Practical GPC Characterization of Poly(β-peptide)s and Poly(β-peptoid)s

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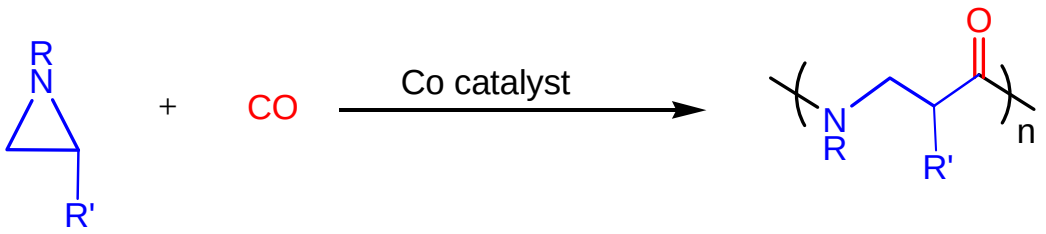
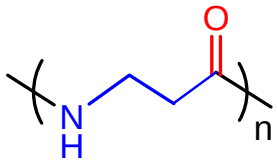
Poly(β-peptide)s and Poly(β-peptoid)s

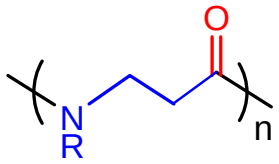


R = H, Poly(β-peptide)

R = Alkyl, Poly(β-peptoid)



Poly(β-alanine)

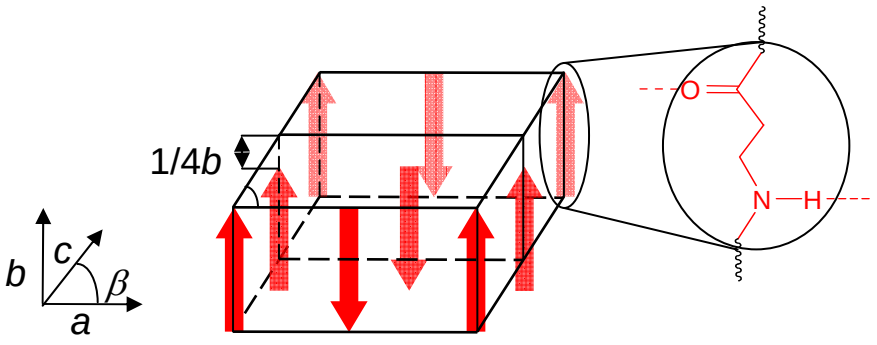


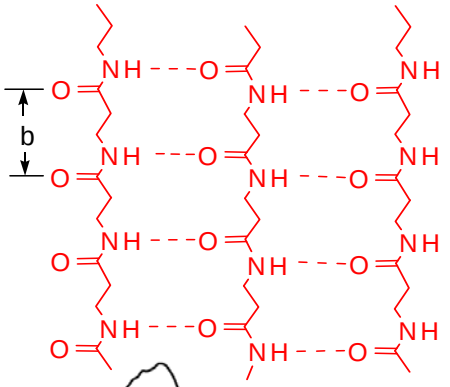
Poly(β-alaninoid)

R = Me, Et, etc.

Why are they interesting?

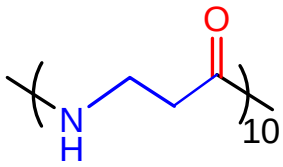
Sheet-Like Structure of Poly(β-Alanine)



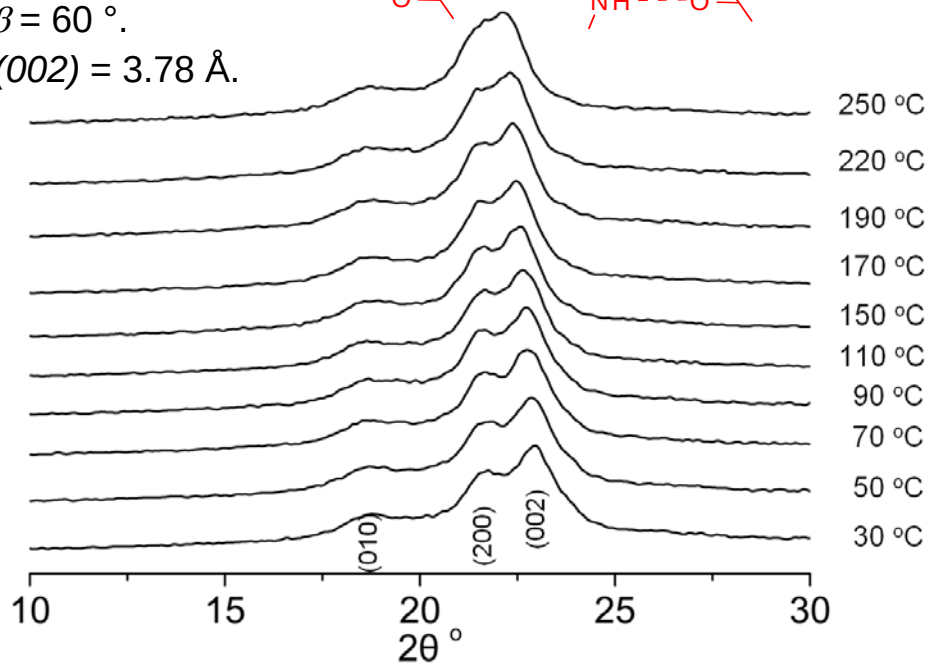


a = 9.33 Å, *b* = 4.78 Å, *c* = 8.73 Å, β = 60 °.

d(200) = 4.04 Å, *d(010)* = 4.78 Å, *d(002)* = 3.78 Å.



Insoluble in anything except acids and HFIPA

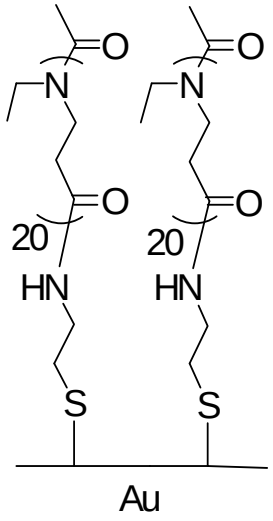


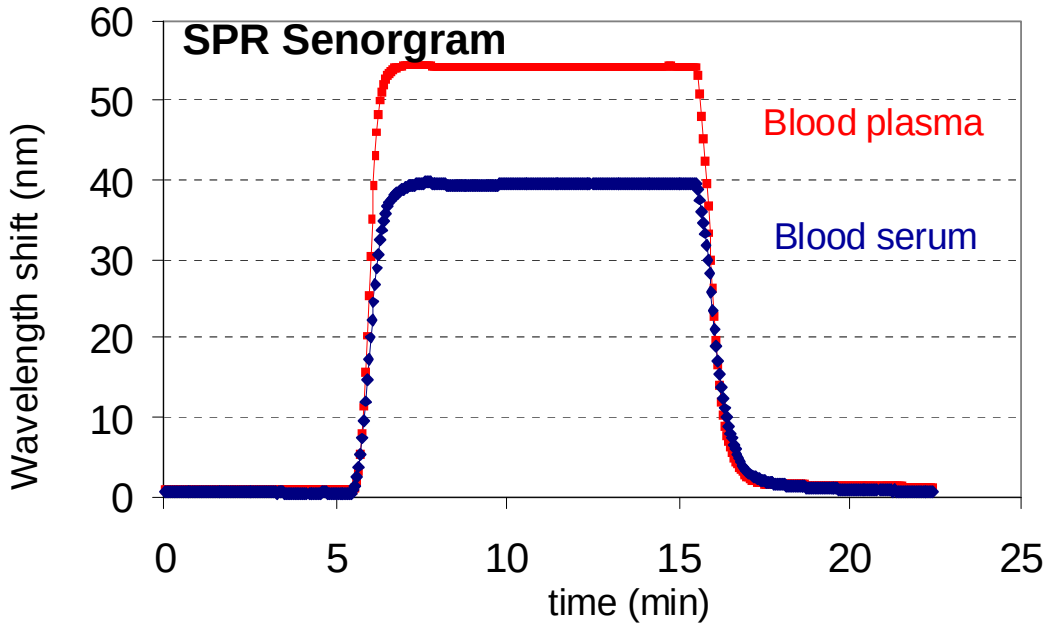
J. Masamoto, K. Sasaguri, C. Ohizumi, H. Kobayashi, *J. Poly. Sci. Part A-2*, 1970, **8, 1703-1711**.

Nonfouling Poly(Ethyl-β-Alanoid)s

Highly soluble in water; resist protein adsorption

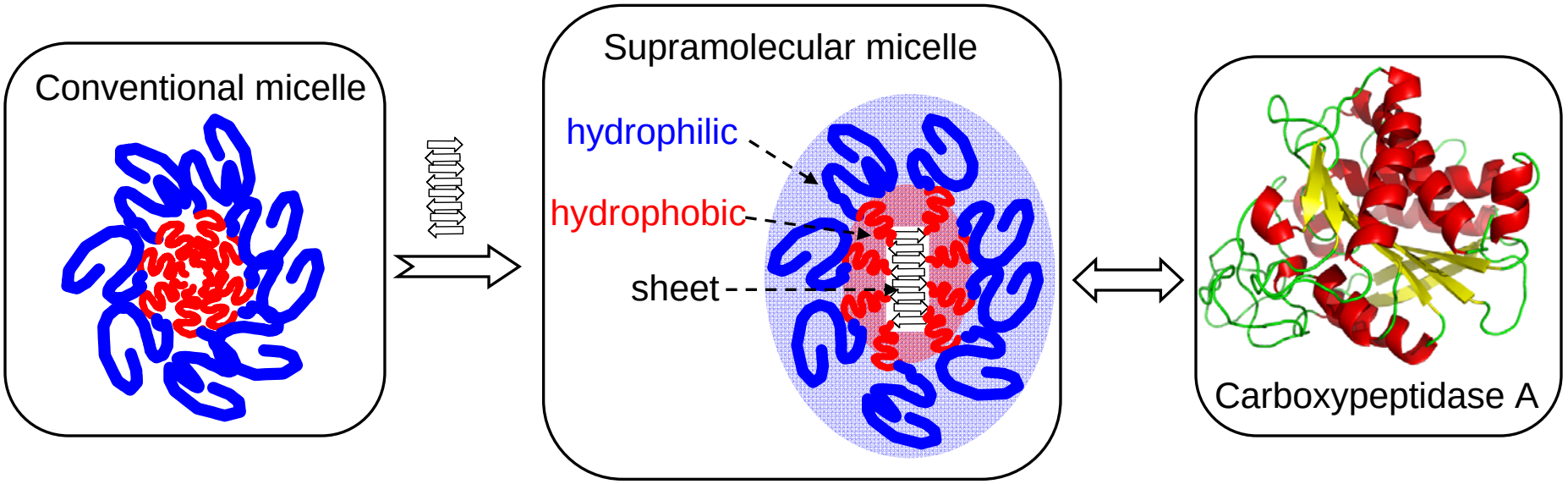
entry	Adsorbed mass (pg/mm^2)		
	Fibrinogen	BSA	Lysozyme
Bare gold	3844 (±723)	1387 (±582)	1443 (±375)
PEtA-20	5 (±4)	0 (±3)	13 (±13)

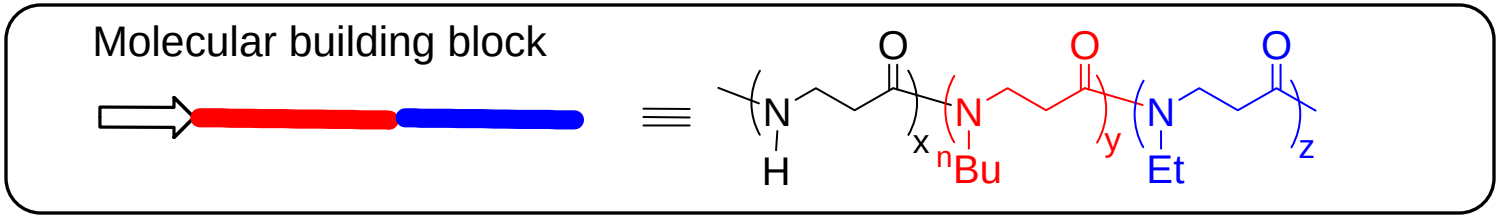




Shaohui Lin, Li Jia, Manuscript submitted.

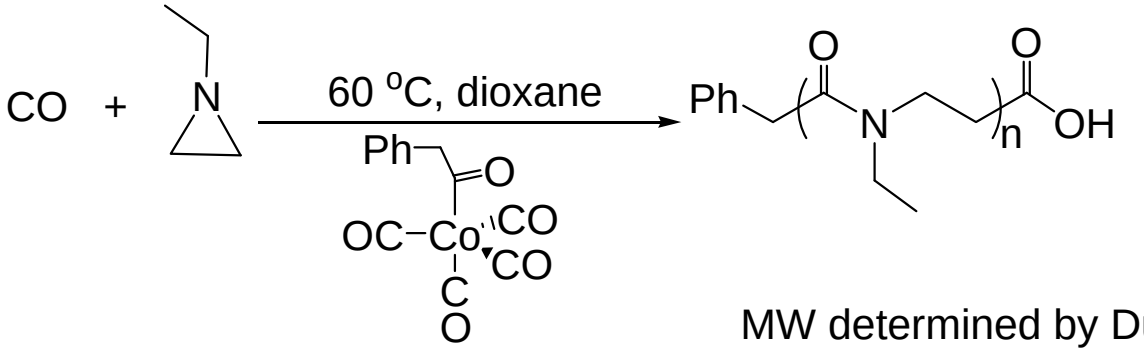
Synthetic Globular Protein Mimics

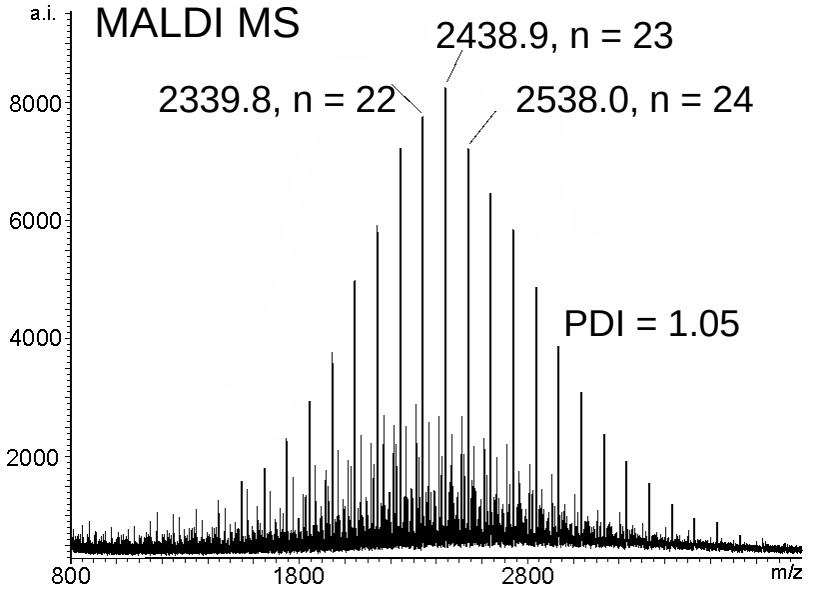




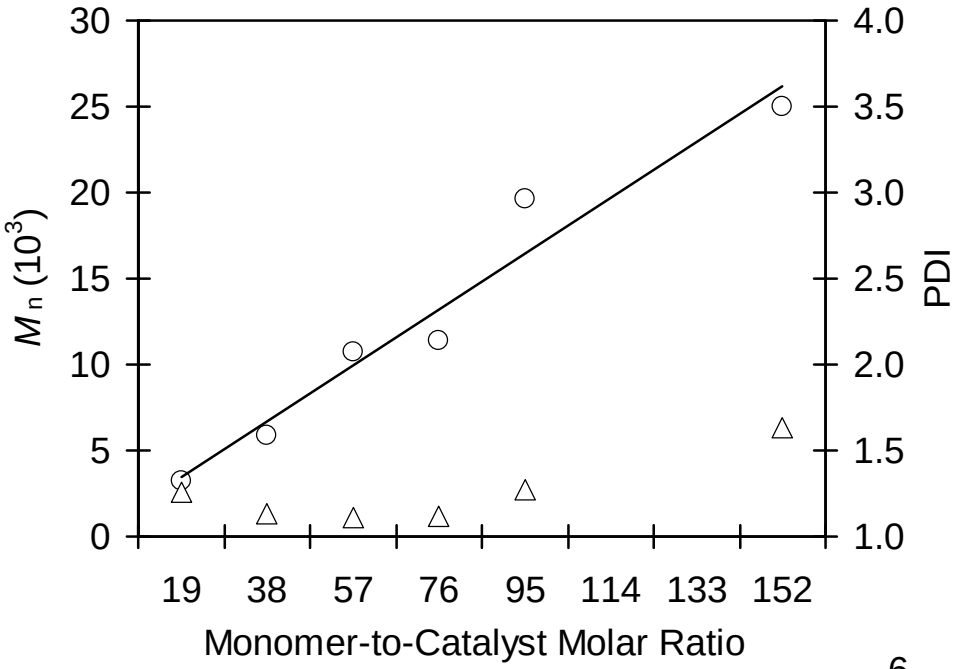
Need a solvent that can solvate all three blocks for GPC!!

Previous MW Characterization



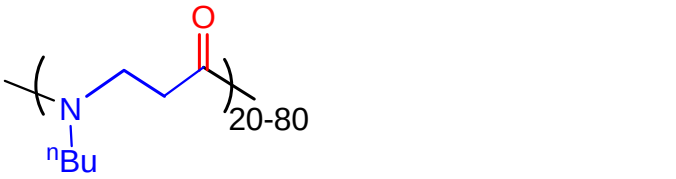


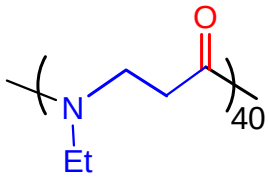
MW determined by DuPont using GPC-MALLS detector and HFIPA as mobile phase.



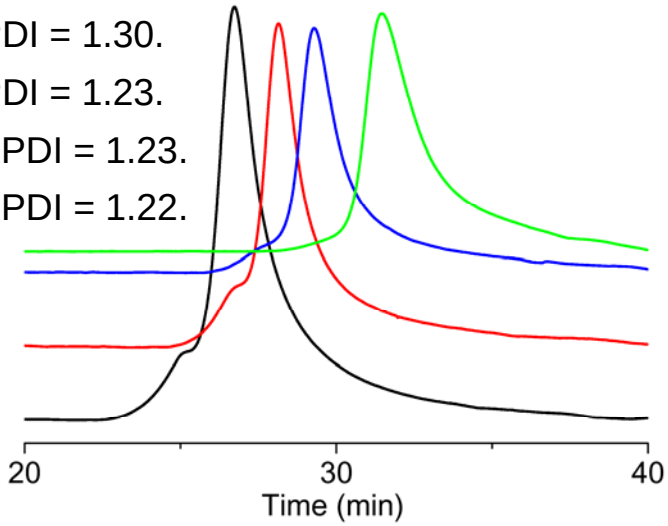
Jia, L. et al *J. Am. Chem. Soc.* **2002**, 7282.

GPC in Chloroform

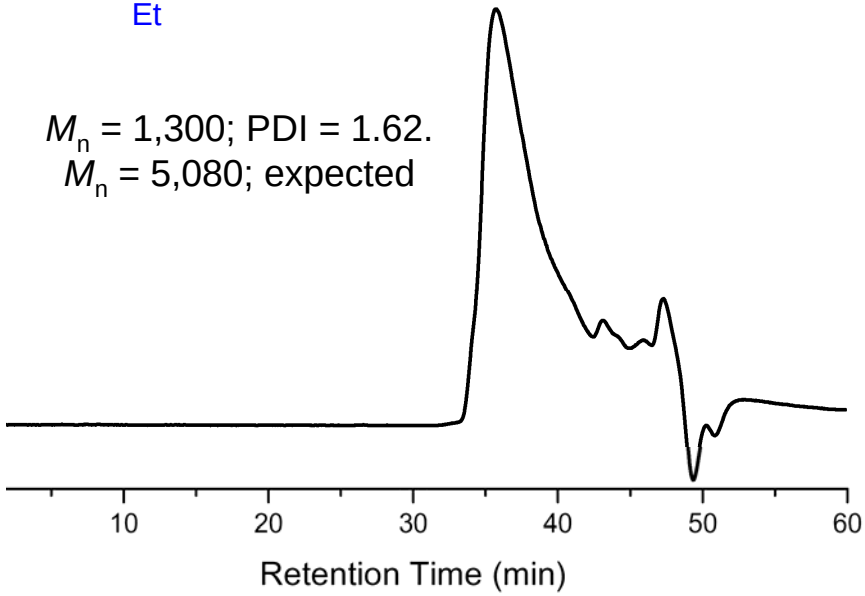




M_n = 2,950; PDI = 1.30.
M_n = 6,827; PDI = 1.23.
M_n = 11,081; PDI = 1.23.
M_n = 15,972; PDI = 1.22.

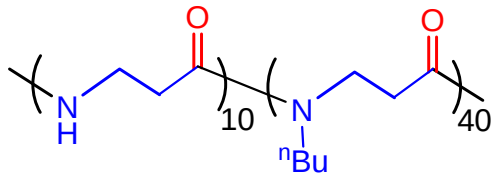


M_n = 1,300; PDI = 1.62.
M_n = 5,080; expected

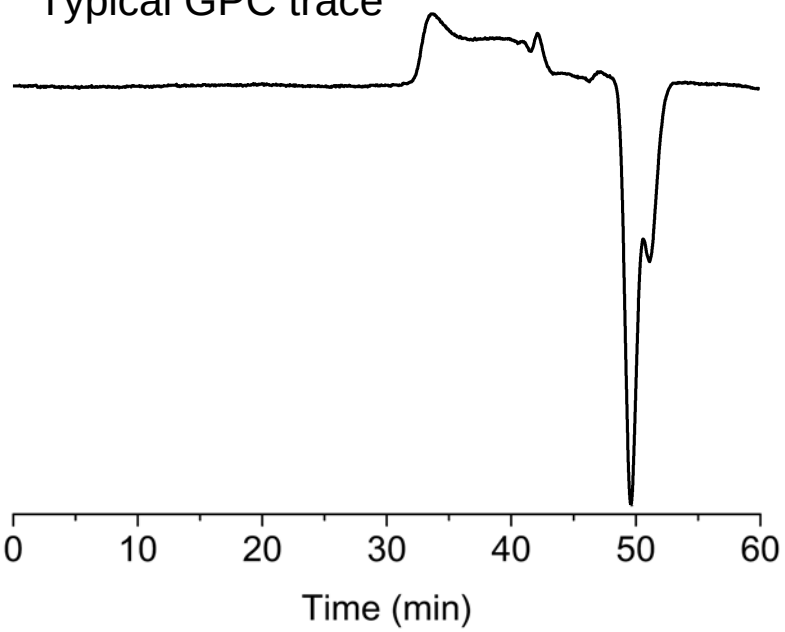


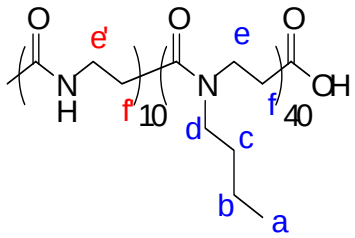
- Poly(n-butyl-β-alanoid)s appear to behave normally.
- Poly(ethyl-β-alanoid) interacts with GPC columns from several vendors. An irregular tail is always observed.
- The MWs of poly(ethyl-β-alanoid) relative to polystyrene STDs are significantly lower than expected.

GPC in Chloroform

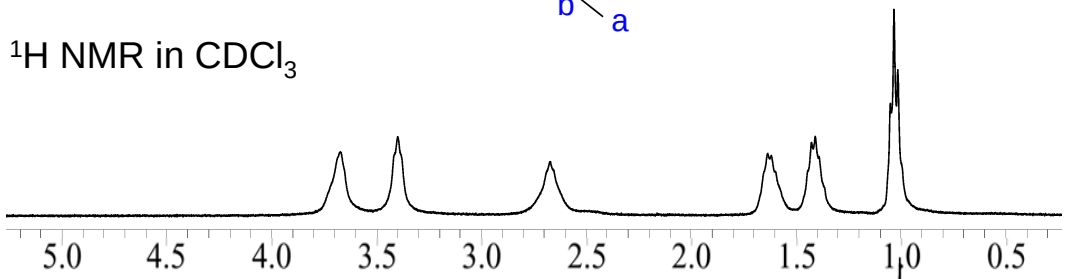


Typical GPC trace

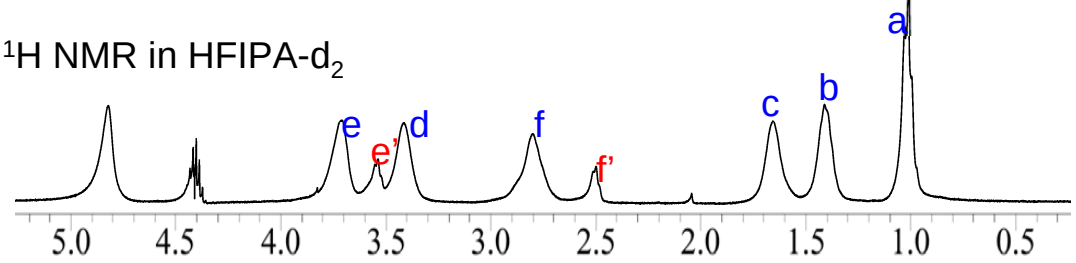




^{1}H NMR in $CDCl_3$

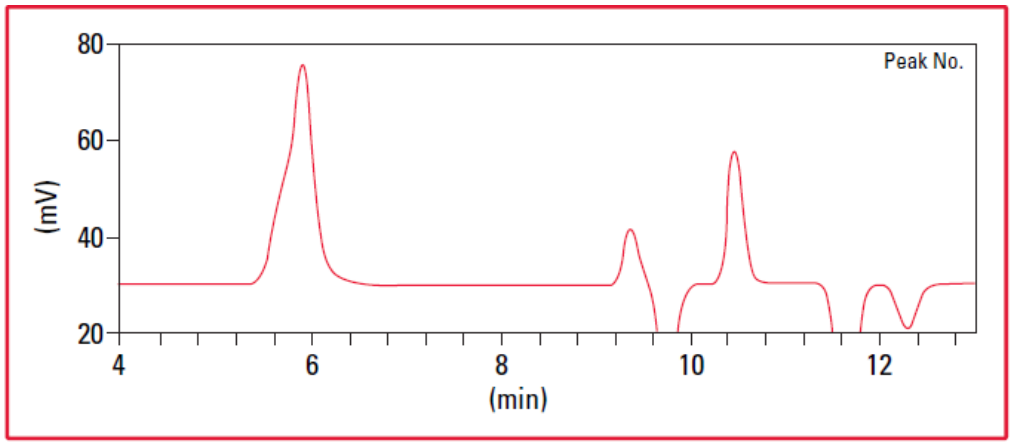


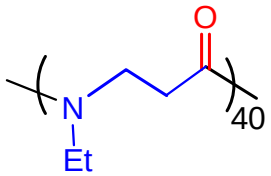
^{1}H NMR in HFIPA-d_2



β-Alanine block forms sheet-like supramolecular structure.

GPC Characterization in HFIPA

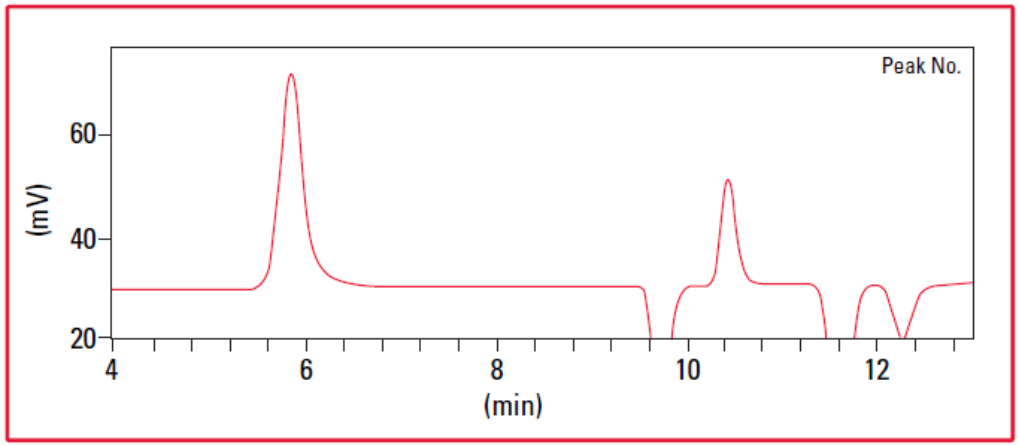


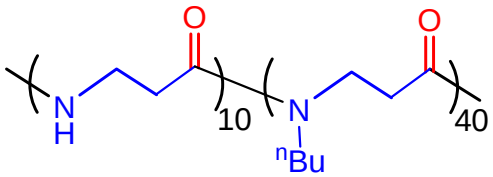


M_n = 30,007 relative to PMMA STDs

M_n = 3,996 expected

PDI = 1.22





M_n = 24,969 relative to PMMA STDs

M_n = 5,790 expected

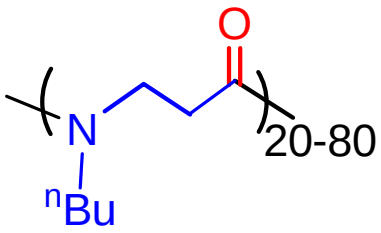
PDI = 1.20

Courtesy of Tosoh

Our Solutions to the GPC Challenge

- A substantially cheaper solvent.
  HFIPA,$(CF_3)_2CHOH$: $ 207 for 100 g
  TFEA, CF_3CH_2OH: $394 for 2 kg, 10 time cheaper.

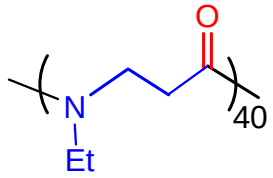
- A method or standard samples for calibration.

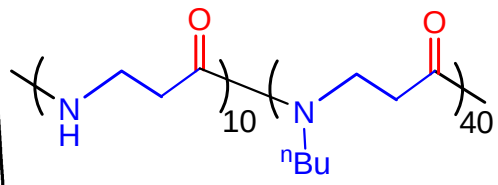


- EcoSEC system and
  Semi-Micro columns

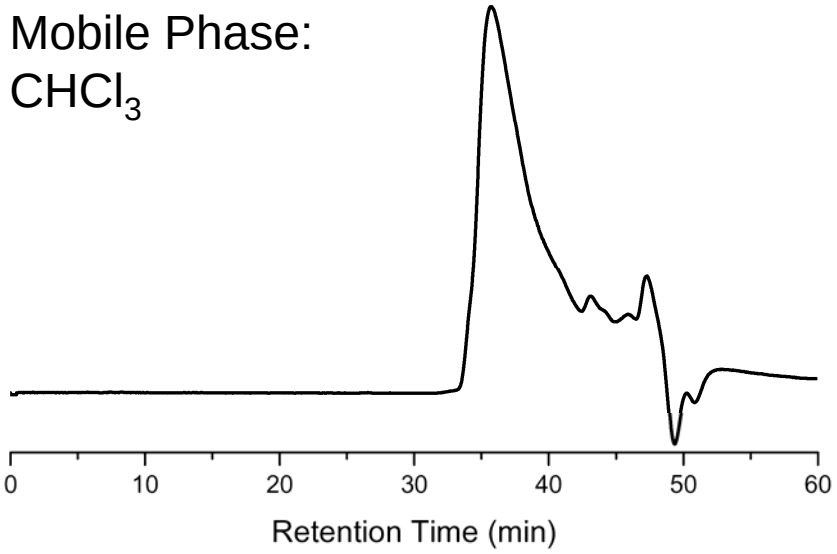
Combination of TFEA Mobile Phase and Semi-Micro Columns

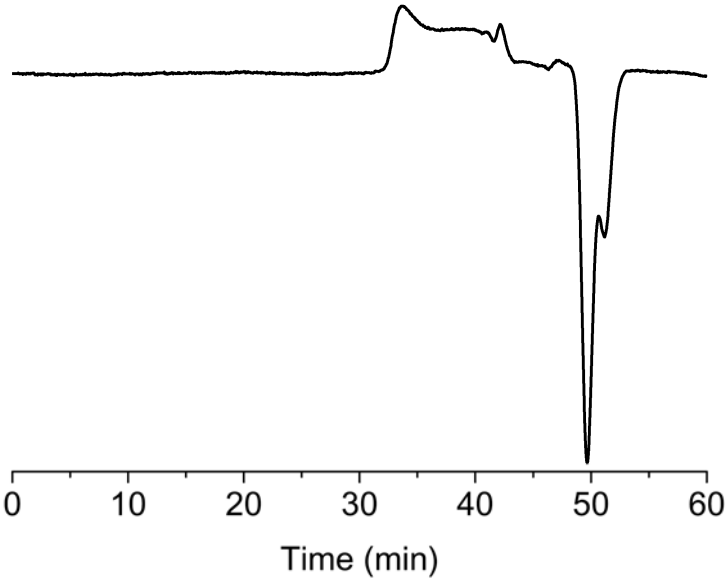
Mobile phase:
CF_3CH_2OH





Mobile Phase:
$CHCl_3$





Solvent Cost Comparison

Case: Column switch, instrument stabilization, and 30 samples.

2 Tosoh SuperH 3000 column x 2

Total flow rate, 0.70 mL/min, 25 min per sample

$200

TFEA

2 Tosoh SuperH 3000 column x 2

Total flow rate, 0.70 mL/min, 25 min per sample

$2000

HFIPA

2 Conventional hi. res. column x 2

Total flow rate, 1.00 mL/min, 50 min per sample

$550

TFEA

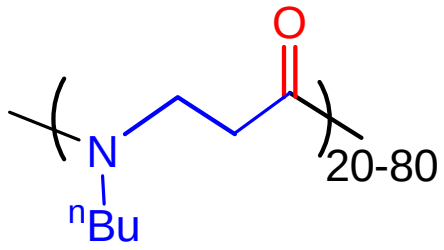
2 Conventional hi. res. column x 2

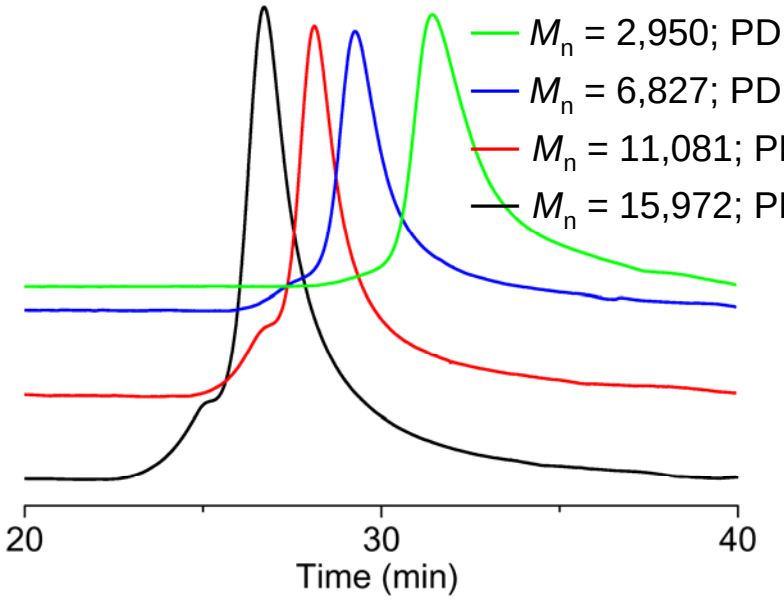
Total flow rate, 1.00 mL/min, 50 min per sample

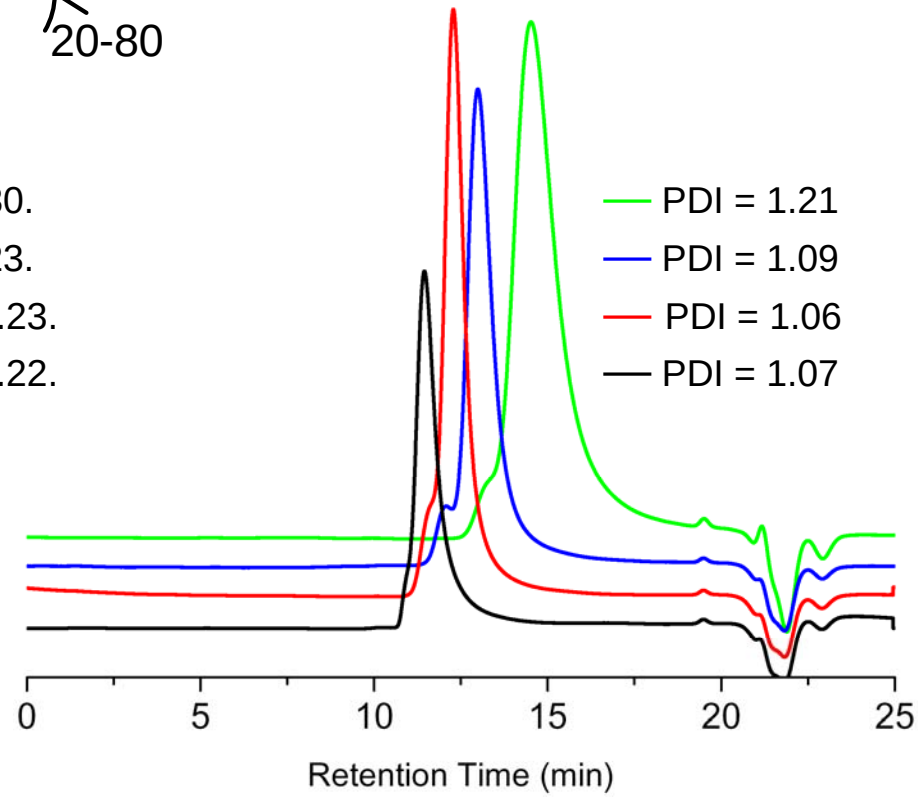
$5500

HFIPA

Poly(Butyl-β-Alanoid) Standards



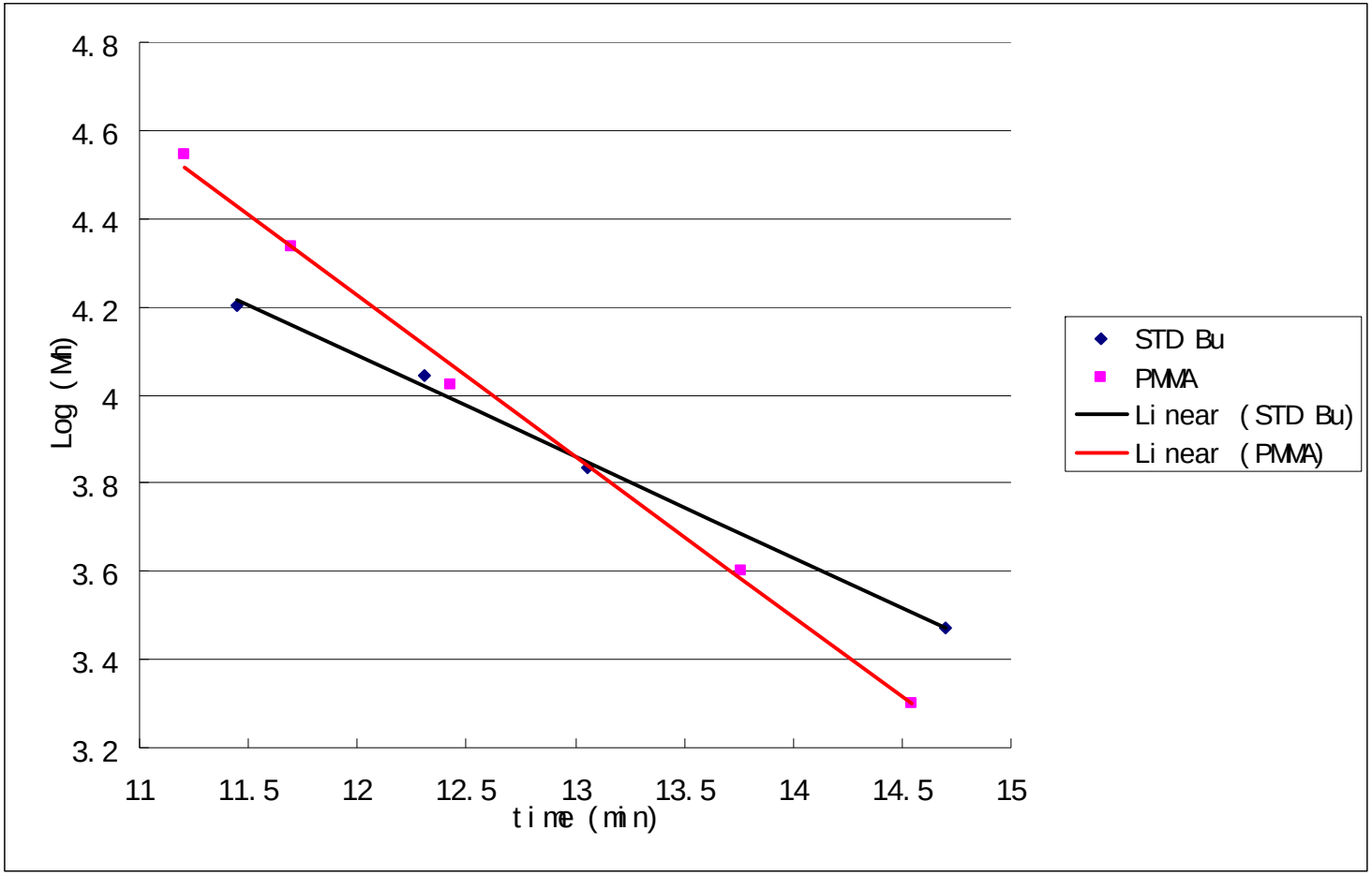




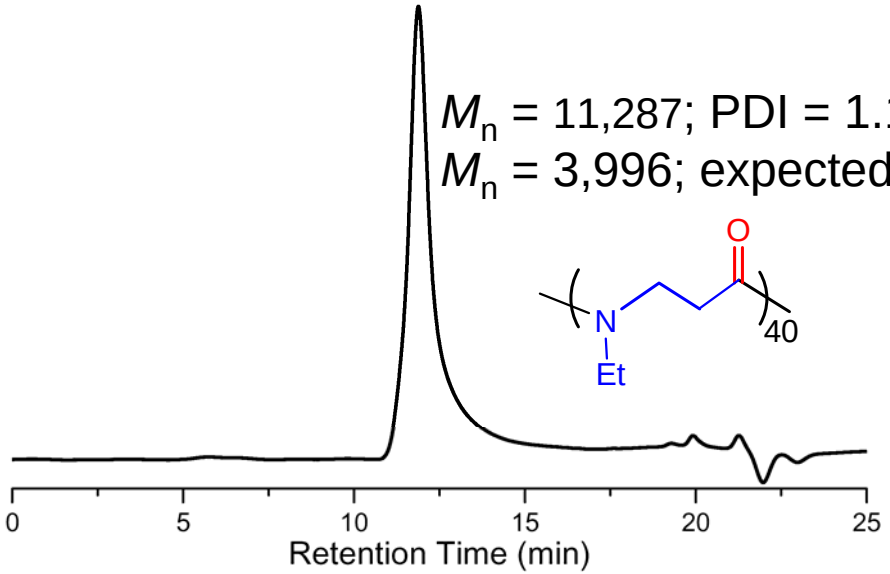
$CHCl_3$, two conventional columns
MW relative to polystyrene STDs.

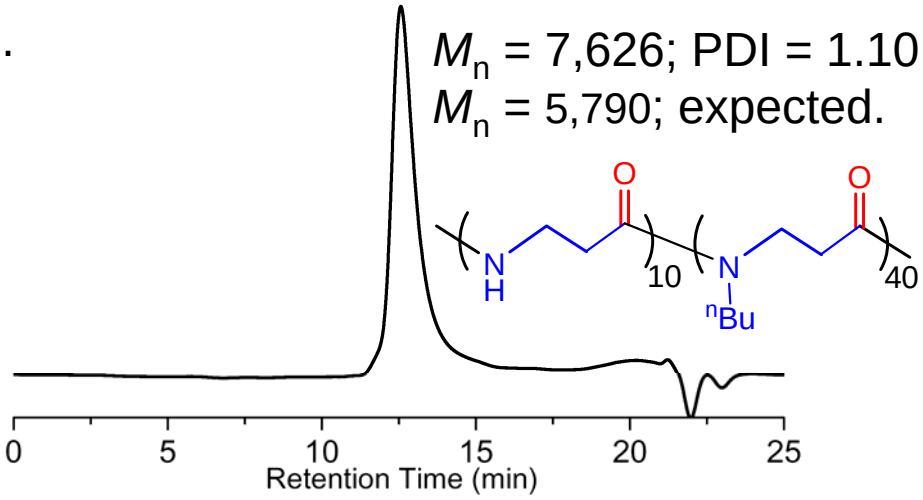
TFEA, two Tosoh SuperH 3000 Column

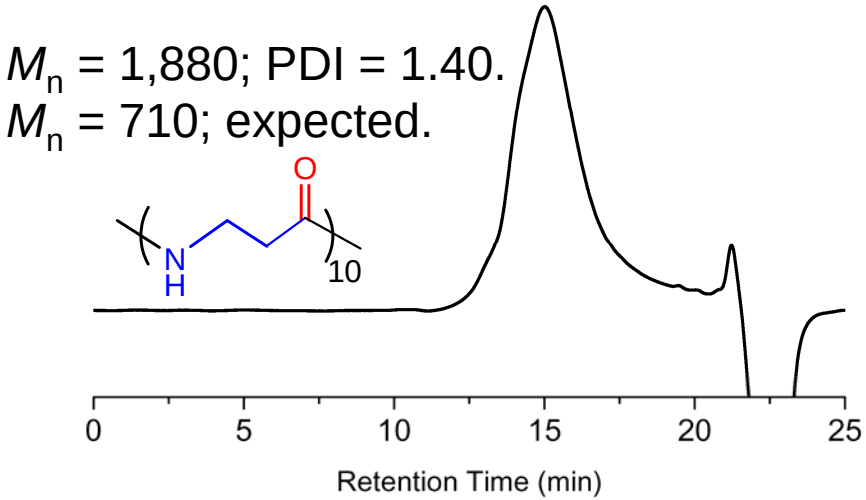
Comparison of PMMA and Poly(^{n}Bu-β-Alanoid) Calibration



MWs Relative to Poly(^{n}Bu-β-Alanoid)s







Conclusion

- TFEA is an viable economical alternative to HFIPA for GPC analysis of poly(β-petide)s and poly(β-peptoid)s.

- TFEA appears to strongly solvate these polymers and prevents polymer-column interaction like HFIPA.

- TFEA is capable of breaking supramolecular aggregates held together by fairly strong intermolecular interactions like HFIPA.

- Relative molecular weight determination is highly errant by simple calibration with standard samples even when the standard samples have similar chemical structures using either TFEA or HFIPA as the mobile phase.