https://doi.org/10.17952/38EPS.2026.P313

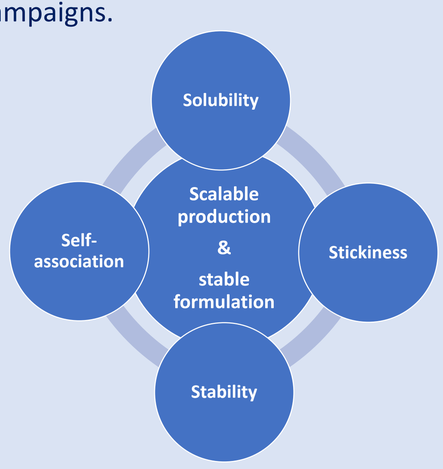


Developability Screening of Pharmaceutical Peptides

Marie Pedersen, Rodrigo Ochoa, Mathias Norrman, Christian Tornøe, Sebastian Swanson (Novo Nordisk A/S)
Jacob Larsen, Stephanie Hansen, Alexander Büll (Danish Technical University)

DEVELOPABILITY

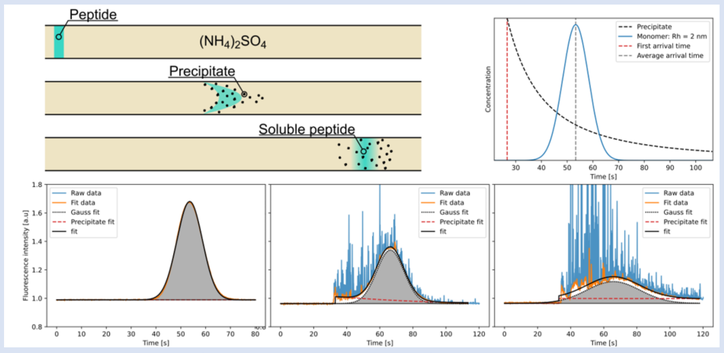
To transform peptides into safe bio-pharmaceutical, they must be soluble, stable and manufacturable in addition to having suitable biological properties.
Fast developability screens addressing key biophysical properties increase chances of success during design-make-test-analyze campaigns.



SCREENING PLATFORM

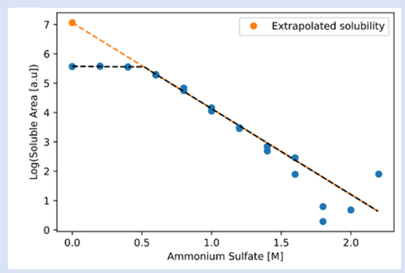
Precipitation of peptides injected in nL volumes by Taylor Dispersion Analysis in Fida1 / FidaNEO (FidaBio)

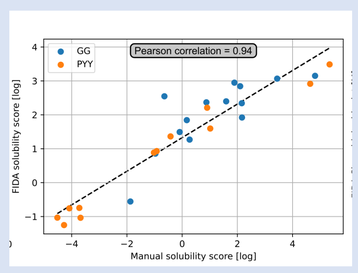




0 M Ammonium Sulfate | 1 M Ammonium Sulfate | 1.3 M Ammonium Sulfate

A 42 nL peptide plug is injected into a capillary and mixed with running buffer containing increasing ammonium sulfate. As solubility decreases, soluble peptide and precipitate separate according to Taylor-Aris theory of transient incomplete separation(Aris 1956). Fitting the signals yields a typical precipitation profile as seen in traditional forced precipitation methods from which we derive a solubility score. We compared peptide solubility quantified using the Fida platform with solubility scores obtained with manual equilibration experiment and find good correlation (Pearson corr = 0.94).





Solubility Profiling of Therapeutic Peptides by Taylor Dispersion Induced Precipitation using Nanoliter Sample Volumes
Larsen JA, Ochoa R, Norrman M, Büll A, Pedersen MØ
2026 Preprint ChemRxiv

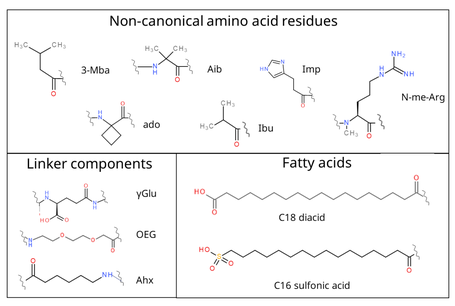
R. Aris, On the dispersion of a solute in a fluid flowing through a tube, *Proceedings of the Royal Society of London. A. Mathematical and Physical Sciences* **1956**, *235*, 67-77

LEARNINGS FROM TWO PEPTIDE FAMILIES: Y2 agonists (PYY) & GLP1/glucagon receptor dual agonists

PEPTIDE LIBRARY

Name	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	Linker	Fatty acid
GG-1151	H	Acb	Q	G	T	F	T	S	D	L	S	K	Y	L	D	L	R	R	A	R	D	F	V	Q	W	L	L	K*	T	-	-	2·γGlu-2·OEG-2·γGlu	C18 diacid
GG-1177	H	Aib	Q	G	T	F	T	S	D	L	S	K	Y	L	E	S	K	R	A	R	E	F	V	Q	W	L	L	K*	T	-	-	2·γGlu-Ser-Glu-Ser-2·γGlu	C18 diacid
GG-1359	Imp	Aib	H	G	T	F	T	S	D	V	S	K	Y	L	E	E	Q	A	A	R	E	F	I	A	W	L	L	K*	T	-	-	2·γGlu-2·OEG	C18 diacid
GG-1139	H	Acb	Q	G	T	F	T	S	D	L	S	K	Y	L	E	S	R	R	A	R	E	F	V	Q	W	L	L	K*	T	-	-	γ·Glu-2·OEG-2·γGlu	C18 diacid
GG-1155	H	Acb	Q	G	T	F	T	S	D	L	S	K	Y	L	D	L	K	R	A	R	E	F	V	Q	W	L	L	K*	T	-	-	2·γGlu-Ser-Gly-Glu-Ser-Gly	C18 diacid
GG-1166	H	Aib	Q	G	T	F	T	S	D	L	S	K	Y	L	D	L	R	R	A	Q	D	F	V	Q	W	L	L	K*	T	-	-	2·γGlu-Ser-Glu-Ser-2·γGlu	C18 diacid
GG-1197	H	Aib	Q	G	T	F	T	S	D	L	S	K	Y	L	D	A	R	R	A	R	D	F	V	Q	W	L	L	K*	T	-	-	3·γGlu-2·OEG	C18 diacid
GG-1223	H	Aib	Q	G	T	F	T	S	D	Y	S	K	Y	L	E	S	R	R	A	R	D	F	V	K*	W	L	I	S	T	-	-	3·γGlu-2·OEG	C18 diacid
GG-1305	Imp	Acb	H	G	T	F	T	S	D	V	S	K	Y	L	E	E	Q	A	A	R	E	F	I	A	W	L	L	K	K*	-	-	2·γGlu-Ser-Gly-Glu-Ser-Gly	C18 diacid
GG-1380	Imp	Aib	H	G	T	F	T	S	D	V	S	R	Y	L	E	G	Q	A	A	R	E	F	I	A	W	L	L	K*	T	-	-	2·γGlu-Ser-Gly-Glu-Ser-Gly	C18 diacid
GG-1383	H	Acb	Q	G	T	F	T	S	D	V	S	K	Y	L	E	S	R	R	A	R	E	F	V	Q	W	L	I	K*	T	-	-	2·γGlu-2·OEG-2·γGlu	C18 diacid
GG-1385	H	Aib	Q	G	T	F	T	S	D	L	S	K	Y	L	D	A	R	R	A	R	D	F	V	Q	W	L	I	N	K*	-	-	gGlu-2·OEG-2·γGlu	C18 diacid
GG-1387	H	Aib	Q	G	T	F	T	S	D	L	S	K	Y	L	D	L	R	R	A	R	E	F	V	Q	W	L	I	N	K*	-	-	gGlu-2·OEG-2·γGlu	C18 diacid
GG-1400	Imp	A	H	G	T	F	T	S	D	V	S	K	Y	L	E	G	R	A	A	R	E	F	I	A	W	L	L	K*	G	G	G	3·γGlu-2·OEG	C18 diacid

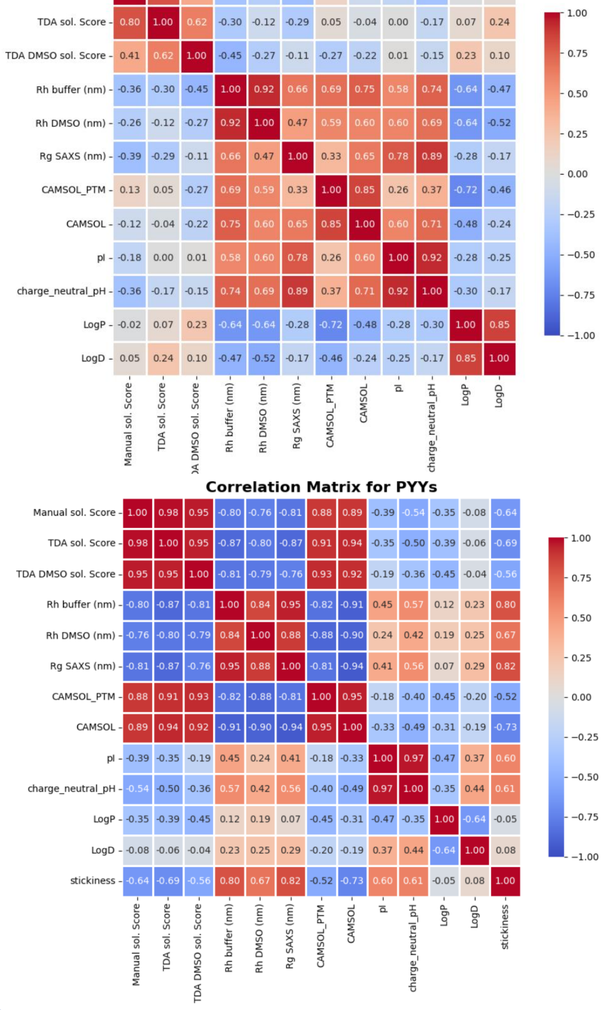
Name	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	Linker	Fatty acid
PYY-1562	3-Mba	R	P	E	K*	P	G	E	D	A	S	P	E	E	L	Q	R	Y	Y	A	S	L	R	H	Y	L	N	W	V	T	R	Q	N-Me-Arg	Y	γ·Glu-2·OEG	C16 Sulfonic acid
PYY-1875	3-Mba	R	P	E	K*	P	P	E	D	A	S	P	E	E	L	Q	R	Y	Y	A	S	L	R	H	Y	Y	N	W	L	T	R	Q	R	Y	γGlu-Ahx	C18 diacid
PYY-1679	3-Mba	R	P	E	A	P	G	K*	D	A	S	P	E	E	L	Q	R	Y	Y	A	S	L	R	H	Y	L	N	W	V	T	R	Q	N-Me-Arg	Y	γGlu	C16 Sulfonic acid
PYY-1686	3-Mba	R	P	E	K*	P	G	E	D	A	S	P	E	E	L	Q	R	Y	Y	I	S	L	R	H	Y	L	N	W	V	T	R	Q	R	Y	γGlu-3·OEG	C18 diacid
PYY-1688	3-Mba	R	P	E	A	P	G	K*	D	A	S	P	E	E	L	Q	R	Y	Y	I	S	L	R	H	Y	L	N	W	V	T	R	Q	R	Y	γGlu-2·OEG	C18 diacid
PYY-1696	3-Mba	R	P	E	K*	P	G	E	D	A	S	P	E	E	L	S	R	Y	Y	I	S	L	R	H	Y	L	N	W	V	T	R	Q	N-Me-Arg	Y	γGlu-2·OEG	C18 diacid
PYY-1698	3-Mba	R	P	E	A	P	G	K*	D	A	S	P	E	E	L	S	R	Y	Y	I	S	L	R	H	Y	L	N	W	V	T	R	Q	N-Me-Arg	Y	γGlu-2·OEG	C18 diacid
PYY-1699	3-Mba	R	P	E	A	P	G	K*	D	A	S	P	E	E	L	S	R	Y	Y	I	S	L	R	H	Y	L	N	W	V	T	R	Q	R	Y	γGlu-2·OEG	C18 diacid
PYY-1700	3-Mba	R	P	E	A	P	G	K*	D	A	S	P	E	E	L	S	R	Y	Y	I	S	L	R	H	Y	L	N	W	V	T	R	Q	N-Me-Arg	Y	γGlu-2·OEG	C16 Sulfonic acid
PYY-1709	Aib	E	P	E	K*	P	G	E	D	A	S	P	E	E	L	Q	R	Y	Y	A	S	L	R	H	Y	L	N	W	V	T	R	Q	N-Me-Arg	Y	γGlu-2·OEG	C18 diacid
PYY-1710	Ibu	R	P	E	K*	P	G	E	D	A	S	P	E	E	L	Q	R	Y	Y	A	S	L	R	H	Y	L	N	W	V	T	R	Q	N-Me-Arg	Y	γGlu-2·OEG	C18 diacid
PYY-1713	Y	E	P	E	K*	P	G	E	D	A	S	P	E	E	L	Q	R	Y	Y	A	S	L	R	H	Y	L	N	W	V	T	R	Q	N-Me-Arg	Y	γGlu-2·OEG	C18 diacid



We selected a library of 26 lipidated therapeutic peptides from two discontinued discovery programs targeting obesity. The first group comprised 14 GLP-1/glucagon co-agonists (GG). The second group contained 12 selective Y2 receptor agonists derived from peptide YY (PYY). The library included a broad range of peptides, from early research to preclinical and clinical-stage molecules, providing a relevant test set for comparing solubility and assembly behavior.

Correlations

GG and PYY families showed different correlation patterns linking solubility and oligomer size with calculated properties demonstrating the importance for experimental solubility profiling for new peptide classes

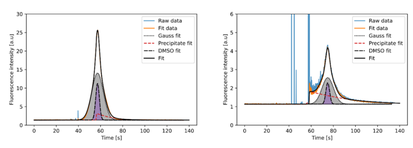


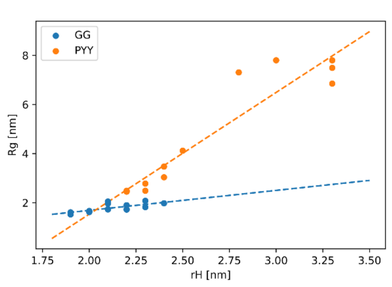
Solubility, Size & Stickiness – all in one assay consuming < 1 µg

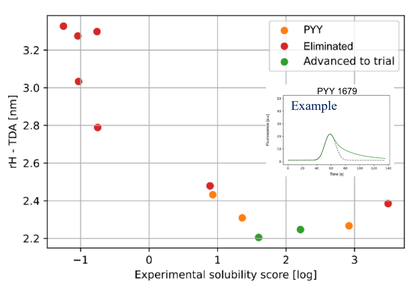
Size
Taylor Dispersion Analysis estimates peptide size from diffusion-driven peak broadening (Taylor 1953). Applying the Stokes–Einstein relation gives an apparent hydrodynamic radius (rH), a readout of oligomerization. We compared rH with SAXS-derived radius of gyration (Rg) to validate the measurements.

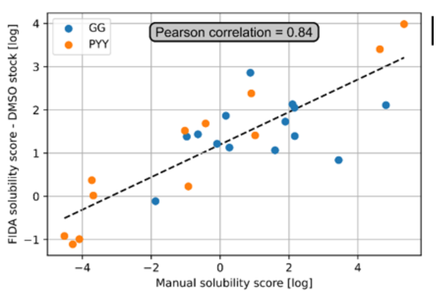
Stickiness
Peptide stickiness appears as tailing in the trace at 0 M ammonium sulfate, indicating interaction with the glass capillary. Combining stickiness, solubility, oligomer size and salt sensitivity flagged 7 of 12 PYY candidates as potentially unsuitable. The two clinical-stage peptides showed favorable profiles.

Compatible with DMSO stocks
DMSO plugs required a modified fitting model to account for DMSO fluorescence and delayed precipitation. Despite this complexity, solubility scores correlated well with aqueous and manual measurements.



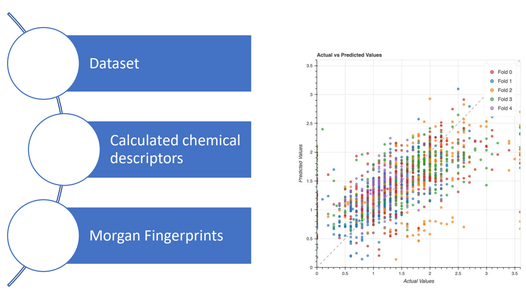






OUTLOOK: ML model

We have demonstrated that we can train a predictive model on in-house solubility data (Sebastian Swanson). For more about chemical descriptors, see Rodrigo Ochoa (poster 251)



G. I. Taylor, Dispersion of soluble matter in solvent flowing slowly through a tube, *Proceedings of the Royal Society of London. A. Mathematical and Physical Sciences* **1953**, *219*, 186-203.