This collaboration addresses fundamental and applied experimental investigations to improve manufacturability of nano and microparticle therapies.

4. **Wendelsbergs beräkningskemi, Sweden**

This collaboration will develop next-generation modeling tools for drug absorption through oral and inhaled administration of small molecules and lipid nanoparticles.

5. **Monash Institute of Pharmaceutical Sciences and Starpharma, Australia**

This collaboration will work with Professor Chris Porter at Monash Institute of Pharmaceutical Sciences with his lymphatic delivery expertise to explore the ability of Starpharma's DEP dendrimer technology to deliver drugs to the lymphatic system and to explore the impact this has on the drug's efficacy in tumour models. This also extends our collaboration with Starpharma to further explore their technology.

6. **Cardiff University, UK**

In collaboration with Professor Arwyn T. Jones, we are working together with the School of Pharmacy and Pharmaceutical Sciences, Cardiff University to characterise and understand the intracellular delivery and trafficking pathways for mRNA delivery systems in different tumour cell lines. By understanding the biology driving this phenotype we aim to explore how it can be applied to develop improved strategies for the intracellular delivery of nucleic acids and other macromolecules.

7. **University of Cambridge, UK**

In collaboration with Professors Ian Paterson and David Spring, we are working to further understand and advance Antibody Drug Conjugate (ADC) Chemistry. Innovative science is key to the progression of next generation therapeutics, where the potential of targeted therapy avoids dose limiting toxicity of chemotherapy, which occurs because of its effects on normal cells. The development of new linkers and warheads by synthetic chemists will be crucial to advancing the field and the next generation of ADCs.

8. **University of Notre Dame, US**

In collaboration with Professor Olaf Wiest, we develop methods for predicting chemical reaction selectivity with high accuracy. Our novel methods for predicting stereoselectivity can aid selection of optimal catalysts for asymmetric reactions. We are currently broadening the methods to allow other types of chemoselectivity predictions, as well as following reactions in enzymes with a much higher precision than previously possible.

9. **University of Nottingham, UK**

As part of an EPSRC Impact Fellowship awarded to Professor Cameron Alexander, Polymer Therapeutics at University of Nottingham and in collaboration with Professor Stewart Martin, Cancer and Radiation Biology, Dr Anna Grabowska, Cancer Biology and Dr Keith Spriggs, Gene Regulation we are investigating novel polymer chemistries, with the aim of achieving radioactivity triggered materials for enhanced cancer therapy.

10. **University of Oxford, UK**

In collaboration with the Oxford Institute of Biomedical Engineering and the Oxford Centre for Drug Delivery Devices, we are working with Professors Constantin Coussios, Bob Carlisle and Robin Cleveland from the Biomedical Ultrasonics, Biotherapy and Biopharmaceuticals Laboratory (BUBBL) in the Institute of Biomedical Engineering, we are working to investigate the use of shock waves, ultrasound and nanobubble mediated sonoporation to enhance intracellular delivery of nucleic acids.

Client List

AstraZeneca

www.astrazeneca.com
Pharmaceutics

- Solubility simulations.
- Nucleation and growth of nano and micro particles in solution.
- Simulation of pellets.
- Drug absorption in lung & gastrointestinal tract and pharmacokinetics.
- Drug databases.

Arcam

www.arcam.com
CAD to metal

- Mass and heat transport in vacuum.

Accelrys

www.accelrys.com
Scientific software

- Organic crystal calculations.

Cheminova
(now FMC Agricultural Solutions)

www.fmcagro.dk
Crop protection

ElectroHeat Sweden AB

www.electroheat.com
Industrial furnaces and heat treatment equipment

- Heat exchanger.

Empereal PKGDS renewable energy Pvt. Ltd

www.empereal.com
Renewable energy based company

PowderPro

www.powderpro.se
Freeze granulation

- Nanoparticle science.

SCA Hygiene Products AB
(now Essity)

www.essity.com
Incontinence care, baby diapers and feminine care

- Polymer science.

SSAB

www.ssab.com
Steel

- Polymer science.

Statoil

www.statoil.com
Oil and gas

- Refinary technology.

Toyota Motor Europe

www.toyota-europe.com
Car industry

- Simulation of combustion chemistry.

University Contacts

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Johan Bergenholtz
Associate Professor, Physical Chemistry

Kalle Sigfridsson
Associate Professor, Pharmaceutical Technology

Leif Eriksson
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beräkningskemi = computational chemistry

The name Wendelsbergs beräkningskemi stems from the Wendelsberg Castle and a park near our office. The castle and park were built by the German-Swedish manufacturer Bruno Wendel in 1888.

Please contact us in Swedish, Danish, English or German.

The Wendelsberg Castle

The Wendelsberg Park

Wendelsberg Chemistry
Wendelsberg Chemistry AB is a subsidiary to Wendelsbergs beräkningskemi AB. It is administratively responsible for projects outside Europe.

Corporate identification number
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