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Institute of Organic Chemistry: 1983–2008

Jay S. Siegel* and Heinz Heimgartner*

Abstract: The developments at the Institute of Organic Chemistry UZH over the past 25 years are discussed with new perspectives being sought through the engagement of a strong international team of professors and the establishment of research groups led by assistant professors. Innovation and change mark the OCI's attitude to the future illustrated by the modern Batchelor's and Master's programs, the 'institute within the institute' the 'Labor für Prozessforschung' (LPF) which uniquely trains post-doctoral students in process chemistry, the encouragement of entrepreneural activity, and the training of apprentices.

Keywords: Institute of Organic Chemistry UZH · Laboratory for Process Chemistry

Introduction

Curricular structure and university administration in Zurich have undergone substantial changes since the 150th anniversary. In 1983, there were three chemical institutes: Inorganic, Physical and Organic. The Institute of Organic Chemistry was run by a fledgling directorate, which had an operational history of only six years since the passing of Hans Schmid. With the development of the new Irchel campus, the OCI had accessed exceptional state of the art laboratories and infrastructure while transitioning to a site away from the traditional center of the university.

The traditional power structure of UZH was also transforming. Already at this time, thoughts of an independent university administration were immerging. In 1984, the position of 'Rektor' was exalted within the Cantonal hierarchy and two 'Prorektor' positions were created. By 1994, a concept of 'Uni2000' was in the works. The concept of university 'self-administration' came officially on March 15, 1998, completely revolutionizing the operations of UZH.

This quarter of a century of reform moved UZH away from direct influence of the 'Erziehungsdirektion' and gave the University directorate independent operational and budgetary responsibility. The same period for the OCI signaled a convergence of core-altering events. Amidst a loss of patriarchal guidance, a change in the Cantonal educational administration policy, a '1999 Bologna' declaration for curricular reform in Europe, and a decreasing number of chemistry students, the OCI had to chart new waters in search of a modern identity.

New 'Digs' – Irchel at Age 30

The first stage of the Irchel campus came on line in 1978, and was fully operational by the 150th anniversary of UZH in 1983. The OCI moved into labs built during the first construction phase. The construction followed well the design of master architect Max Ziegler, and provided state of the art laboratories blended within an architectural style that promoted interaction and exchanges. The wide halls, ample meeting spaces, elegant spiral staircases, and a unified building network, all integrated within a park of the architect's design, created an atmosphere of positivism and creativity.

On a personal note, JSS remembers his first visit to Irchel in 1983 to visit the Dreiding group meeting. Coming from Princeton, an idyllic campus on its own, the Irchel experience and its proximity to the center of Zurich was nonetheless exceptional and impressive.

Considering only the question of wear and tear, the labs are unparalleled in the degree of maintenance that they have enjoyed.

Correspondence: Prof. Dr. J. S. Siegel
Prof. Dr. H. Heimgartner
Institute of Organic Chemistry
University of Zurich
Winterthurerstrasse 190
CH-8006 Zurich
Tel.: +41 44 635 4281
Fax: +41 44 635 6888
E-mail: jss@oci.uzh.ch

Nonetheless, during this period, building technology and infrastructure needs have increased enormously. In this regard the labs are still competitive, but given the leading position of UZH as a European research university, the time is nigh for a technological/infrastructure renovation. Indeed, one of the biggest steps to be made toward a 'greener' research environment in Zurich will be to invest in technologically state-of-the-art chemistry laboratories.

Now, as the concept of the 'zero carbon house' becomes more popular,[1] and technological developments make it more realizable, it is time to consider the 'zero carbon laboratory' as ideal, even if the concept is unattainable based on the inherent nature that chemical research must at its core deal with the processing of chemicals.

With Irchel phase 5 nearing and phase 6 in discussion, a demonstration of leadership would come through development of a model laboratory of the future with all the power, safety and utility of the highest class, but coupled to technology that would showcase exceptional efficiency and sustainability.

Faculty in Transition

The number of 'Lehrstühle' in Organic Chemistry declined dramatically during the past 25 years from six in 1983 to formally three in 2000. A combination of decreasing student numbers and a misunderstanding of the magnitude of the role of chemistry in the human endeavor led the then Prorektor Künzle to propose that Chemistry could be covered by a total of nine 'Lehrstühle' distributed equally over three institutes. No matter how untenable the decision, it placed a pressure on the faculty to regroup. As a result, as retirements occurred, selected successors were not approved.

The faculty progression of the 1980s followed through the retirement of Max Viscontini 1983, Andre Dreiding 1987, and Conrad Eugster 1988, of which two were replaced by the recruitment of Hans-Jürgen Hansen 1988 and John A. Robinson 1989. During the 1990s, Walter Thiel was attracted to Zurich, but before the decade passed Andrea Vasella 1993 and Walter Thiel 1998 were recruited away to ETH-ZH and MPI Mühlheim, respectively. The quality of the lost faculty is reflected in part by the power of the institutions that recruited them. Add to this loss of faculty in their prime, the retirement of Wolfgang von Philipsborn 1997, and the picture becomes dark, indeed (Fig. 1).

Proper replacement of these key faculty from the international scene became difficult in light of such a regressive policy toward Chemistry. Thus, the dawning of Uni2000 looked bleak for one of UZH's charter science faculties – one that supported the growth and prestige of UZH through a strong international reputation and two illustrious Nobel Prize winners. That any institution would turn its back on a core competence of Natural science cannot be explained on scientific or thematic grounds. Chemistry in the context of a modern natural science philosophy remains a central and enabling discipline of thought, innovation and economy.

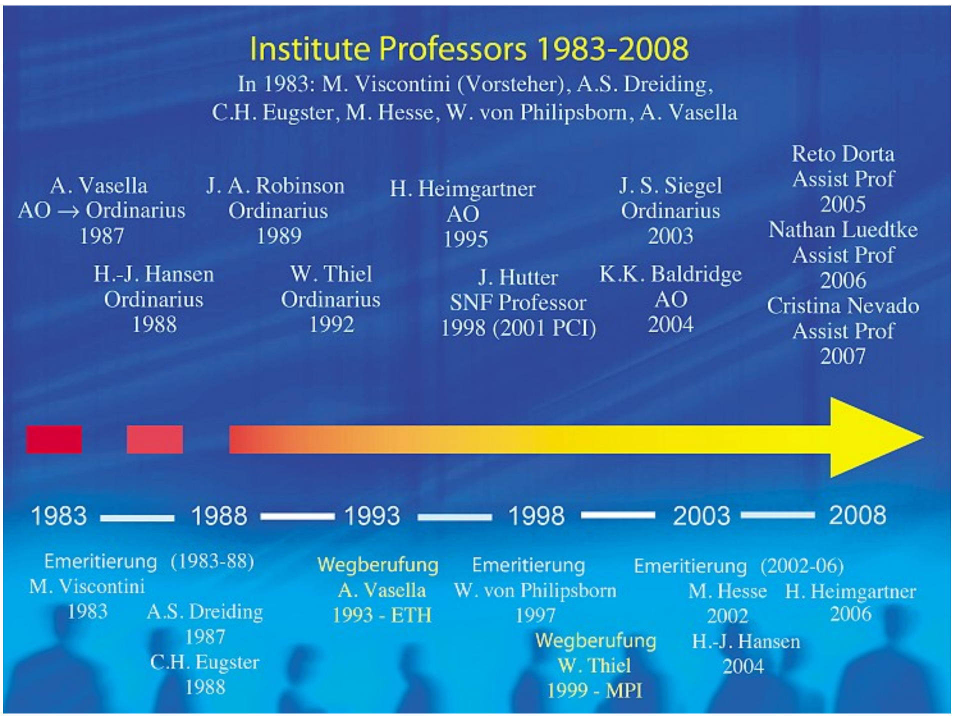

Fig. 1. Timeline of professors in OCI 1983–2008

The first decade of the new millennium was slated for three more retirements: Manfred Hesse 2002, Hans-Jürgen Hansen 2004, and Heinz Heimgartner 2006. A substantial commitment to rebuilding of Organic Chemistry was imperative, particularly in light of the tremendous appreciation and support for Organic Chemistry at the neighboring ETH. The international role of chemistry at UZH was in jeopardy.

The recruitment of Jay S. Siegel 2003 and Kim K. Baldridge 2004 brought a distinctly new perspective to the OCI. It seemed that the instigation of a model alternative to the 'Lehrstuhl' system would be necessary if OCI was to regain its prowess as a strong institute with international leading representation in research and teaching. The forging of a new plan for building up an international program would require identification of new resources for personnel, finances, and global networking. The UZH and Zurich community had to develop a greater appreciation of what they had to lose if chemistry disappeared or continued but not in a leading role on campus.

Independence for young investigators in the US assistant professor system has often been compared to the strong mentoring and guidance offered to European habilitants. An important goal became finding a way to blend the spontaneous and entrepreneurial offerings of the US system with the traditional exactness and steadfastness of Switzerland.

The OCI plan was to recognize the habilitation as a personal development program in research, and an assistant professor as a professional rank in the academic hierarchy. As such, all institute co-workers overseeing analytical facilities were encouraged to enhance the research component of their positions and to advance themselves through habilitation to 'Privatdozent' status. Their professional career development became then oriented toward an eventual Titular Professorship in recognition of their internationally leading contributions to research.

Contemporary with promoting the independent status of researchers already in the institute, the future recruitment and development of the faculty should focus on the appointment of assistant professors with exceptional talent. These young and creative minds provide the best indicators of the future directions for research in chemistry and the best chance for an organization to achieve success. It comes down to applying a well distributed management principle to the academic setting: 1) Recruit the best young minds; 2) Give them the best resources; and 3) GET OUT OF THEIR WAY.

The concept of the program is that diversity in research through numerous independent young program leaders will stimulate scientific discovery and discourse.

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Ultimately this kind of creative environment is renewing UZH's reputation as an attractive center for students and researchers from all corners of the world and at every age level.

Habilitation as Instrument of Personal Development

Tried and true the concept of the habilitation embodies the idea of higher personal development through the deeper pursuit of a scientific thesis. If the PhD dissertation is a demonstration of a candidate's coming of age as an independent thinker and researcher, then habilitation demonstrates the candidate's ability to develop an independent area of research. The achievement of habilitation leads to the granting of a right to lecture (*venia legendi*) in one's area of expertise and thereby instruct others in the methods of that discipline.

The century old tradition of developing young talent through support of habilitation research has continued over the last 25 years. Roughly 15 habilitation thesis have been submitted to the faculty since 1980, seven of them in the last five years (Table).

Several successful habilitations have led to academic careers. Heinz Heimgartner 1980 remained in the OCI and advanced through Titular Professor to ad personam Professor and member of the OCI directorate. During his career, he built a world-famous reputation in heterocyclic chemistry, including attaining the Kametani award for Heterocyclic Chemistry. He was also mentor to two distinguished alumni, Peter Wipf and Daniel Obrecht, one a well-known professor of chemistry at the University of Pittsburgh, the other the successful founder of Polyphor AG in Allschwil CH.

Peter Rüedi 1984 and Stefan Bienz 1995 remain in the OCI as Titular Professors. Professor Rüedi researches natural product chemistry and phosphate processing enzymes. Professor Bienz focuses on synthetic methodologies based on organosilicon compounds.

Table. Habilitations at OCI 1980–2008

Year	*Name*	*Title*	*Future*
1980	Heinz Heimgartner	*3-Amino-2H-azirine, neue Synthone für heterocyclische Verbindungen*	Tit.-Prof. 1987; AO 1995; emeritiert 2006
1982	Lienhard Hoesch	*Nitrene beim Aufbau und Abbau von Polyazaverbindungen*	1987 Institut für Pflanzenbiologie
1984	Peter Rüedi	*Natürlich vorkommende Chinomethide*	Tit.-Prof. 1998
1985	Wolf-Dietrich Woggon	*Beiträge zur Biosynthese von Arthropoden-Allomonen*	AO 1995 Uni Basel
1985	Martin Karpf	*Organische Synthesen bei hohen Temperaturen: Entdeckung, Untersuchung und Anwendung der α-Alkinon Cyclisierung“*	1988 F. Hoffmann-La Roche
1994	Georg Fráter	*Stereochemische und mechanistische Untersuchungen zur Synthese von Sesquiterpenen und Sesquiterpenoiden*	Tit.-Prof. 2002 (extern, Givaudan)
1995	Stefan Bienz	*Enantioselective Synthesis Using Amino Acid or Silicon Based Chiral Auxiliaries and Synthesis of Polyamine Toxins from Spiders and Wasps*	Tit.-Prof. 2002
1998	Michael Bühl	*Theoretische Untersuchungen von Strukturen, Reaktivitaeten und NMR-chemischen Verschiebungen von Fullerenen, schwereren Hauptgruppenverbindungen und Uebergangsmetallkomplexen*	1999 MPI Mülheim 2008 Chair Comp. Chem. - St. Andrews
2003	Andreas Rippert	*A Diverse Ligandothek Based on Axially Chiral Backbones Used in Selective Transition-Metal Catalysis*	2004 Kantonspolizei Zürich
2004	Anthony Linden	*Structural Diversity in Organoammonium Chloromercurate(II) and Bromothallate(III) Salts*	1990 X-Ray Lab
2005	Nathaniel Finney	*Molecular Recognition and Physical Organic Chemistry at the Interface of Basic and Applied Research*	2004 OCI
2005	Oliver Zerbe	*Umhabilitation – ETH Zürich*	2003 OCI/NMR
2006	Reza Fallahpour	*Umhabilitation – Uni Basel*	2005 OCI
2007	Karl-Heinz Ernst	*Expression and Amplification of Molecular Chirality at Metal Surfaces*	(extern - Empa)
2008 ex	Laurent Bigler		2000 OCI/MS

Wolf-Dietrich Woggon 1985 went on to become professor in Basel and today heads the Department of Chemistry in Basel. Michael Bühl 1994 is now Chair for Computational Chemistry at the University of St. Andrews after an interim period at the MPI Mühlheim. The influence of UZH habilitants in the academic community continues.

The personal development achieved through a habilitation study can have an impact in the industrial world as well. Georg Fràter 1994 led for many years the chemical research at Givaudan in Dübendorf. In parallel, he lectured in Fragrance Chemistry at UZH and become Titular Professor in 2002. In his present position as President of the Swiss Chemical Society, he continues to serve a leadership role in chemistry.

Martin Karpf 1985 joined the ranks at Hoffmann La Roche in 1988 and focused on the area of process chemistry. He has had numerous successful campaigns in developing economical methods for the synthesis of blockbuster active pharmaceutical ingredients. Recently, he has received much attention for his team's work on the synthesis of oseltamivir (Tamiflu). The quality of his lectures on process chemistry is known worldwide. His team was awarded the Swiss Chemical Society's Sandmeyer Prize for industrial chemistry. Dr. Karpf also serves that society as Treasurer. The earmark of research, teaching and service branded during his UZH experience is clear.

The most recent habilitations reflect the OCI's new establishment of an instrumentation-oriented cadre of independent research scholars. Oliver Zerbe, Anthony Linden, and Nathaniel Finney 2004, all lead programs that have a strong component involving analytical methods. Reza Fallahpour brings the design and synthesis of novel ligands directed toward applications in photovoltaic cells. Karl-Heinz Ernst 2007 marks an inaugural collaboration between UZH and Empa and expands the OCI research spectrum to surface and material science.

Building through Young Talent

In 2004, the OCI made a commitment to rebuild by way of assistant professor appointments (Fig. 2). The first appointment was Reto Dorta, recipient of an Alfred Werner Fellowship from the 'Stiftung für Stipendien auf dem Gebiet Chemie'. The following year, Nathan Luedtke was appointed to the position opened by the retirement of Hans-Jürgen Hansen. The success of our assistant professor program convinced the faculty to give the green light on the hire of another assistant professor to fill the position vacated by the retirement of Heinz Heimgartner. Cristina Nevado was recruited and appointed in 2007 to fill this position.

Fig. 2. OCI assistant professors Reto Dorta, Nathan Luedtke, and Cristina Nevado

Assistant Professor Profiles

Reto Dorta studied chemistry at the University of Neuchâtel and the University of Salerno. He joined Professor Georg Süss-Fink's group at the University of Neuchâtel for his Diploma work (1997) and subsequently moved to the Weizmann Institute of Science (Israel), where he earned his doctoral degree under Professor David Milstein in 2002. He then transferred to the University of New Orleans for a one-year postdoctoral stay with Professor Steven P. Nolan. Soon after joining Prof. John E. Bercaw at the California Institute of Technology for a second postdoc, he was awarded an Alfred Werner Assistant Professorship and moved to UZH in 2005.

Research in the Dorta group is directed toward the preparation of reactive transition metal complexes for stoichiometric and catalytic applications. The focus of attention is the development of new chiral and non-chiral auxiliary ligand systems that are able to bind, activate, and functionalize substrates at a metal center. Specific emphasis is put on the development of new chiral ligand families for asymmetric catalysis and new, highly electron-donating ligands for late transition metals. The ultimate goal of the research program is to identify complexes for new, more selective or more widely applicable catalytic transformations.

Representative publications:

'A Chiral Bis-Sulfoxide Ligand in Late-Transition Metal Catalysis; Rhodium-Catalyzed Asymmetric Addition of Arylboronic Acids to Electron-Deficient Olefins', R. Mariz, X. Luan, M. Gatti, A. Linden, R. Dorta, *J. Am. Chem. Soc.* **2008**, *130*, 2172.

'd^8 Rhodium and Iridium Complexes of Corannulene', J. S. Siegel, K. K. Baldridge, A. Linden, R. Dorta, *J. Am. Chem. Soc.* **2006**, *128*, 10644.

'Steric and Electronic Properties of N-Heterocyclic Carbenes; A Detailed Study on their Interaction with $Ni(CO)_4$', R. Dorta, E. D. Stevens, N. M. Scott, C. Costabile, L. Cavallo, C. D. Hoff, S. P. Nolan, *J. Am. Chem. Soc.* **2005**, *127*, 2485.

Nathan Luedtke was born in the United States, and attended high school near Seattle, Washington. In 1996 he received his bachelor's degree from the University of Washington where he worked as a teaching assistant for the Department of Chemistry. During his studies at the University of Washington he conducted original research investigating DNA–small molecule interactions with Paul Hopkins (Organic Chemistry), and DNA origins of replication in *S. cerevisiae* with Walt Fangman (Genetics).

Luedtke received his doctoral degree in 2003 from the University of California, San Diego where he studied small molecule–RNA binding interactions in the laboratory of Yitzhak Tor. During his PhD work he received numerous awards for teaching and research, as well as a doctoral fellowship from the State of California to investigate the anti-HIV potential of RNA ligands.

From 2003–2006 Nathan worked as an NIH Postdoctoral Fellow in the Laboratory of Alanna Schepartz (Yale University). During this time he investigated a variety of topics at the interface of chemistry and biology, including the application of small fluorescent molecules to study protein folding in living cells. Since October 2006, Nathan has been an Assistant Professor of Organic Chemistry at the University of Zürich where he is investigating the chemistry and biology of DNA.

Watson and Crick's model of fully hydrated (B-form) duplex DNA inspired the mechanistic understanding of the replication and flow of genetic information known as the central dogma of biology. Since then, DNA has been regarded as a uniform double helix and a passive library of genetic information. DNA structure, however, is highly dynamic and its functions are potentially diverse.

While it is now widely recognized that the three-dimensional folded structure of RNA is essential for its proper function, much less is known about how DNA folding and dynamics are involved in the regulation gene expression, chromosome stability, cellular replication, and programmed cell death. Research in the Luedtke Lab is focused on the design, synthesis, and evaluation of chemical probes for diverse secondary and tertiary structures of DNA that have been implicated in these activities. It is hoped that structure-specific probes capable of reporting and/or stabilizing DNA structures like hairpins, G-quadruplexes, and i-motifs will provide new tools for determining the presence and function of these structures *in vivo*.

One potential application of this work is the development of new anti-cancer agents. Many of the currently used anti-cancer therapies utilize chemical agents that bind to duplex DNA non-specifically (*e.g.* cisplatin, mitomycin C, daunomycin, *etc.*). The use of small molecules that can target DNA in a structure-selective fashion may dramatically decrease the side effects of these treatments. Indeed, two new molecules prepared in the Luedtke Lab that bind to G-quadruplex DNA selectively also exhibit promising anti-cancer activities in cell cultures.

Representative publications:

'Surveying Polypeptide and Protein Domain Conformation and Association with FlAsH and ReAsH', N. W. Luedtke, R. J. Dexter, D. B. Fried, A. Schepartz, *Nature Chemical Biology* **2007**, *3*, 779.

'Lanthanide-mediated Phosphoester Hydrolysis and Phosphate Elimination from Phosphopeptides', N. W. Luedtke, A. Schepartz, *Chem. Commun.* **2005**, 5426.

'Cellular Uptake of Aminoglycosides, Guanidinoglycosides, and Poly-arginine', N. W. Luedtke, P. Carmichael, Y. Tor, *J. Am. Chem. Soc.* **2003**, *125*, 12374.

Cristina Nevado was born in Madrid, where she graduated in chemistry at the Universidad Autónoma de Madrid in 2000. In October 2004 she received her PhD in organic chemistry at the same university working with Prof. Antonio M. Echavarren in the cyclization of enynes catalyzed by platinum and gold complexes. In December 2004 she joined the group of Prof. Alois Fürstner at the Max-Planck-Institut für Kohlenforschung (Germany) where she was part of the team who conquered the first total synthesis of Iejimalide B, a marine macrolide possessing a very sensitive architecture. Since May 2007 she is Assistant Professor in Organic Chemistry at the University of Zürich.

Rooted in the wide area of Organic Chemistry, her research program is focused on complex chemical synthesis and new organometallic reactions. Central to her interest is the total synthesis of natural products with challenging architectures and relevant biological properties. Her driving force stems from the discovery and application in synthesis of new methodologies based on late transition metal catalyzed reactions.

Representative publications:

'Total Synthesis of Iejimalide A-D and Assessment of the Remarkable Actin-Depolymerizing Capacity of these Polyene Macrolides', A. Fürstner, C. Nevado, M. Waser, M. Tremblay, C. Chevrier, F. Teply, C. Aïssa, E. Moulin, O. Müller, *J. Am. Chem. Soc.* **2007**, *129*, 9150.

'Total Synthesis of Iejimalide B', A. Fürstner, C. Nevado, M. Tremblay, C. Chevrier, F. Teply, C. Aïssa, M. Waser, *Angew. Chem., Int. Ed.* **2006**, *45,* 5837.

'Non-Stabilized Transition Metal Carbenes as Intermediates in Intramolecular Reactions of Alkynes with Alkenes', A. M. Echavarren, C. Nevado, *Chem. Soc. Rev.* **2004**, *33*, 431.

Molecular Design and Synthesis

The Bologna declaration in its call for a European space for higher education, set as key goals global attractiveness with pan European compatibility. The call encourages diversity in curriculum and specifically speaks of deviation from traditional structures.

Chemistry is ripe for such a movement. The classical idea of partitioning chemistry into Inorganic, Organic, and Physical, or even Biochemistry, is a political remnant kept from dying a peaceful death by specific institute and lehrstuhl academic structures. Most chemists learned a generation or more ago that the distinction between organic and inorganic compounds is taxonomic and not physically meaningful. It is well understood that synthesis in absence of analysis is equally meaningless. Theoretical/computational models and physical measurements guide our thinking from natural products to materials.

What unifies chemistry today is our ability to design and synthesize molecular systems in a directed line of investigation. This principle may have an engineering slant *en route* to an optimized molecule for a specific application or it may have a fundamental discovery slant, wherein the variation in the structure/properties of the molecule serves as the dependent/independent variable of the scientific study.

Molecular design and synthesis is also what makes chemistry so central to many other areas like medical, life, earth and materials science. Still, our curricula tend to parallel classical object-based structures, when what a modern chemist needs is an education oriented toward modeling, designing, synthesizing and analyzing of molecular systems. New classes and courses of study are needed to match the modern focus of chemical research.

A plan for the future is to create a new kind of curriculum for the molecular sciences based on the idea of preparing students with a philosophy in mind that, control of molecular structure and properties is paramount. This philosophy unifies theory, synthesis, and analysis in the pursuit of contemporary goals in chemical science. Given this perspective, an entering student can early in his or her career make personal career choices that affect the nature of the course of study without sacrificing the broad and fundamental training needed to be successful as a chemist.

This perspective on chemistry is a positive outcome of the forced transition of the OCI faculty. With an emphasis on the synthesis of molecular architectures with specific function, the research programs of John Robinson and Jay Siegel represent well the molecular design and synthesis paradigm. From biomimetic scaffolds to novel aromatic materials, the two research teams are highly active in the international chemistry arena.

The fundamental modeling tools for the design of new molecules come from computational chemistry. Computational Chemistry during the period 1992–1999 was strongly represented in the institute through the research of Professor Walter Thiel and his 'habilitant' Michael Bühl. After their departure, Jürg Hutter came to the OCI as an SNF professor, but moved to a permanent Associate Professor position in the Physical Chemistry Institute in 2001.

In 2004, with the arrival of Kim Baldridge, Computational Chemistry was revitalized at OCI. Along with a strong program in computational science, she brought expertise in global network 'Grid Computing'. The Baldridge group built a multinode supercomputer cluster of Dell processors, as their core facility. Over time, this facility has expanded and presently includes several computer clusters and 'fat' memory machines.

Professor Profiles:

Kim K. Baldridge studied Chemistry and Mathematics at the University of Minot, North Dakota, with a minor in physics. This was followed by a Master's Degree in Mathematics from North Dakota State University, NDSU, North Dakota, 1985. She received her PhD in Theoretical Chemistry from NDSU in 1988, working with Mark Gordon and Don Truhlar, on QM algorithms for 'reaction path following' (GAMESS, Gaussian) and application of QM methods to aromatic constructs. She then spent a year as a postdoctoral researcher at Wesleyan University, Connecticut, USA, with Dave Beveridge, working on hybrid QM/classical methods.

From 1989–2004, Kim Baldridge followed a split career track at the San Diego Supercomputer Center (Director of Integrative Computational Sciences) and University of California, San Diego (full professor, 2001–4). In 2004, she became a Professor of Theoretical and Computational Chemistry in the Institute of Organic Chemistry at the University of Zurich, where activities include QM computational methods development and application, and development of high performance and grid computing methods. She received the Agnes Fay Morgan Award (2002), was appointed Fellow of the American Physical Society (2000) and Fellow of the American Association of the Advancement of Sciences (2001).

Kim Baldridge's research is at the interface of Theoretical Methods development and applications of computational methods to problems across several disciplines, highlighted with experimental collaborations. The research involves utilization of computational methodologies for prediction of chemical and physical properties, in conjunction with experiments, to enhance the understanding of control within technologically and biologically important chemical structures and reaction processes.

A large variety of computational tools, including a variety of computational chemistry software, visualization and analysis tools, and computer, grid, and middleware technologies for enabling computation on a wide variety of compute platforms and environments, are applied in her research as well as teaching efforts.

Representative publications:

'Steric Isotope Effects Gauged by the Bowl-Inversion Barrier in Selectively Deuterated Pentaarylcorannulenes', T. Hayama, K. K. Baldridge, Y.-T. Wu, A. Linden, J. S. Siegel, *J. Am. Chem. Soc.* **2008**, *130*, 1583.

'A Simple Model System for the Study of Carbohydrate-Aromatic Interactions', G. Terraneo, D. Potenza, A. Canales, J. Jimenez-Barbero, K. K. Baldridge, A. Bernardi, *J. Am. Chem. Soc.* **2007**, *129*, 2890.

'Stereoselectivity and Expanded Substrate Scope of an Engineered PLP-dependent Aldolase', F. P. Seebeck, A. Guainazzi, C. Amoreira, K. K. Baldridge, D. Hilvert, *Angew. Chem., Int. Ed.* **2006**, *45*, 6824.

Fig. 3. Kim Baldridge, John Robinson, Jay Siegel

John Robinson studied chemistry at University College, London, where he was awarded the B.Sc. degree in 1974. He completed his PhD at Cambridge University in 1977, under the supervision of Professor A. R. Battersby. With a Royal Society Postdoctoral Fellowship, he subsequently carried out postdoctoral work in the Biochemistry Institute of the University of Karlsruhe, before joining the Chemistry Department of Southampton University, UK in 1979 as a lecturer. In 1987, he became senior lecturer, and was awarded the Hickinbottom Prize of the Royal Society of Chemistry. He moved to Zurich as Full Professor of Organic Chemistry in 1989.

There are two main research areas within the Robinson group, one concerned with the synthesis and biological activity of protein epitope mimetics (PEMs), and the other with the study of antibiotic biosynthesis, in particular, the glycopeptide antibiotic vancomycin. These research foci fall within the broad area of chemical biology/ biological chemistry. Most of the research is concerned with the synthesis of biologically active molecules, and studies of their interactions with proteins. The work, therefore, draws upon the methods of chemistry, as well as of biochemistry, biophysics and biology.

Representative publications:

'Design of β-Hairpin Peptidomimetics that Inhibit Binding of α-Helical HIV-1 Rev Protein to the Rev Response Element RNA', K. Moehle, Z. Athanassiou, K. Patora, A. Davidson, G. Varani, J. A. Robinson, *Angew. Chem., Int. Ed.* **2007**, *46*, 9101.

'Synthetic Virus-like Particles from Self-assembling Coiled-coil Lipopeptides and their Use in Antigen Display to the Immune System', F. Boato, R. M. Thomas, A. Ghasparian, A. Freund-Renard, K. Moehle, J. A. Robinson, *Angew. Chem., Int. Ed.* **2007**, *46*, 9015.

'Oxidative Phenol Coupling Reactions Catalyzed by OxyB: A Cytochrome P450 from the Vancomycin Producing Organism. Implications for Vancomycin Biosynthesis', K. Woithe, N. Geib, K. Zerbe, D. B. Li, M. Heck, S. Fournier-Rousset, O. Meyer, F. Vitali, N. Matoba, K. Abou-Hadeed, J. A. Robinson, *J. Am. Chem. Soc.* **2007**, *129*, 6887.

Jay S. Siegel earned a BSc in Chemistry from California State University - Northridge (1980), followed by an MA (1982) and PhD (1986) from Princeton working with Professor Kurt Mislow in the area of Structural Chemistry and Stereochemistry. During his studies at Princeton (1983), he received a Swiss Universities Grant (*cf.* Fulbright Grants) to study crystallography at the Swiss Federal Institute of Technology in Zurich, with Professor Jack D. Dunitz. After earning his PhD, he was awarded a NSF-CNRS postdoctoral fellowship (1985) to study supramolecular chemistry at the University of Louis Pasteur in Strasbourg with Jean-Marie Lehn. He began his independent career as Assistant Professor of Chemistry at UCSD (1986), was promoted to Associate Professor (1992) and Full Professor (1996). He was a US-NSF Presidential Young Investigator (1988), an American Cancer Society Jr. Fellow (1990), an Alfred P. Sloan Fellow (1992), and an Arthur C. Cope Scholar by the ACS (1998). He was elected fellow of the American Association for the Advancement of Science (1998) and the Royal Society of Chemistry (2007). He has been visiting professor at Princeton, Caltech, University of Basel, the Weizmann Institute and Tokyo Institute of Technology. In 2003, he was appointed as Professor and co-director of the Organic Chemistry Institute of the University of Zurich and Director of its laboratory for process chemistry research (LPF). He is co-Editor in Chief of *Topics in Stereochemistry* and chairs the editorial advisory board of *Organic and Biomolecular Chemistry*, as well as the EUCHEMS Organic Chemistry Division.

Molecular design, chemical synthesis, and structure/function analysis constitute the three principle components of modern stereochemistry as practiced in the Siegel group. Robust transmission of structural and stereo-chemical information is fundamental to selective chemical processes like (bio)molecular recognition, enantioselective reactions, and the assembly of designed materials. Beyond symmetry and molecular bonding, stereochemical investigations draw upon concepts from many disciplines and implement techniques such as synthetic methodology, X-ray crystallography, NMR spectroscopy, and computational theory. As a result, research in this area combines synthetic and physical organic chemistry with an eye toward issues of material and life science.

Representative publications:

'Synthesis of 2,6-Diarylphenyl-dimethylsilyl Cations: Polar-π Distribution of Cation Character', S. Duttwyler, Q.-Q. Do, A. Linden, K. K. Baldridge, J. S. Siegel, *Angew. Chem., Int. Ed.* **2008**, *47*, 1719.

'Synthesis, Structure, and Isomerization of Decapentynylcorannulene: Enediyne Cyclization/Interconversion of $C_{40}R_{10}$ Isomers', T. Hayama, Y.-T. Wu, A. Linden, K. K. Baldridge, J. S. Siegel, *J. Am. Chem . Soc.* **2007**, *129*, 12612.

'Buckybowls on Metal Surfaces: Symmetry Mismatch and Enantiomorphism of Corannulene on Cu(110)', M. Parschau, R. Fasel, K.-H. Ernst, O. Gröning, L. Brandenberger, R. Schillinger, T. Greber, A. P. Seitsonen, Y.-T. Wu, J. S. Siegel, *Angew. Chem., Int. Ed.* **2007**, *46*, 8258.

Analytical Infrastructure for the Molecular Sciences – AIMS

The growing dependence of chemistry on instrumentation is a common experience of every scientific generation. In the last 25 years, the computer revolution has opened the floodgates to data collection, remote/automated operation, and advanced numerical modeling. The synergy between computer interfacing and electronic micronization has made it possible to place instruments like 700 MHz NMRs, and ICR mass spectrometers in the hands of the bench chemist. Gone are the days where a single advanced research group in

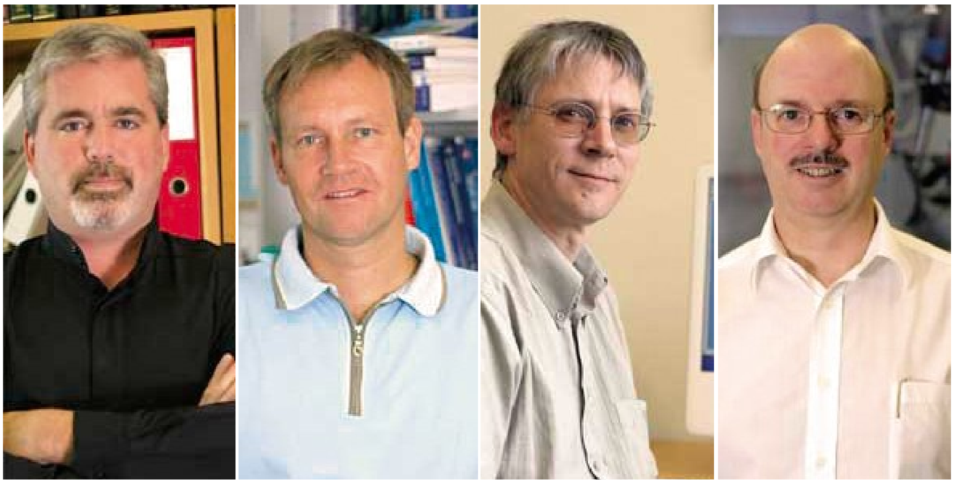

Fig. 4. Nathaniel S. Finney, Oliver Zerbe, Stefan Bienz and Anthony Linden

an institute owns, operates and services the research instrument for the institute. An essential part of the training of a modern chemist involves learning the ins-and-outs of modern instrumentation. The utilization of such instruments by so many researchers makes the development of common research infrastructure centers practical and attractive.

In OCI, the Analytical Infrastructure for the Molecular Sciences (AIMS) has had its inception. Six community infrastructure services are individually overseen by an independent research scientist, with assistance from a team of technical operators and faculty user-group oversight. At present, Nuclear Magnetic Resonance spectroscopy, Mass Spectroscopy, X-ray Crystallography, Absorption/Emission Spectroscopy, Microanalysis and Computational chemistry have infrastructure status supported by the OCI. Robotic automized synthesis is in development.

NMR and MS, under the guidance of Wolfgang von Philipsborn and Manfred Hesse, were among the first of such services to be established. During the time of Hans Schmid the essential value of such instrumentation was recognized. At that time, these techniques were in the research and development phase and required research professors at the forefront of the technological developments. Routine student use of such temperamental instruments was ill advised.

Presently, PD Dr. Oliver Zerbe (Fig. 4) and Dr. Laurent Bigler oversee NMR and MS, respectively. With close to ten NMR instruments including the flagship 600 and 700 MHz instruments with cryoprobes, chemistry is well outfitted for NMR studies of all types. New acquisition in MS is anticipated, and high resolution, electrospray and MALDI capabilities makes the OCI facility a draw for researchers worldwide wishing to do analytical studies as well as metabolic profiling.

Around 1980 the first X-ray diffractometer came to the OCI. A real step forward was made with the appointment of PD Dr. Anthony Linden in 1990 (Fig. 4). He acquired a new instrument in 1992 and another in 2001. As of 2005, automated powder diffraction was added through the purchase of a new powder diffractometer. Dr. Linden is now editor of *Acta Crystallographica* and is co-organizer of the Zurich School for Crystallography. He and Hans-Beat Bürgi offer the school as a practical 'hands-on' training in the solving of X-ray crystal structures.

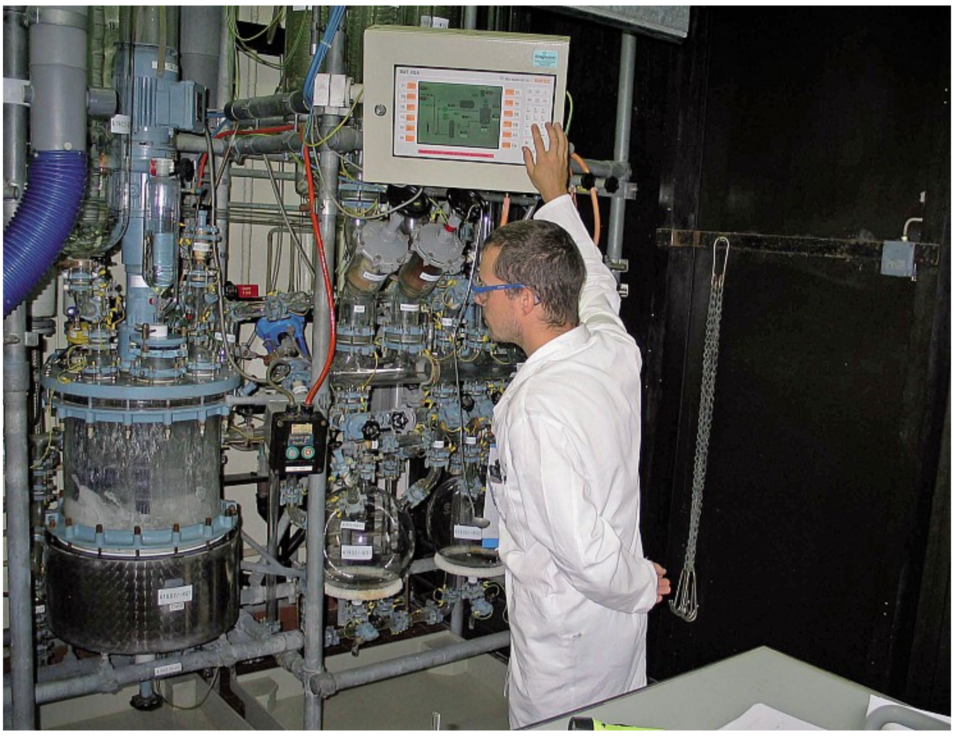

Fig. 5. The 'Labor für Prozessforschung' (LPF)

Organic Chemistry at the Academic-Industry Interface

The OCI holds a unique position among leading research universities of the world in having an institute dedicated to the training of postdoctoral researchers in the skills of process chemistry. The 'Labor für Prozessforschung' (LPF) was profiled in the September 2006 issue of CHIMIA. As of 1996, the LPF was run by Max Rey of Cilag AG as an outsourcing arm of the process R+D division. Numerous industrial processes were developed under Max's leadership. With Max's untimely death in 2002 a new model for operations was sought. Since the restructuring of the LPF in 2004 by its Director Jay S. Siegel, it has been led by a phenomenal team of chemists who live at the academic–industry interface. Nathaniel S. Finney (Fig. 4), Thomas Bader, Walter Ganci and Michael Müller form a leadership team that has numerous successes in industrial scale process chemistry under their belt in just these few years. They have also trained and placed into industry over 20 postdoctoral scientists.

Building on the tradition of active pharmaceutical ingredient (API) synthesis, which started with Carbogen's founders (T. Herzig, D. Beer and R. Julina), the LPF operations include generic API target selection, patent and safety assessment, route selection, methods development, scale-up to 100 l, GMP production and analytics, and finishing process evaluation (*e.g.* polymorph studies). This *institute within an institute* supports between 25–30 co-workers of which about half are postdoctoral scientists on two-year contracts. Support for this endeavor comes exclusively through industrial partnerships (Fig. 5). AZAD Pharmaceuticals and Fine Chemicals (Mike Baronien) has been the LPF's major benefactor and partner since 2003. Close relations are also enjoyed with Cilag AG Schaffhausen.

One of the future developments for process chemistry is automation and design synthesis optimization. Nathaniel Finney has been a major motivating force in this area. In addition to his independent research program on chemical sensors and the photophysics of fluorescent molecules, Nat serves as the chemical advisor to the LPF. In this capacity he provides important input to the chemical methods and technologies to be implemented. Through partnerships with Swiss companies like Systag and Mettler, advances in automation and safety evaluation have made great strides. Nat's research collaborations at PSI and the OCI purchase of a new automated powder diffractometer, have opened the door to polymorph studies that combine sampled screening and detailed structure analysis, two important aspects for the characterization of APIs.

Spawning new industrial or entrepreneurial ventures is a specialty of the OCI. Polyphor AG, established by Daniel and Jean-Pierre Obrecht, is another shining example of success. Working together with John Robinson, Polyphor developed its base technologies from within the walls of the OCI. Today Polyphor is a thriving life science company.

An additional place where the OCI makes an impact at the border between academics and industry is through our 'Lehrlingslabor' (Fig. 6). After many years in dormancy, the OCI program is again active. In 2007, a dedicated laboratory for the training of apprentices was newly outfitted. Six-to-eight working places for entering apprentices are available to learn the art and science of practical chemistry. The program is expected to have an equilibrium population of between 15 and 20 apprentices over the three-year training period. Within the formal apprentice laboratory, an extension of the introductory course as well as advance synthesis and analytical laboratory classes are conducted. During the second and third years, apprentices move directly into research groups to gain further experience in modern practices.

The apprentice program is oriented as an OCI service to Zurich's Cantonal goal of offering meaningful apprentice studies that can lead to gainful industrial employment and/or further personal development through higher educational programs. Also, the OCI is open to industrial partnerships and small companies who would like to have apprentices but are not set up to offer the basic training classes, and should contact the OCI director, Jay Siegel.

More Changes for the Better

The next 25 years at the OCI will also embody many structural and programmatic changes. The ability to incorporate productive change into an organization's daily routine is a hallmark of success in 21st century. The youthful composition of the OCI and its entrepreneurial attitude toward all ventures in science makes for a winning program. The opportunities for students, researchers and private sector partners are enormous. The doors of the OCI are wide open and welcome to all comers to share in the next 175 years. The OCI offers a program of which our alumni can be proud; and, the citizens of Zurich can have confidence that their OCI is working well for their future well-being.

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[1] a) *http://www.zerocarbonhaouse.com/*
b) *http://en.wikipedia.org(wiki/Zero_energy_building*

Fig. 6.
The 'Lehrlingslabor'