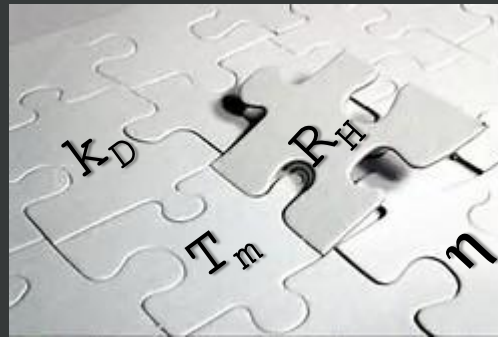
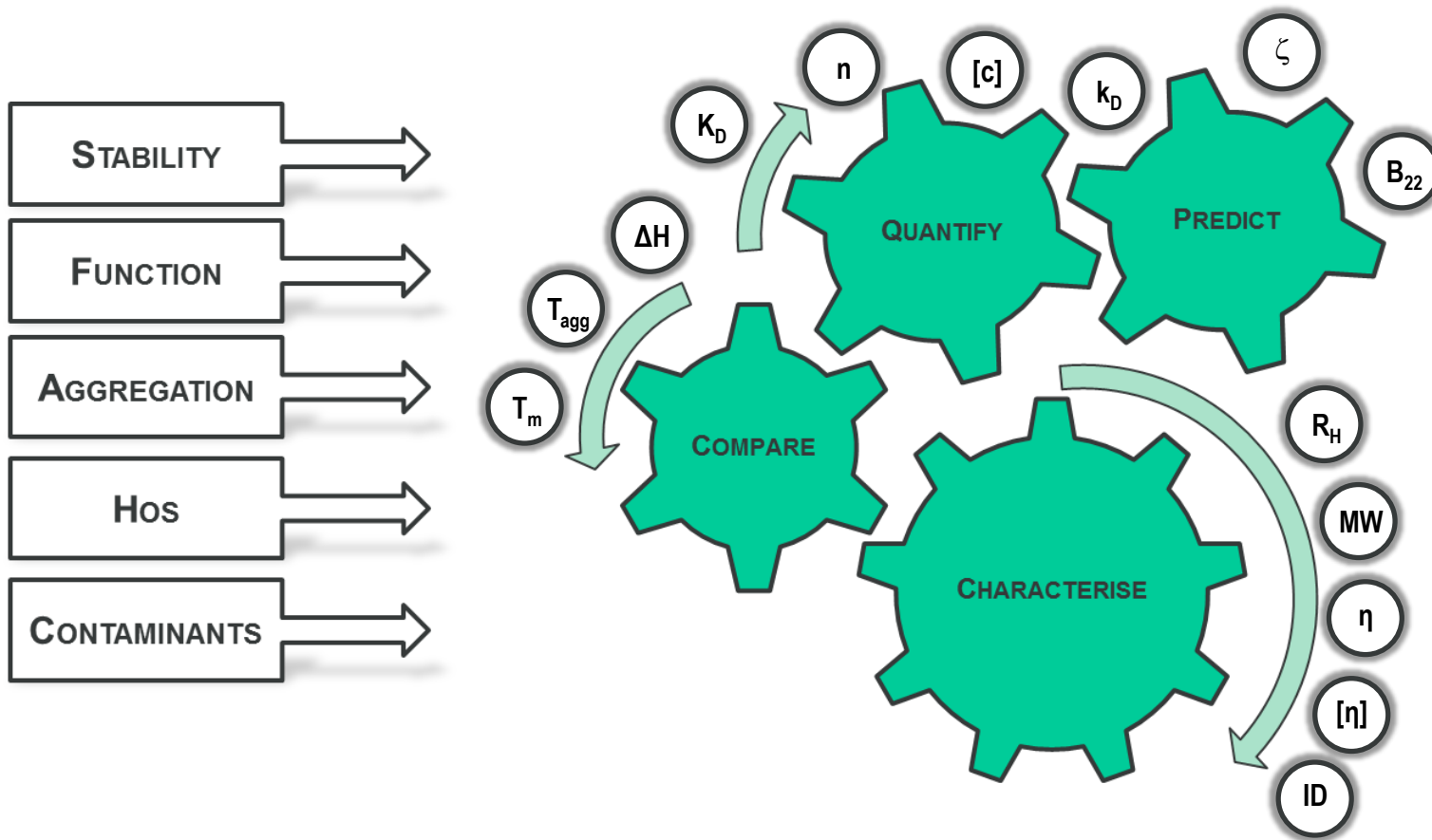




# From Molecular Interactions to Successful Products: Solutions from our Biosciences Portfolio





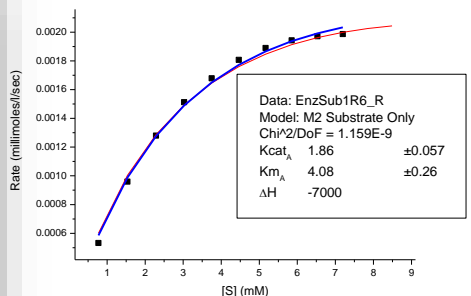
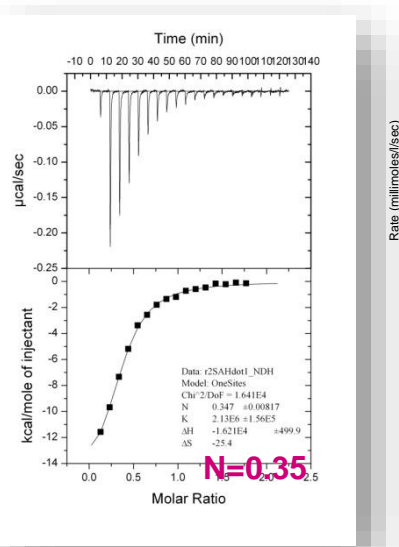
Our biosciences portfolio offers an array of orthogonal & complementary solutions to profile and control key characteristics and quality attributes



# Molecular Interactions: Calorimetry, DLS and TDA



## Affinity



## R<sub>H</sub> & Self-association

mAbs 7:1, 77-83; January/February 2015; Published with license by Taylor & Francis Group, LLC

**Early developability screen of therapeutic antibody candidates using Taylor dispersion analysis and UV area imaging detection**

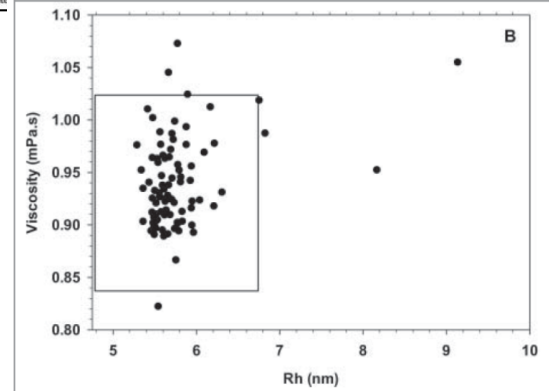
Alexandra Lavoisier and Jean-Marc Schlaeppi\*

Biologics Center, Novartis Institute

**Methodologies for the rapid determination of the diffusion interaction parameter using Taylor dispersion analysis**

Sevi Latunde-Dada,\*<sup>a</sup> Rachel Bott,<sup>a</sup> David Barker<sup>a</sup> and Oksana Iryna Leszczyszyn<sup>a</sup>

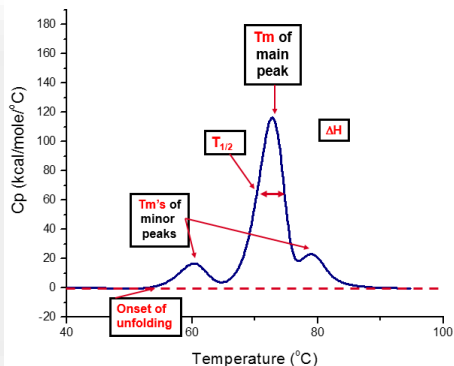
*Anal. Methods*, 2016, **8**, 386-392  
DOI: 10.1039/C5AY02614H  
Received 30 Sep 2015, Accepted 27 Nov 2015  
First published online 02 Dec 2015



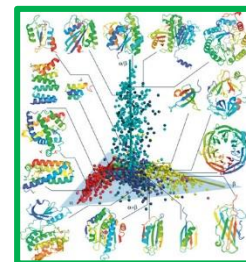
# Formulation Stability: DSC, DLS, SEC-MALS, TDA



## Conformational stability



## Novel therapeutics



European Journal of Pharmaceutical Sciences 93 (2016) 21–28

Taylor Dispersion Analysis as a promising tool for assessment of peptide-peptide interactions

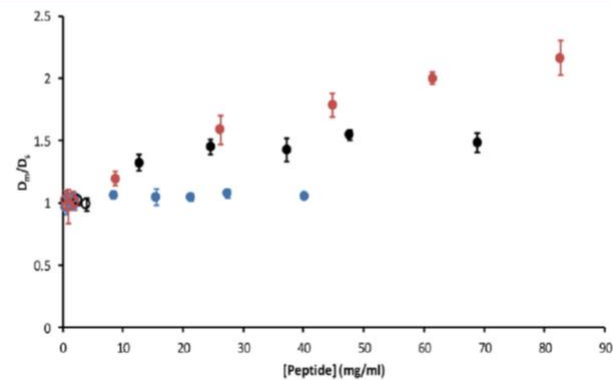
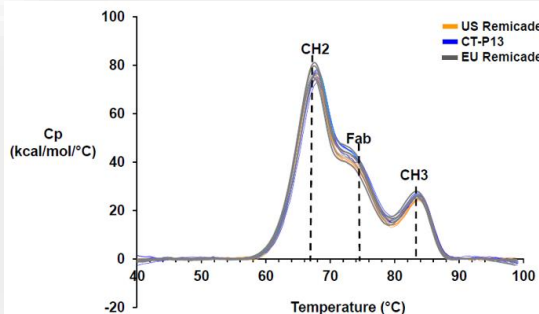
Ulrich B. Høgstædt<sup>a,b</sup>, Grégoire Schwach<sup>b,c</sup>, Marco van de Weert<sup>a</sup>, Jesper Østergaard<sup>a,\*</sup>

<sup>a</sup> Department of Pharmacy, Faculty of Health and Medical Sciences, University of Copenhagen, Universitetsparken 2, DK-2100 Copenhagen, Denmark

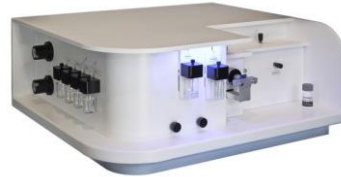
<sup>b</sup> Early Stage Development, Ferring Pharmaceuticals A/S, Kay Fiskers Plads 11, DK-2300 Copenhagen S, Denmark

<sup>c</sup> F. Hoffman-La Roche Ltd., Pharmaceuticals Division, Grenzacherstr. 124, CH-4070 Basel, Switzerland

## HOS Similarity



# Sub-visible particles: Archimedes, NTA, G3-ID

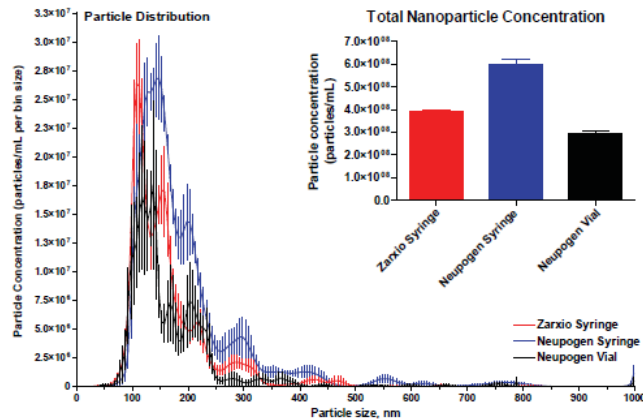


■ Sub-micron [particle]

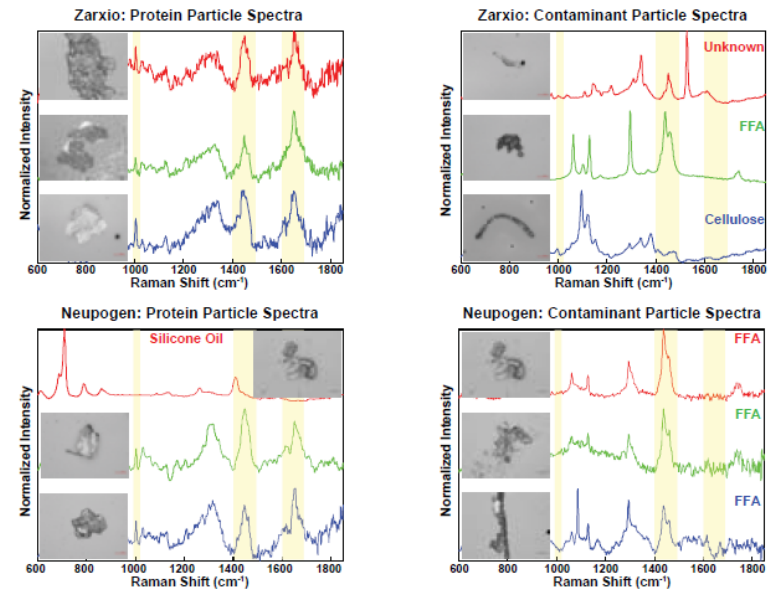
■ Particle ID



## Nanoparticle Characterization



## Particle Identification by Raman Microscopy



# From molecular interactions to successful products...

POSTER

Meet the Malvern team who can show you how:

- Oksana Barker (née Leszczyszyn)  
Senior Applications Development Scientist
- Natalia Markova  
Scientific Marketing Leader: Biosciences
- Maria Walton  
Biosciences Sales Specialist

Markos Trivariotis, Rachel Bott, Seyi Latunde-Dada, David Barker, Oksana I. Leszczyszyn.  
Malvern Instruments Ltd, Malvern, Worcestershire, UK

ASSESSING AN INTERACTION PARAMETER FOR BIOFORMULATION STABILITY IN A SINGLE MEASUREMENT: EXPLOITING CONCENTRATION GRADIENTS FROM TAYLOR DISPERSION

### Introduction

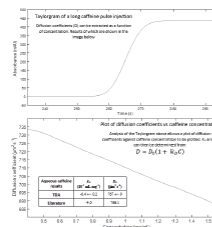
Reversible Self-Association can be a first step for the formation of aggregates and it can lead to high viscosity and poor stability of protein formulations. One metric to assess the propensity for self-association, and therefore the stability of a formulation, is the diffusion interaction parameter,  $k_D$ .

$$D = D_0 (1 + k_D C)$$

Taylor Dispersion Analysis (TDA) is an absolute method for determining the Diffusion Coefficient. Using the Viscotek TD, the  $k_D$  can be calculated from the concentration gradient in a single TDA measurement.

### Extracting the diffusion interaction parameter ( $k_D$ ) from a single TDA measurement

A long particle injection (2-3  $\mu$ L) creates a concentration gradient which is recorded as an absorbance trace. Analysis of the trace allows the calculation of the diffusion coefficient at each concentration along the gradient.



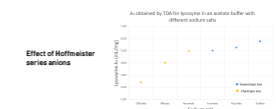
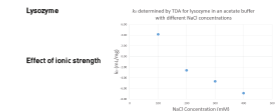
A linear fit to the resulting plot gives the self-diffusion coefficient,  $D_0$  and the interaction parameter,  $k_D$ . A negative  $k_D$  indicates self-association while a positive sign points to repulsive interactions.

### Assessing protein stability in different buffers

BSA

	$k_D$ (L/mol)	$D_0$ (cm <sup>2</sup> /s)
TBA	0.5	0.3
BSA-MNH	1.0E-05	1.0E-05
BSA-MNH-MNH	0.0001	0.0001

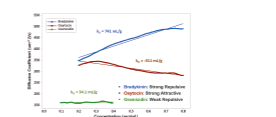
### Assessing protein stability in different buffers



### Interaction parameter of peptides using TDA

Peptides present a challenge for DLS: small size and dilute solutions make ID determination difficult. With TDA the diffusion coefficient of small molecules and peptides is easily accessible. The ID of three peptides was measured.

Peptide	Amphipathic	Hydrophobic	Hydrophilic	$k_D$ (L/mol)	$D_0$ (cm <sup>2</sup> /s)
Peptide 1	+	-	-	0.0001	1.0E-05
Peptide 2	-	+	-	0.0001	1.0E-05
Peptide 3	-	-	+	0.0001	1.0E-05



### References

1. Salyba, A. et al. Diffusion and sedimentation interaction parameters for measuring the second virial coefficient and their utility as predictors of protein aggregation, *Biophys. J.* 99 (2010) 2002-2005.
2. Rubin, J. et al. Combining aggregation kinetics and molecular diffusion in protein-wastewater salt systems observed with dynamic light scattering, *J. Phys. Chem. C* 114 (2010) 4530-4537.
3. Latunde-Dada, S. et al. Methodologies for the rapid determination of the diffusion interaction parameter using Taylor Dispersion Analysis, *Anal. Methods* 3 (2011) 186-192.
4. Hoppel, C. B. et al. Taylor Dispersion Analysis as a promising tool for assessment of peptide-protein interactions, *Eur. J. Pharm. Sci.* 50 (2012) 2-15.

