



Universiteit
Leiden
The Netherlands

Boosting mass spectrometry-based analytics for biopharma Gstöttner, C.J.

Citation

Gstöttner, C. J. (2021, November 30). *Boosting mass spectrometry-based analytics for biopharma*. Retrieved from <https://hdl.handle.net/1887/3245884>

Version: Publisher's Version

License: [Licence agreement concerning inclusion of doctoral thesis in the Institutional Repository of the University of Leiden](#)

Downloaded from: <https://hdl.handle.net/1887/3245884>

Note: To cite this publication please use the final published version (if applicable).

Boosting

mass spectrometry-based

analytics for biopharma

Christoph Johann Gstöttner

ISBN: 978-94-6419-333-6

© 2021 Christoph Johann Gstöttner. All rights reserved. No part of this book may be reproduced, stored in a retrieval system, or transmitted in any form or by any means without permission of the author or the journals holding the copyrights of the published manuscripts. All published material was reprinted with permission.

The work presented in this thesis was performed at the Center for Proteomics and Metabolomics, Leiden University Medical Center, The Netherlands.

This work was supported by the European Commissions Horizon 2020 project “Analytics for Biologics” (Grant agreement ID 765502).

Cover Design and Layout: Christoph Johann Gstöttner

Printed by: Gildeprint BV, Enschede, The Netherlands

Financially supported by: Roche Diagnostics GmbH, Penzberg, Germany

Boosting mass spectrometry-based analytics for biopharma

Proefschrift

ter verkrijging van de graad van doctor aan de Universiteit Leiden,
op gezag van rector magnificus prof. dr. ir. H. Bijl,
volgens besluit van het college voor promoties
te verdedigen op dinsdag 30 november 2021
klokke 16.15 uur

door

Christoph Johann Gstöttner
Geboren te Zwiesel, Duitsland
op 25 januari 1993

Promotor: Prof. dr. M. Wuhrer

Co-promotor: Dr. E. Domínguez Vega

Leden promotiecommissie: Prof. dr. R.E.M Toes

Prof. dr. R. P.H. Bischoff,
*Department of Analytical
Biochemistry, Rijksuniversiteit Groningen,
The Netherlands*

Dr. I. Kohler,
*Division of BioAnalytical Chemistry,
Amsterdam Institute of Molecular and Life Sciences,
Vrije Universiteit Amsterdam, The Netherlands*

Dr. A. Gargano,
*Faculty of Science, Van 't Hoff Institute for Molecular
Sciences, university of Amsterdam, The Netherlands*

“If at first the idea is not absurd, then there is no hope for it.”

Albert Einstein

Table of Contents

Chapter 1	Introduction	9
Chapter 2	Fast and automated characterization of antibody variants with 4D-HPLC/MS	35
Chapter 3	Fast analysis of antibody-derived therapeutics by automated multidimensional liquid chromatography – mass spectrometry	53
Chapter 4	Monitoring glycation levels of a bispecific monoclonal antibody at subunit level by ultrahigh resolution MALDI FT-ICR mass spectrometry	71
Chapter 5	Characterization and prediction of positional 4-hydroxyproline and sulfotyrosine, two post-translational modifications that can occur at substantial levels in CHO cells-expressed biotherapeutics	97
Chapter 6	Intact and subunit-specific analysis of bispecific antibodies by sheathless CE-MS	125
Chapter 7	Sheathless CE-MS as a tool for monitoring exchange efficiency and stability of bispecific antibodies	147
Chapter 8	Affinity capillary electrophoresis – mass spectrometry as tool to unravel proteoform-specific antibody-receptor interactions	159
Chapter 9	Structural and functional characterization of SARS-CoV-2 RBD domains produced in mammalian cells	183
Chapter 10	Discussion and future perspectives	207
	Nederlandse Samenvatting	222
	English Summary	225
	Curriculum Vitae	229
	List of Publications	230
	PhD Portfolio	233
	Acknowledgments	236

