Prof. Dr. Ulrich Schwaneberg

PERSONAL INFORMATION

Name: **Schwaneberg, Ulrich**

Researcher unique identifier(s): E-7234-2014
(Web of Science or search term Schwaneberg U)

Nationality: German

Date of birth: **17.June.1969**

URL for web site: http://www.biotec.rwth-aachen.de/

Family status: Married, four children

EDUCATION

1996 - 1999 Dr. rer. nat. (PhD)
Faculty of Chemistry, Institute of Technical Biochemistry,
University Stuttgart, Germany (Group of Prof. R. D. Schmid)

1990 - 1996 Diploma in Chemistry
Faculty of Chemistry, Institute of Technical Biochemistry,
University Stuttgart, Germany (Group of Prof. R. D. Schmid)

PREVIOUS POSITIONS

1999 – 2001 Postdoc at the California Institute of Technology (CalTech Fellowship),
Division of Chemistry & Chemical Engineering, Pasadena, USA
(Group of Prof. F. Arnold; Nobel prize winner 2018 in chemistry)

2002 - 2008 Professorship at the Jacobs University Bremen (renamed in 2006; International University Bremen), Faculty of Science, Bremen, Germany

CURRENT POSITION(S)

Since 01/2009 Head of the Institute of Biotechnology; (since 1/2014 reduced to a **50 %** appointment); Faculty of Natural Science, Mathematics and Informatics, **RWTH Aachen University**, Germany

Since 01/2014 Member of the Board of Scientific Directors at **DWI-Leibniz Institute for Interactive Materials** (**50 %** appointment; located at the RWTH Aachen Campus Melaten), Leibniz Gemeinschaft, Germany

FELLOWSHIPS AND AWARDS

2018 **Innovation award** of the BioRegions' Germany

2016 **BMBF-awardee** for the next generation of bioprocesses (**1,75 Mio €**)

2015 Specially appointed professor at Osaka University (visiting professorship)

2014-2016 RWTH Aachen Performance Awards

Since 2013 Visiting Professorship for Senior International Scientists of the Chinese Academy of Science (Sabbatical in 2014 at the TIB in Tianjin)

1999 – 2001 Caltech Post-doc Fellowship

INSTITUTIONAL RESPONSIBILITIES (notable activities)

Since 2015 Speaker of Henkel Innovation Campus for Advanced and Sustainable Technologies HICAST

Since 2010 Representative of RWTH Aachen in the board of directors and deputy director of the whole **Bioeconomy Science Center** (**58.5 Mio € for 10 years**; see www.biosc.de

2012 – 2014 Dean of the 'Department' of Biology (Aachener Biologie und Biotechnologie ABBt; 18 professors Fachgruppe Biologie), RWTH Aachen University, Germany

(e.g. development of a structural and development plan with three focus areas)

Since 2013 Member of the committee for development of the RWTH research profile area 'Molecular Science', RWTH Aachen University, Germany

2013 Successful development of a research agenda and defence of the **DWI's** application to become an **institute of national interest within the Leibniz Association** (**DWI - Leibniz Institute for Interactive Materials**), Aachen, Germany)

COMMISSIONS OF TRUST & MEMBERSHIPS (selected)

Since 2017 Member of the Max Planck School of Physics, Chemistry and Construction of Life

Since 2017 Member of Deutsche Phosphor-Plattform DPP e.V., Frankfurt am Main, Germany

Since 2015 Member of Kuratorium Fraunhofer Institute for Applied Polymer Research (IAP) in Potsdam, Germany

Since 2014 Member of the Technology Advisory Board of Henkel AG & Co, Düsseldorf, Germany

2010-2015 Board member of MedLife e.V. (former LifeTec Aachen), Aachen, Germany

Since 2010 Member of Cluster Industrielle Biotechnologie e.V. CLIB 2021, Düsseldorf, Germany

Since 2010 Member of MedLife e.V. (former LifeTec Aachen), Aachen, Germany

Since 2009 Founder and advisor of SeSaM-Biotech GmbH, Aachen, Germany (SeSaM has since 2017, 8 full-time coworkers; http://www.sesam-biotech.com/)

Since 2004 Member at DECHEMA, Frankfurt, Germany

Since 2002 Served repeatedly as reviewer and evaluator in several panels of DFG-, DBU-, BMBF-, DAAD-, Fondazione Cariplo and VW-Foundation (tenure-track evaluations of Lichtenberg professorships)

KEY PERFORMANCE PARAMETERS

- Researcher unique identifier(s): E-7234-2014 (Web of Science or search term Schwaneberg U)
  Web of Science **Core** Collection:
  - >**200 Publications** in peer reviewed journals (186 found in Web of Science Core Collection) *h*-Index: 32 // 3,544 Citations (on 20.02.2018) e.g. 2017: 20 peer-reviewed manuscripts with an average impact factor of 4.26
  - **World-leading group in the protein engineering** by directed evolution (400-500 publications per year in "directed evolution" since 2009; search term "directed evolution; analyse results by author): **3rd** rank: overall years // **1st**: 2012, 2013, 2014; 2nd in 2015, 2017

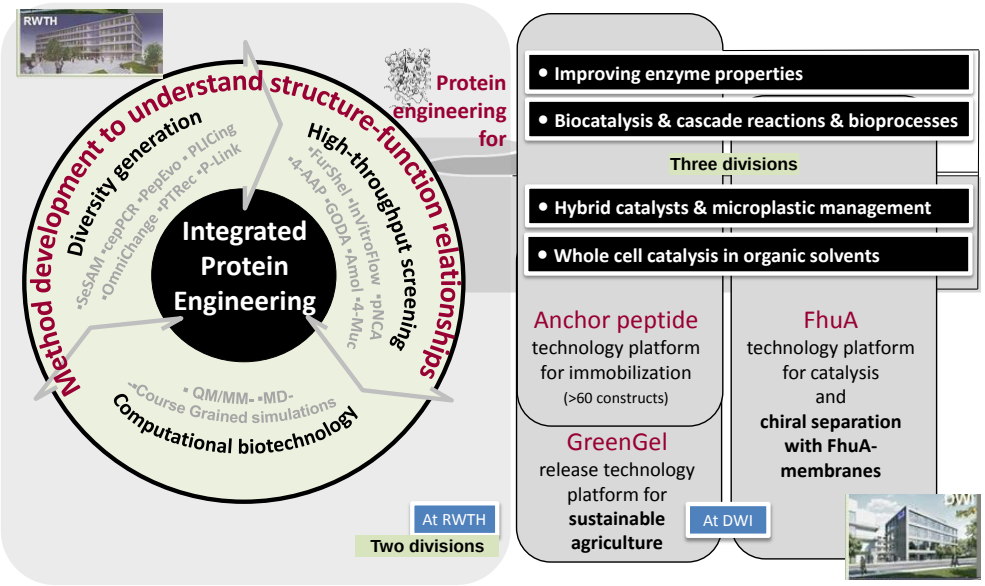
- **Group size**
  55 PhDs, post-docs, and staff

COLLABORATIONS WITH INDUSTRY

- Since 2015 Coordinator ("Sprecher") of the Henkel Innovation Campus for Sustainable and Advanced Technologies (**HICAST**) at RWTH Aachen University
  Link: http://www.rwth-aachen.de/cms/root/Die-RWTH/Aktuell/Pressemitteilungen/Maerz/~hrbf/HICAST-Exzellenz-fuer-nachhaltige-Tech/?lidx=1
  Direct invest of 5 Mio € for five years by Henkel company. Three PIs (Professors Richtering, Palkovits, and Schwaneberg (coordinator) for fundamental understanding of interactions between enzymes, textiles (surfaces) and detergents in order to develop more sustainable laundry products. HICAST is based on eight years of continuous collaborations with Henkel (4 joint patents) and is according to Burno Piacenza (board member and executive vice president of Henkel) the largest research investment which Henkel ever made with at a university
- **Joint patents** with BASF SE (8), Evonik (2), DSM (1), Roche (1), Henkel (5), B.R.A.I.N (2)
  - **Four enzymes** were **commercialized** by the above mentioned industrial partners; one additional is currently at DSM in the phase of upscaling
- Main **academic PI** in the industrial Innovationsallianz FuPol (Functional Polymers; 4 industrial partners) and PI in the EU Robox project (8 industrial partners), EU Marie Sklodowska-Curie Action (MSCA) ITN PAcMAN and OXYTRAIN (4 industrial partners),
- **Cofounder of SeSaM-Biotech** GmbH. One Start-Up company is in process of establishment in 2019 based the ***green*Release** technology for plant health (Microgel containers which bind through anchor peptides on plant leaves and which are load with fungicides)
- **Direct funding from companies** since 2011: 180-400 T€ per year

GROUP ORGANISATION

Our group is organised in five divisions (blue squares) at the RWTH Aachen University and the DWI-Leibniz Institute for Interactive Materials.



All five divisions work together to generate a fundamental understanding of protein properties on a molecular level and to use the discovered principles for efficient process development as well as design of interactive materials for a sustainable bioeconomy. Application of directed evolution methodologies for material science application and integration of tailormade biological building blocks into polymers to functionalize polymers (e.g. antimicrobial coatings; chiral membranes) for for applictions in medicine (e.g. stent functionalisations), plant health (greenRelease technology), and hybrid catalysis.

Organisation of the group

With **external coaches** with have developed role descriptions (for PhDs, post-docs, staff, subgroup leaders, professor) and implemented several measures for an efficient group organisation, which are evaluated and adjusted in yearly group retreats. Highlights are **taskforces** (in which each co-worker participates to better the group), the **GRC** (Group Research Council) representing PhDs & post-docs and participating in the weekly **GMB** meetings (main decision board). Further structures comprise a buddy and PhD mentoring system, weekly **SGL** (subgroup leader meetings), bimonthly **PDM** meetings (Project Development Meetings), a scientific coordinator and a position for strategic institute development (patent filing & support of core technologies and start-ups).

Representative publications to the core group technologies and applications fields; Stand 2017

Selected publications which represent the **group's research profile and competences in protein engineering and applications areas in integrated bioeconomy with biohybrid materials:**

A: *Protein engineering: Lessons and strategies for efficient enzyme design*
B: *Protein engineering: Methods for diversity generation & high-throughput screening*
C*: Next generation biokatalysis & discovered protein reengineering principles*
D*: Application fields: Valorisation from renewable resources & biohybrid release systems for a sustainable and integrated bioeconomy*

A: Protein engineering: lessons and strategies for efficient enzyme design: Zhao, J., Frauenkron-Machedjou, V. J., Kardashliev, T., Ruff, A. J., Zhu, L., Bocola, M., Schwaneberg, U. (2017). Amino acid substitutions in random mutagenesis libraries: lessons from analyzing 3000 mutations. **Appl. Microbiol. Biotechnol.**, 101, 3177-3187. **//** Cheng*, F., Zhu*, L., Schwaneberg, U. (2015). Directed evolution 2.0: improving and deciphering enzyme properties. **Chem. Commun**., 51, 9760-9772. (review; KnowVolution strategy) // Frauenkron-Machedjou, V. J., Fulton, A., Zhu, L., Bocola, M., Zhu, L., Jaeger, K.-E., Schwaneberg, U. (2015). Towards understanding directed evolution: more than half of all amino acid positions contribute to ionic liquid resistance of *Bacillus subtilis* lipase A**. ChemBioChem**, 16, 937-945. // Zhao, J., Kardashliev, T., Ruff, A. J., Bocola, M., Schwaneberg, U. (2014). Lessons from diversity of directed evolution experiments by an analysis of 3000 mutations. **Biotechnol Bioeng**, 111, 2380-2389. // Ruff, A. J., Dennig, A., Schwaneberg, U. (2013). To get what we aim for: progress in diversity generation methods**. FEBS J**., 280, 2961-2978 (review).

B: Methods for *diversity generation*: Yang, J., Ruff, A. J., Arlt, M., Schwaneberg, U. (2017). Casting epPCR (cepPCR): A simple random mutagenesis method to generate high quality mutant libraries. **Biotechnol. Bioeng.**, first published online: May 02 2017, DOI: 10.1002/bit.26327 // Belsare, K. D., Ruff, A. J., Martinez, R., Shivange, A. V., Mundhada, H., Holtmann, D., Schrader, J., Schwaneberg, U. (2014). **MAP2.03D**: a sequence/structure based server for protein engineering. **Synth. Biol.**, 1, 139-150. //Marienhagen, J., Dennig, A., Schwaneberg, U. (2012). Phosphorothioate-based DNA Recombination: an enzyme-free method for the combinatorial assembly of multiple DNA fragments (**PTRec**). **BioTechniques, Rapid Dispatch**, 1-6. // Dennig, A., Shivange, A.V., Marienhagen, J., Schwaneberg, U. (2011). **OmniChange**: The sequence independent method for simultaneous site-saturation of five codons, **PLoS One**, 6, e26222. (➔ generates 3.2 million protein variants in one afternoon; granted IP) // Wong, T. S., Tee, K. L., Schwaneberg, U. (2004). Sequence Saturation Mutagenesis (**SeSaM**): A novel method for directed evolution, **Nucleic Acids Res.** 32, e26. (plus four subsequent ones; granted IP). **Methods for *high-throughput screening:*** Körfer, G., Pitzler, C., Vojcic, L., Martinez, R., Schwaneberg, U. (2016). In vitro flow cytometry-based screening platform for cellulase engineering. **Scientific Reports**, Publication Date (Web): May 17, 2016. DOI: 10.1038/srep26128. // Cheng, F., Kardashliev, T., Pitzler, C., Shehzad, A., Lue, H., Bernhagen, J., Zhu, L., Schwaneberg, U. (2015). A competitive flow cytometry screening system for directed evolution of therapeutic enzyme**. ACS Synth. Biol**., 4, 768-775. // Pitzler, C., Wirtz, G., Vojcic, L., Hiltl S., Böker, A., Martinez, R. Schwaneberg, U. (2014). A fluorescent hydrogel-based flow cytometry high-throughput screening platform for hydrolytic enzymes. **Chemistry & Biology**, 21, 1733-1742. // Ruff, A. J., Dennig, A., Wirtz, G., Blanusa, M., Schwaneberg, U.

(2012). Flow cytometer-based high throughput screening system for accelerated directed evolution of P450 monooxygenases. **ACS Catalysis**, 2, 2724-2728.

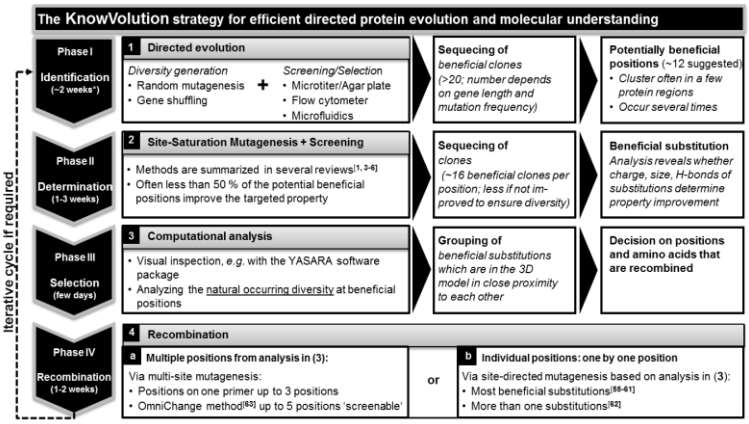
C: ***Next generation biokatalysis & discovered protein reengineering principles***: Markel*, U., Zhu*, L., Frauenkron-Machedjou, V. J., Zhao, J., Bocola, M., Davari, M. D., Jaeger, K.-E., Schwaneberg, U. (2017). Are Directed Evolution Approaches Efficient in Exploring Nature's Potential to Stabilize a Lipase in Organic Cosolvents? **Catalysts**, 7, 142 // Belsare, K. D., Horn, T., Ruff, A. J., Martinez, R., Magnusson, A., Holtmann, D., Schrader, J., Schwaneberg, U. (2016). Directed evolution of P450cin for mediated electron transfer. **PEDS**, 30, 119-127. Dhoke, G. V., Davari, M. D., Schwaneberg, U., Bocola, M. (2015). QM/MM calculations revealing the resting and catalytic states in zinc-dependent medium-chain dehydrogenases/reductases. **ACS Catalysis**, 5, 3207-3215. // Dennig, A., Lülsdorf, N., Liu, H., Schwaneberg, U. (2013). Regioselective o-hydroxylation of monosubstituted benzenes by P450 BM3. **Angew. Chemie**, 53, 8459-8462. // Arango Gutierrez, E., Meier, T., Duefel, H., Mundhada, H., Bocola, M., Schwaneberg, U. (2013). Reengineered glucose oxidase for amperometric glucose determination in diabetes analytics. **Biosensors & Bioelectronics**, 50, 84-90. // Müller, C. A., Akkapurathua, B., Winkler, T., Staudt, S., Hummel, W., Gröger, H., Schwaneberg, U. (2013). In vitro double-oxidation of n-heptane with direct co-factor regeneration. **Adv. Syn. & Cat**., 355, 1787-1798. // Kuper, J., Wong, T.S., Roccatano, D., Wilmanns, M., Schwaneberg, U. (2007). Understanding the mechanism of organic co-solvent inactivation in heme monooxygenase P450 BM-3, **JACS**, 129, 5786-5787. Sauer, D. F., Himiyama, T., Tachikawa, K., Fukumoto, K., Onoda, A., Mizohata, E., Inoue, T., Bocola, M., Schwaneberg, U., Hayashi, T., Okuda, J. (2015). A highly active biohybrid catalyst for olefin metathesis in water: impact of a hydrophobic cavity in a β-barrel protein. **ACS Catalysis,** 5, 7519-7522. // Philippart, F., Arlt, M., Gotzen, S., Tenne, J., Bocola, M., Chen, H.H., Zhu, L., Schwaneberg, U.*, Okuda, J.* (2013). A hybrid ring-opening metathesis polymerization catalyst based on engineered ß-barrel protein FhuA. **Chemistry**, 19, 13865-13871. // Onaca, O., Sarkar, P., Roccatano, D., Friedrich, T., Hauer, B., Grzelakowski, M., Güven, A., Fioroni, M., Schwaneberg, U. (2008). Functionalized nanocompartments (synthosomes) with a reduction-tiggered release system, **Angew. Chem.** Int Ed, 47, 7029-7031.

D: ***Application fields: Valorisation from renewable resources & biohybrid release systems for a sustainable***

and integrated bioeconomy: Meurer, R. A., Kemper, S., Knopp, S., Eichert, T., Jakob, F., Goldbach, H. E., Schwaneberg*, U., Pich*, A. (2017). Biofunctional Microgel-Based Fertilizers for Controlled Foliar Delivery of Nutrients to Plants. **Angewandte Chemie**, 56, 1-7 // Peng, H., Rübsam, K., Jakob, F., Schwaneberg, U., Pich, A. (2016). Tunable Enzymatic Activity and Enhanced Stability of Cellulase Immobilized in Biohybrid Nanogels. Biomacromolecules, 17, 3619-3631. // Peng, H., Kather, M., Rübsam, K., Jakob, F., Schwaneberg, U., Pich, A. (2015). Water-soluble reactive copolymers based on cyclic N-vinylamides with succinimide side groups for bioconjugation with proteins. **Macromolecules**, 48, 4256-4268. // van Rijn, P., Tutus, M., Kathrein, C., Zhu, L., Wessling, M., Schwaneberg, U., Böker, A. (2013). Challenges and advances in the field of self-assembled membranes**. Chem. Soc. Rev**., 42, 6578-6592 //.

Three highlighted publications with a summary of max. 1000 characters

Highlight **1**: *Protein engineering strategy* ***KnowVolution***



Cheng, F., Zhu*, L., Schwaneberg, U. (2015). Directed evolution 2.0: improving and deciphering enzyme properties. Chem. Commun., 51, 9760-9772* (review).

The protein engineering strategy KnowVolution balances throughput and time requirements for designing efficient enzymes. KnowVolution is divided in four phases: I. Identification of potential beneficial positions, II. Determination of beneficial substitutions at positions from

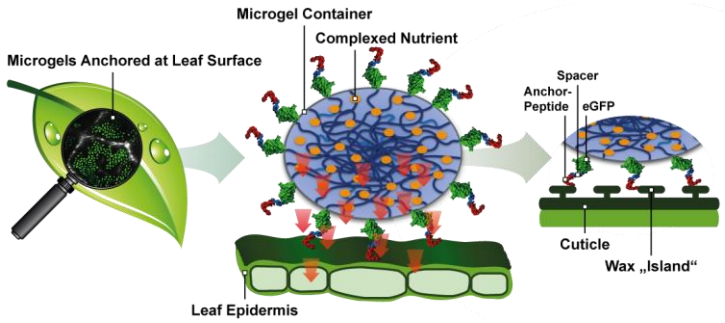
I., III. Structural analysis to determine whether substitutions might interact or not (cooperative), and IV. Recombination of beneficial positions/substitutions depending on analysis on III to maximize property improvements. Minimizing the number of substitutions in phase II. proved to be essential to generate robust enzymes with only slightly reduced thermal resistance and unaltered substrate preference. In addition, the chemical interactions for each beneficial substitution is discovered which enables a deep molecular understanding of the improved enzyme property. Three of the reported examples in the review were commercialized by industrial partners.

Highlight **2**: *High-throughput screening technology for directed enzyme evolution* (patent filed)

Körfer, G., Pitzler, C., Vojcic, L., Martinez, R., Schwaneberg, U. (2016). In vitro flow cytometry-based screening platform for cellulase engineering. Scientific Reports, 32, 629-634.

In order to make directed enzyme evolution a standard tool in process development, the development times for improving enzyme properties have to be significantly reduced and throughput has to be significantly increased due to the complexity of the protein sequence space.
*The InVitroFlow technology is a cell-free directed evolution system that enables to sample up to 10^9 events per day offering coverage of a significant fraction of the generated sequence space in order to identify beneficial positions beyond the possibility of traditional screening formats. Validation was performed after sampling of 1.4 * 10^7 events which improved the activity of a cellulase from 16.5 to 220.6 U per mg in one round of evolution. Traditional directed evolution campaigns in 96-MTP formats yield usually improvements of a factor of 1.5 to 2.5 per round of evolution. In summary, the InVitroFlow technology offers exciting novel possibilities to evolve cell toxic proteins and proteins from human or animal origin using cell-free expression systems based on wheat germ and other eukaryotic cell extract.*

Highlight **3**: *Example of **integrated bioeconomy 2.0** technology platform (patent filed)*



Meurer, R. A., Kemper, S., Knopp, S., Eichert, T., Jakob, F., Goldbach, H. E., Schwaneberg, U., Pich*, A. (2017). Biofunctional Microgel-Based Fertilizers for Controlled Foliar Delivery of Nutrients to Plants. Angewandte Chemie, 56, 1-7.*
**shared corresponding authorship*

The release technology platform (named GreenGel) serves as a broadly applicable and robust release system for sustainable agriculture. Main advantages of the GreenRelease technology over existing release technologies are: the controlled release of compounds over weeks/months, minimized losses due to a high rainfastness, plant compatibility, and tunable biodegradability. The amount of applied fungicides/herbicides can be reduced and thereby environmental contamination will be minimized ("achieve more with less"). GreenGel is based on engineered peptides that act as adhesion promotors to wax layer of plants and that decorate microgels. The microgels are a novel type of soft particles which were developed in the SFB985 Microgels by the Pich group and serve as containers for all kinds of compounds. Microgels are produced in kg scale

(8-10 € per kg) and can usually be loaded with 30-50 % of the polymer dry weight (upper publication 50 % load with Fe^{3+} micronutrient).