From Stereocontrolled Glycosylation to Automated Chemical Synthesis

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From the building blocks of nature to disease-battling pharmaceuticals, carbohydrates have had a profound impact on evolution, society, economy, and human health. Numerous applications of these essential biomolecules in many areas of science and technology exist, most of which can be found at the forefront of therapeutic agent and diagnostic platform development. Although carbohydrates are desirable for the pharmaceutical and biomedical communities, these molecules are very challenging targets for chemists because of the need for functionalization, protecting and leaving group manipulations, controlling anomeric stereoselectivity, separation, and analysis. The development of practical methods for the synthesis of building blocks,¹ chemical glycosylation,^{2, 3} and glycan assembly⁴ represent demanding areas of research.

At the core of this presentation is the development of new methods, strategies, and technologies for the chemical synthesis of glycans. These tools will be discussed in light of recent results related to the development of new glycosylation reactions,⁵⁻⁷ methods for controlling the stereoselectivity,^{8, 9} and HPLC-based automated synthesis.¹⁰⁻¹² The effectiveness of methods developed will be illustrated by the synthesis of glycopharmaceuticals.¹³ This work has been generously supported by the National Institutes of Health and the National Science Foundation.

References

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BIOGRAPHICAL SKETCH



Alexei Demchenko was born (1965), raised, and educated in Moscow, Russia. He graduated from the Mendeleev University of Chemical Technology of Russia with a Diploma (M.S.) in Chemical Engineering (1988) before joining the laboratory of the late Professor Kochetkov at the Zelinsky Institute of Organic Chemistry in Moscow. In 1993, he was awarded a Ph.D. in organic chemistry by the Russian Academy of Sciences for his work on the development of thiocyanate methodology for glycosylation. After two post-doctoral years under Kochetkov, he joined Professor Boons' group at the University of Birmingham (UK) as a BBSRC post-doctoral research fellow. In 1998, he moved to the Complex Carbohydrate Research Center, University of Georgia (USA) as a research associate. In 2001, he joined the faculty at the University of Missouri - St. Louis (UMSL) as an Assistant Professor where he was promoted to the rank of Associate Professor with tenure (2007) and Professor (2011). In 2014, Demchenko was appointed Curators' Distinguished Professor of Chemistry and Biochemistry. In 2021, Demchenko joined the faculty at Saint Louis University as Professor and Department Chair.

Professor Demchenko received a number of professional recognitions and awards including a CAREER award by the National Science Foundation (2005), the New Investigator Award by the Division of Carbohydrate Chemistry of the American Chemical Society (ACS, 2007), the UMSL Chancellor's Award for Excellence in Research and Creativity (2013), the ACS St. Louis Award (2014), the UMSL Senior Investigator of the Year Award (2017), Fellows Award by the Academy of Science – St. Louis (2020), the UMSL Co-Investigators of the Year Award (with Keith Stine, 2020), the Melville L. Wolfrom Award by the Division of Carbohydrate Chemistry and Chemical Glycobiology of the ACS (2024), and the ACS Midwest Award (2024).

With participation of 175 trainees, Professor Demchenko has co-authored 235 articles (Scopus *H*-index 49, Scholar *H*-index 53) and has given 185 invited lectures and seminars. His research interests are in the area of synthetic carbohydrate chemistry that include: streamlined synthesis of carbohydrate building blocks; novel glycosylation reactions; methods for stereocontrolling the glycosidic bond formation; strategies for expeditious assembly of complex glycans and glycoconjugates; synthetic vaccines and glycopharmaceuticals; human milk oligosaccharides and other food additives and ingredients; solid phase and automated synthesis; modification and conjugation of glycans to protein carriers, surfaces, and nanoparticles. His research program has been funded by grants from a variety of sources totaling \$13.3M.

Professor Demchenko has served in many editorial roles and organized several international conferences including the 2015 Gordon Research Conference on Carbohydrates. From 2019, he has served as President of the U.S. Advisory Committee for the International Carbohydrate Symposia. Professor Demchenko was the 2020-2021 Chair of the Division of Carbohydrate Chemistry of the ACS. Demchenko is the National Representative of the USA for the International Carbohydrate Organization.

PROFESSIONAL EXPERIENCE AND APPOINTMENTS

2021 - Professor and Chair, Department of Chemistry, Saint Louis University, USA

- 2014 2021 Curators' Distinguished Professor of Chemistry and Biochemistry, UM St. Louis, USA
- 2011 2014 Professor of Chemistry and Biochemistry, UM St. Louis, USA
- 2007 2011 Associate Professor and Director of Graduate Studies, UM St. Louis, USA
- 2001 2007 Assistant Professor of Chemistry and Biochemistry, UM St. Louis, USA
- 1998 2001 Research Associate (Boons), Complex Carbohydrate Research Center, Georgia, USA
- 1995 1998 BBSRC Post-Doctoral Research Fellow (Boons), University of Birmingham, UK
- 1993 1995 Research Associate (Kochetkov), Zelinsky Institute of Organic Chemistry, Moscow, Russia

EDUCATION, DEGREES

- 1988 1993 Ph.D. in Organic Chemistry (Kochetkov), Zelinsky Institute of Organic Chemistry, Russia
- 1982 1988 M.S. in Chemical Engineering, Mendeleev University of Chemical Technology of Russia

RESEARCH INTERESTS

- Streamlined synthesis of regioselectively protected carbohydrate building blocks
- Novel glycosylation reactions. Stereocontrol and mechanism of chemical glycosylation
- Expeditious strategies for the synthesis of complex oligosaccharides and glycoconjugates
- Synthetic glycopharmaceuticals (anti-cancer, anti-bacterial, anti-septic, etc.)
- Human milk oligosaccharides and other food additives and ingredients
- Solid phase and surface chemistry: application to automated glycan synthesis

SELECTED AWARDS

- 2024 The Midwest Award, American Chemical Society, St. Louis Section
- 2024 The Melville L. Wolfrom Award, American Chemical Society, CARB Division
- 2020 Co-Investigators of the Year Award (with K. J. Stine), UM St. Louis Office of Research
- 2020 Outstanding Scientists Awards Fellows Award, Academy of Science St. Louis
- 2017 Senior Investigator of the Year Award, UM St. Louis Office of Research
- 2014 St. Louis Award, American Chemical Society, St. Louis Section
- 2013 Chancellor's Award for Excellence in Research and Creativity, UM St. Louis
- 2007 New Investigator Award, American Chemical Society, CARB Division
- 2005 CAREER Award, National Science Foundation

SELECTED PROFESSIONAL ACTIVITIES AND HONORS

- 2022 Fellow of the Saint Louis University Research Institute
- 2020 Fellow of the Academy of Science St. Louis
- 2020 2021 Chair, Division of Carbohydrate Chemistry, American Chemical Society
- 2019 The National Representative of the USA for the International Carbohydrate Organization
- 2019 President of the U.S. Advisory Committee for the International Carbohydrate Symposia
- 2015 Chair, Gordon Research Conference on Carbohydrates
- 2012 2021 Associate Editor, Journal of Carbohydrate Chemistry

SELECTED RESEARCH SUPPORT

- 2006 2027 National Science Foundation (CHE-0547566, 1058112, 1800350, 2147156, **2350461**)
- 2006 2028 National Institutes of Health, NIGMS (R15 GM077170, R21 GM072693, R03 Al067494, R01 GM090254, R01 GM111835, U01 GM120673, **R35 GM152125**)

RECENT PUBLICATIONS (SELECTED FROM 230; SCOPUS H-INDEX 49, SCHOLAR H-INDEX 53)

- G. A. Kashiwagi, L. Petrosilli, S. Escopy, et. al., *Chem. Eur. J.* **2024**, 30, e202401214 (Front cover)
- Y. Singh, S. Escopy, M. Shadrick, et. al. Chem. Eur. J., 2023, 29, e202302288
- A. Dent, S. Escopy, A. V. Demchenko. *Chem. Eur. J.*, **2023**, *29*, e202300873
- Y. Singh, S. A. Geringer, and A. V. Demchenko. Chem. Rev., 2022, 122, 11701-11758
- S. Escopy, A. V. Demchenko. Chem. Eur. J., 2022, 28, e202103747 and e202201180
- S. Escopy, Y. Singh, K. J. Stine, A. V. Demchenko. *Chem. Eur. J.*, **2021**, 27, 354-361 (Hot paper)
- S. A. Geringer, Y. Singh, D. J. Hoard, A. V. Demchenko. Chem. Eur. J., 2020, 26, 8053-8063
- M. P. Mannino, A. V. Demchenko. *Chem. Eur. J.*, **2020**, *26*, 2927-2937 and 2938-2946 (Hot papers)
- Y. Singh, A. V. Demchenko. Chem. Eur. J., 2020, 26, 1042-1051 (Hot paper, front cover)
- Y. Singh, A. V. Demchenko. Chem. Eur. J., 2019, 25, 1461-1465 (Top downloaded paper 2018-19)

BOOKS EDITED

Handbook of Chemical Glycosylation, A. V. Demchenko Ed., Wiley-VCH, 2008

Frontiers in Modern Carbohydrate Chemistry, A. V. Demchenko Ed., ACS Symp. Ser., 960, 2007