Professor Stefan Matile

Curriculum Vitae

2003 – present	Full Professor, Department of Organic Chemistry, University of Geneva, Geneva, Switzerland
2014 – present	National Centre of Competence in Research (NCCR) Molecular Systems Engineering, Founding Member, WP co-Leader, Steering Committee
2021 – present	Director, Department of Organic Chemistry, U Geneva (same 2004-05, 08-09, 11-14)
1989	Diploma under the Supervision of Professor W.-D. Woggon, Department of Chemistry, University of Zurich, Zurich, Switzerland
1994	Ph.D. under the Supervision of Professor W.-D. Woggon, University of Zurich
1994 – 1996	Swiss NSF Postdoctoral Research Fellow, Department of Chemistry, Columbia University, New York, NY, USA, with Professor K. Nakanishi
1996 – 1999	Assistant Professor of Chemistry, Department of Chemistry, Georgetown University, Washington, DC, USA
1999 – 2003	Associate Professor of Organic Chemistry, University of Geneva
2000 – 2005	National Research Program (NRP) Functional Supramolecular Materials, Project Leader
2010 – 2022	National Centre of Competence in Research (NCCR) Chemical Biology, Founding Member, WP Leader, Steering Committee
2013 – 2016	Vice-President, School of Chemistry and Biochemistry, University of Geneva
2016 – 2019	President, School of Chemistry and Biochemistry, University of Geneva

Research Interests

Translational supramolecular chemistry, at the interface of synthetic organic, biological and materials chemistry, with a passion for unorthodox interactions, expecting that the integration of new ways to get into contact on the molecular level will ultimately solve otherwise intractable challenges in science and society. Recent highlights are the discovery of fluorescent probes to image physical forces in biology (flippers, commercialized), catalysis with anion-π interactions, chalcogen and pnictogen bonds, and dynamic covalent exchange cascades to enter into cells and hinder viruses to do the same (thiol-mediated uptake, antivirals). Topics of longstanding interest are multistep organic synthesis, multicomponent surface architectures, ion transport, and molecular tongues and leaves (sensors, photosystems).

Recent Key Publications (total 365, 65 *JACS/Au*, etc, society journals preferred)

- Chen, X.-X.; Bayard, F.; Gonzalez-Sanchis, N.; Pamungkas, K. K. P.; Sakai, N.; Matile, S. "Fluorescent Flippers: Small-Molecule Probes to Image Membrane Tension in Living Systems," *Angew. Chem. Int. Ed.* **2023**, 62, e202217868.
- Laurent, Q.; Martinent, R.; Lim, B.; Pham, A.-T.; Kato, T.; López-Andarias, J.; Sakai, N.; Matile, S. "Thiol-Mediated Uptake," *JACS Au* **2021**, *1*, 710–728.
- Zhao, Y.; Cotelle, Y.; Liu, L.; Lopez-Andarias, J.; Bornhof, A.-B.; Akamatsu, M.; Sakai, N.; Matile, S. "The Emergence of Anion-π Catalysis," *Acc. Chem. Res.* **2018**, *51*, 2255–2263.
- Humeniuk, H. V.; Gini, A.; Hao, X.; Coelho, F.; Sakai, N.; Matile, S. "Pnictogen-Bonding Catalysis and Transport Combined: Polyether Cation Transporters Made in Situ," *JACS Au* **2021**, *1*, 1588–1593.
- López-Andarias, J.; Eblighatian, K.; Pasquer, Q. T. L.; Assies, L.; Sakai, N.; Hoogendoorn, S.; Matile, S. "Photocleavable Fluorescent Membrane Tension Probes: Fast Release with Spatiotemporal Control in Inner Leaflets of Plasma Membrane, Nuclear Envelope, and Secretory Pathway," *Angew. Chem. Int. Ed.* **2022**, *61*, e202113163.
- Laurent, Q.; Martinent, R.; Moreau, D.; Winssinger, N.; Sakai, N.; Matile, S. "Phosphorothioate Oligonucleotides Enter Cells by Thiol-Mediated Uptake," *Angew. Chem. Int. Ed.* **2021**, *60*, 19102–19106.

Selected Honors

- (CH)-ERC Advanced Investigator Grants (2022, 2010)
- SNSF Level-1 Investigator (2015, 2017), SNSF Excellence Grant (2021, on invitation)
- ERC Advanced Grants Panel (2019-), Swiss ERC Panel (2014)
- Chemistry Europe Fellow (2022)
- Some Lectures (total 305): Heilbronner-Hückel, Molecular Science Frontier (Chinese Academy of Sciences), Krishnan, W. S. Johnson (Stanford), Torkil Holm, Tateshina, Bürgenstock, Asan; Visiting Professor: U Florida (Tarrant), Angers, Warwick, Santiago de Compostela, JSPS (2x)

Major Achievements

Stefan Matile has contributed to the development of "functional supramolecular chemistry" from the beginning, the shift of attention from structure to function, significant function, "translational supramolecular chemistry". In this context, three specific key achievements are

1) The discovery of small-molecule fluorescent probes to image physical forces in biology ("flipper probes").
2) The discovery of anion-π catalysis, chalcogen-bonding catalysis, and pnictogen-bonding catalysis.
3) The identification of thiol-mediated uptake as central network to bring matter into cells (drug delivery), hinder pathogens to enter and cells to move (drug discovery).

1) Among the three, flipper probes [1] are arguably the most popular because chemistry tools to enable the imaging of physical forces in living cells respond to a central need in today's life sciences. He formulated the concept of flipper probes as planarizable push-pull probes, inspired by lobster pigmentation, first in 2012. The first probes that work also in cells appeared six year later. Since then, he has focused on probe targeting within cells, on chalcogen-bonding cascade switches for dual sensing and super-resolution microscopy, and on many collaborations to enable use in the community. Flipper-TR® probes stand as a fine example for translational supramolecular chemistry, moving from the fundamental principles to success on the market.

2) Stefan Matile has introduced anion-π catalysis in 2013 as a new concept to achieve molecular transformation [2]. His general idea, deduced from earlier results on anion transport, is to stabilize anionic transition states on π-acidic aromatic surfaces. Ten years later, he has realized anion-π catalysis for many different catalysts, including fullerenes, carbon nanotubes, π-stacked foldamers, artificial enzymes, electric fields, and for many different reactions, including autocatalytic epoxide-opening polyether cyclizations [3], asymmetric enolate, enamine, iminium, transamination, and Diels-Alder chemistry.

Impressed by the power of anion-π catalysis, he expanded the concept of unorthodox interactions in catalysis to chalcogen bonds in 2017 [4] and pnictogen bonds in 2018 [5]. Access to novel reactivity has been secured with Sb(III) and Sb(V) catalysts for polyether cyclizations and transport-coupled catalysis in membranes [6]. These characteristics justified the definition of s-hole catalysis as non-covalent counterpart of Lewis acid catalysis, complementary to hydrogen-bonding catalysis as non-covalent counterpart of Brønsted acid catalysis, a new field full of promise [6].

3) Stefan Matile has identified thiol-mediated uptake (TMU) as a general system in place to enable and inhibit the entry into cells [7]. Cellular uptake is a central challenge in science and society because this is where our best drugs suffer, from genome editing to RNA vaccines, and where the worst viruses pass. With his introduction of cell-penetrating poly(disulfide)s in 2014 and small-molecule cascade exchangers (CAXs) one year later, he demonstrated that TMU could solve this challenge. Since then, a rapidly growing collection of CAXs has been introduced by his and other groups to deliver otherwise demanding substrates (antibodies, genome editing machinery, oligonucleotide phosphorothioates) into living animals, plant cells and bacteria, and to provide access to modern materials (adaptive, degradable, recyclable). Inhibition of viral entry [8] and cell motility reveal drug discovery potential (anti-viral, anti-thrombotic, anti-tumor), and identify integrins as one out of multiple cellular exchange partners in dynamic networks that account for TMU. Emerging thus as much more important than originally expected, he has shown that it is because of the elusive nature of dynamic covalent cascade exchange chemistry that TMU is not better known and understood. According to these results, the need to crack TMU thus translates into a wonderful challenge in translational supramolecular chemistry.

These three more recent key achievements are complemented by topics of long-standing interest, that is transport across lipid bilayer membranes and ordered surface architectures, to build, *inter alia*, ion channels [9], photosystems [10] and sensors [9] (artificial leaves, tongues, noses).

More: www.unige.ch/sciences/chiorg/matile/ *March 2023*