

ARTICLE

Measurement and modelling solubility of amino acids and peptides in aqueous 2-propanol solutions

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SUPPORTING INFORMATION

Contents

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† Electronic supplementary information (ESI) available. See DOI:

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1. Substances

Table S1 Substances, abbreviations, suppliers, CAS numbers and mass-specific purities and molar mass (M) of the solutes used in this work.

Solute	*Abbrev.*	*Supplier*	*CAS no.*	*Purity / %*	*M / g·mol^{-1}*
Glycine	*Gly*	*ROTH*	*56-40-6*	*≥ 99.0*	*75.070*
L-alanine	*Ala*	*Sigma*	*56-41-7*	*≥ 98.0*	*89.100*
L-valine	*Val*	*Alfa*	*72-18-4*	*> 99.0*	*117.150*
L-leucine	*Leu*	*TCI*	*61-90-5*	*> 99.0*	*131.180*
L-isoleucine	*Ile*	*Sigma*	*73-32-5*	*≥ 99.5*	*131.180*
L-proline	*Pro*	*Bachem*	*147-85-3*	*≥ 99.0*	*115.140*
L-serine	*Ser*	*Bachem*	*56-45-1*	*> 99.0*	*105.100*
L-threonine	*Thr*	*Sigma*	*72-19-5*	*≥ 98.0*	*119.120*
L-aspartic acid	*Asp*	*Sigma*	*56-84-8*	*≥ 99.0*	*133.110*
L-asparagine	*Asn*	*Sigma*	*70-47-3*	*≥ 98.0*	*132.120*
L-glutamic acid	*Glu*	*Sigma*	*56-86-0*	*≥ 99.5*	*147.130*
L-glutamine	*Gln*	*Merck*	*56-85-9*	*> 99.0*	*146.150*
L-arginine	*Arg*	*Merck*	*74-79-3*	*≥ 98.0*	*174.210*
L-histidine	*His*	*Sigma*	*71-00-1*	*≥ 99.0*	*155.160*
L-lysine	*Lys*	*Sigma*	*56-87-1*	*≥ 98.0*	*146.190*
L-phenylalanine	*Phe*	*Merck*	*63-91-2*	*≥ 98.0*	*165.200*
L-tyrosine	*Tyr*	*Bachem*	*60-18-4*	*≥ 98.0*	*181.200*
L-tryptophan	*Trp*	*Merck*	*73-22-3*	*≥ 98.0*	*204.230*
L-cysteine	*Cys*	*Merck*	*52-90-4*	*≥ 98.0*	*121.160*
L-methionine	*Met*	*Merck*	*63-68-3*	*≥ 99.0*	*149.210*
Glycyl-glycine	*Gly-Gly*	*Sigma*	*556-50-3*	*≥ 99.0*	*132.119*
Glycyl-L-alanine	*Gly-Ala*	*Sigma*	*3695-73-6*	*≥ 99.0*	*146.146*
L-alanyl-glycine	*Ala-Gly*	*Sigma*	*687-69-4*	*≥ 99.0*	*146.146*
L-alanyl-L-alanine	*Ala-Ala*	*Sigma*	*1948-31-8*	*≥ 99.0*	*160.173*
Glycyl-L-serine	*Gly-Ser*	*Bachem*	*687-38-7*	*≥ 99.0*	*162.145*
L-seryl-glycine	*Ser-Gly*	*Bachem*	*687-63-8*	*≥ 99.0*	*162.145*
L-alanyl-L-serine	*Ala-Ser*	*Bachem*	*3303-41-1*	*≥ 99.0*	*176.172*
L-seryl-L-alanine	*Ser-Ala*	*Bachem*	*6403-17-4*	*≥ 99.0*	*176.172*
Glycyl-L-proline	*Gly-Pro*	*Bachem*	*704-15-4*	*≥ 99.0*	*172.180*
L-prolyl-glycine	*Pro-Gly*	*Bachem*	*2578-57-6*	*≥ 99.0*	*172.180*
L-alanyl-L-proline	*Ala-Pro*	*Bachem*	*13485-59-1*	*≥ 99.0*	*186.211*
L-prolyl-L-alanine	*Pro-Ala*	*Bachem*	*6422-36-2*	*≥ 99.0*	*186.211*
Glycyl-glycyl-glycine	*Gly-Gly-Gly*	*Sigma*	*556-33-2*	*≥ 98.0*	*189.170*
Glycyl-glycyl-L-alanine	*Gly-Gly-Ala*	*Bachem*	*19729-30-7*	*≥ 99.0*	*203.200*
Glycyl-L-alanyl-glycine	*Gly-Ala-Gly*	*Bachem*	*16422-05-2*	*≥ 99.0*	*203.200*
L-alanyl-glycyl- L-alanine	*Ala-Gly-Ala*	*Bachem*	*37460-22-3*	*≥ 99.0*	*217.225*
L-alanyl-L-alanyl-L-alanine	*Ala-Ala-Ala*	*Bachem*	*5874-90-8*	*≥ 99.0*	*231.252*
L-Leucyl-glycyl-glycine	*Leu-Gly-Gly*	*Bachem*	*1187-50-4*	*≥ 99.0*	*245.279*
Glycyl-L-leucyl-glycine	*Gly-Leu-Gly*	*Bachem*	*2576-67-2*	*≥ 98.0*	*245.279*
Glycyl-glycyl-L-leucine	*Gly-Gly-Leu*	*Bachem*	*14857-82-0*	*≥ 99.0*	*245.279*
Glycyl-L-alanyl-L-leucine	*Gly-Ala-Leu*	*Bachem*	*22849-49-6*	*≥ 99.0*	*259.305*
2-propanol	*2-prop.*	*BDH Chemicals*	*67-63-0*	*≥ 98.5*	*60.100*

2. pKa values

Table S2 pK_a-values of the amino acids measured in this work. All pK_a-values in 10 wt%, 20 wt%, and 30 wt% of 2-propanol are taken from Dey et al.[1]. For the remaining components, the pK_a-values were calculated by the software Chemicalize® and assumed to be solvent-independent. The error of this calculation is assumed not to be greater than 0.01.

Component	pK_{a1}	pK_{a2}	pK_{a3}	pK_{a4}
Gly	10 wt%: 2.42 ± 0.07 20 wt%: 2.61 ± 0.07 30 wt%: 2.79± 0.07	10 wt%: 9.58 ± 0.05 20 wt%: 9.61 ± 0.05 30 wt%: 9.65 ± 0.05	-	
Ala	10 wt%: 2.55 ± 0.06 20 wt%: 2.75 ± 0.06 30 wt%: 2.95 ± 0.06	10 wt%: 9.59 ± 0.05 20 wt%: 9.61 ± 0.06 30 wt%: 9.63 ± 0.06	-	
Val	10 wt%: 2.47 ± 0.08 20 wt%: 2.68 ± 0.08 30 wt%: 2.89 ± 0.09	10 wt%: 9.69 ± 0.05 20 wt%: 9.71 ± 0.05 30 wt%: 9.74 ± 0.05	-	
Leu	10 wt%: 2.55 ± 0.06 20 wt%: 2.73 ± 0.06 30 wt%: 2.91 ± 0.07	10 wt%: 9.52 ± 0.05 20 wt%: 9.53 ± 0.05 30 wt%: 9.53 ± 0.06	-	
Ile	10 wt%: 2.55 ± 0.06 20 wt%: 2.73 ± 0.06 30 wt%: 2.91 ± 0.07	10 wt%: 9.52 ± 0.05 20 wt%: 9.53 ± 0.05 30 wt%: 9.53 ± 0.06	-	
Pro	10 wt%: 2.11 ± 0.07 20 wt%: 2.27 ± 0.07 30 wt%: 2.44 ± 0.07	10 wt%: 10.62 ± 0.04 20 wt%: 10.64 ± 0.04 30 wt%: 10.66 ± 0.04	-	
Ser	10 wt%: 2.35 ± 0.05 20 wt%: 2.46 ± 0.05 30 wt%: 2.57 ± 0.05	10 wt%: 8.97 ± 0.04 20 wt%: 8.99 ± 0.04 30 wt%: 9.01 ± 0.04	15.17	
Thr	10 wt%: 2.32 ± 0.04 20 wt%: 2.45 ± 0.04 30 wt%: 2.57 ± 0.05	10 wt%: 9.00 ± 0.05 20 wt%: 9.00 ± 0.05 30 wt%: 9.01 ± 0.05	14.95	
Asp	1.70	5.11	9.61	
Asn	10 wt%: 2.41 ± 0.06 20 wt%: 2.59 ± 0.06 30 wt%: 2.78 ± 0.07	10 wt%: 8.67 ± 0.05 20 wt%: 8.70 ± 0.06 30 wt%: 8.73 ± 0.06	-	
Glu	1.88	4.27	9.54	
Gln	10 wt%: 2.36 ± 0.09 20 wt%: 2.55 ± 0.09 30 wt%: 2.75 ± 0.10	10 wt%: 9.07 ± 0.05 20 wt%: 9.10 ± 0.05 30 wt%: 9.13 ± 0.05		
Arg	2.41	9.12	12.41	
His	10 wt%: 1.83 ± 0.05 20 wt%: 1.97 ± 0.05 30 wt%: 2.10 ± 0.06	10 wt%: 5.79 ± 0.07 20 wt%: 5.74 ± 0.08 30 wt%: 6.68 ± 0.08	10 wt%: 9.11 ± 0.04 20 wt%: 9.12 ± 0.04 30 wt%: 9.12 ± 0.04	
Lys	2.74	9.44	10.29	
Phe	10 wt%: 2.39 ± 0.04 20 wt%: 2.52 ± 0.04 30 wt%: 2.64 ± 0.04	10 wt%: 9.17 ± 0.07 20 wt%: 9.20 ± 0.08 30 wt%: 9.23 ± 0.08	-	
Tyr	2.20	9.11	10.13	
Trp	2.43	9.44	-	
Cys	2.35	9.05	10.17	
Met	10 wt%: 2.40 ± 0.05 20 wt%: 2.55 ± 0.05 30 wt%: 2.71 ± 0.05	10 wt%: 9.18 ± 0.05 20 wt%: 9.19 ± 0.05 30 wt%: 9.21 ± 0.05	-	
Gly-Gly	3.52	8.14	15.32	-
Gly-Ala	3.61	8.14	13.82	-
Ala-Gly	3.66	8.39	14.32	-
Ala-Ala	3.73	8.39	13.82	-
Gly-Ser	3.36	8.14	12.66	15.11
Ser-Gly	3.44	7.85	13.92	15.15
Ala-Ser	3.48	8.39	12.72	15.11
Ser-Ala	3.51	7.85	13.50	15.13
Gly-Pro	3.61	8.13	-	-

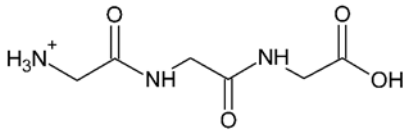
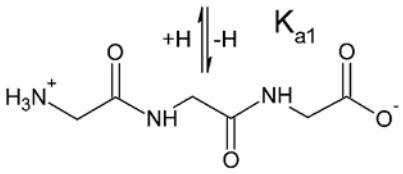
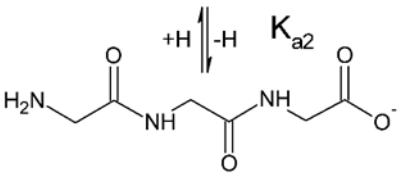
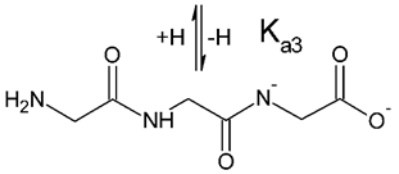
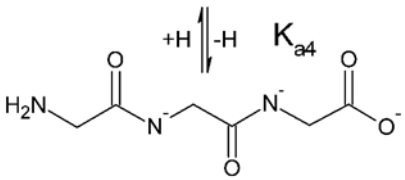
Pro-Gly	3.66	9.81	14.29	-
Ala-Pro	3.71	8.38	-	-
Pro-Ala	3.71	9.81	13.79	-
Gly-Gly-Gly	3.43	7.84	12.54	15.84
Gly-Gly-Ala	3.49	7.84	12.60	14.43
Gly-Ala-Gly	3.53	7.84	12.43	14.61
Ala-Gly-Ala	3.58	8.09	12.64	14.39
Ala-Ala-Ala	3.65	8.09	12.53	14.19
Gly-Gly-Leu	3.72	7.82	12.82	14.16
Gly-Leu-Gly	3.77	7.84	12.61	14.81
Leu-Gly-Gly	3.39	8.13	12.82	-
Pro-Gly-Gly	3.26	9.50	12.60	15.94
Gly-Ala-Leu	3.78	7.84	12.68	14.24

3. pH-dependent solubility

Table S3 Dissociations schemes together with the corresponding Henderson Hasselbalch equation and the components. The derivation principle was taken from A. Avdeef [2] and adapted to the way of dissociation of amino acids and peptides.

Dissociation scheme	Henderson Hasselbalch eq.	Components
$H_3A^+ \rightleftharpoons H_2A^{\pm} \rightleftharpoons HA^- \rightleftharpoons A^{2-}$	$x^L_{HA,tot} = x^L_{HA} \cdot (1 + 10^{pK_{a1}-pH} + 10^{pH-pK_{a2}} + 10^{2pH-pK_{a3}-pK_{a2}})$	Gly-Gly, Gly-Ala, Ala-Gly, Ala-Ala, Pro-Gly, Pro-Ala, Leu-Gly-Gly
$H_4A^+ \rightleftharpoons H_3A^{\pm} \rightleftharpoons H_2A^- \rightleftharpoons HA^{2-} \rightleftharpoons A^{3-}$	$x^L_{HA,tot} = x^L_{HA} \cdot (1 + 10^{pK_{a1}-pH} + 10^{pH-pK_{a2}} + 10^{2pH-pK_{a3}-pK_{a2}} + 10^{3pH-pK_{a4}-pK_{a3}-pK_{a2}})$	Gly-Ser, Ser-Gly, Ser-Ala, Ala-Ser, Gly-Gly-Gly, Gly-Gly-Ala, Gly-Ala-Gly, Ala-Gly-Ala, Ala-Ala-Ala, Gly-Gly-Leu, Gly-Leu-Gly

The derivation of the Henderson Hasselbalch equation is shown below with the dissociation scheme, the charge of the species (S) and the dissociation constants for the tripeptide Gly-Gly-Gly

Species (S)	Charge	Dissociation constants	
	1+	$K_{a1} = \frac{a[S^{\pm}] \cdot a[H^+]}{a[S^+]}$	(S1)
	0	$K_{a2} = \frac{a[S^-] \cdot a[H^+]}{a[S^{\pm}]}$	(S2)
	1-	$K_{a3} = \frac{a[S^{2-}] \cdot a[H^+]}{a[S^-]}$	(S3)
	2-	$K_{a4} = \frac{a[S^{3-}] \cdot a[H^+]}{a[S^{2-}]}$	(S4)
	3-		

Where $a[S^{charge}]$ represent the activity of the single charged species. The total activity a_{tot} is calculated based on the sum of the single activities shown in eq. S5

$$a_{tot} = a[S^{\pm}] + a[S^+] + a[S^-] + a[S^{2-}] + a[S^{3-}] \quad \text{(S5)}$$

Using the eqs. S1 - S5 the total activity can be rewritten based on the dissociation constants and the activity of the proton H^+.

$$a_{tot} = a[S^{\pm}] + a[S^{\pm}] \cdot \frac{a[H^+]}{K_{a1}} + a[S^{\pm}] \cdot \frac{K_{a2}}{a[H^+]} + a[S^{\pm}] \cdot \frac{K_{a2}}{a[H^+]} \cdot \frac{K_{a3}}{a[H^+]} + a[S^{\pm}] \cdot \frac{K_{a2}}{a[H^+]} \cdot \frac{K_{a3}}{a[H^+]} \cdot \frac{K_{a4}}{a[H^+]} \quad \text{(S6)}$$

With eqs. S7 and S8

$$a[H^+] = 10^{-pH} \quad \text{(S7)}$$

$$K_{ai} = 10^{-K_{ai}}; i = 1,2,\dots,n-1, n = number\ of\ species \quad \text{(S8)}$$

The equation can be simplified to

$$a_{tot} = a[S^{\pm}] \cdot (1 + 10^{\mathrm{pK_{a1}-pH}} + 10^{\mathrm{pH-pK_{a2}}} + 10^{\mathrm{2pH-pK_{a2}-pK_{a3}}} + 10^{\mathrm{3pH-pK_{a2}-pK_{a3}-pK_{a4}}}) \quad \text{(S9)}$$

Under the assumption that all activity coefficients of the charged species are equal, the solubility in mole fraction can be calculated using eq. S10

$$x_{tot}^{L} = x_{\pm}^{L} \cdot (1 + 10^{pK_{a1}-pH} + 10^{pH-pK_{a2}} + 10^{2pH-pK_{a3}-pK_{a2}} + 10^{3pH-pK_{a4}-pK_{a3}-pK_{a2}}) \quad \text{(S10)}$$

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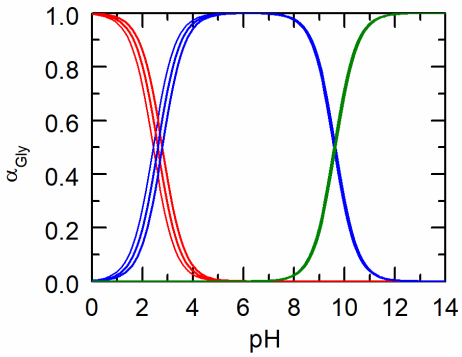
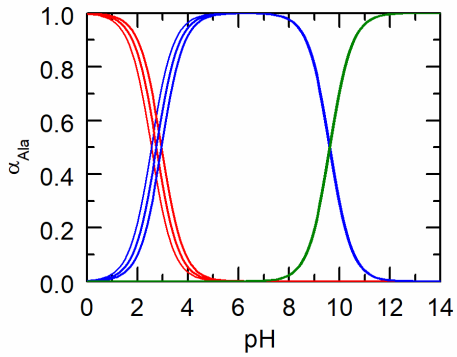
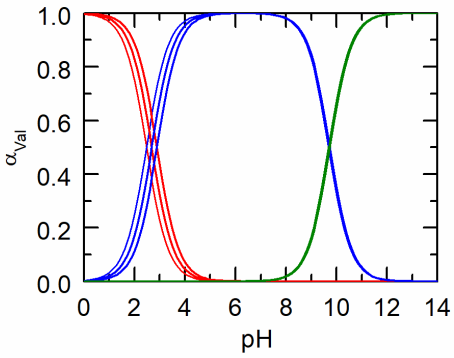
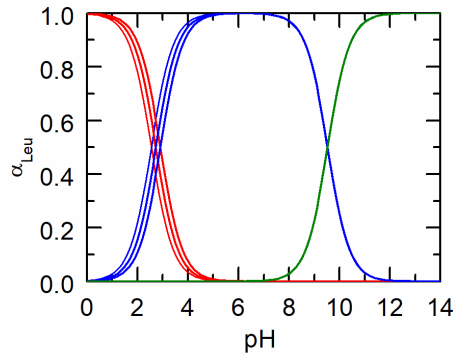
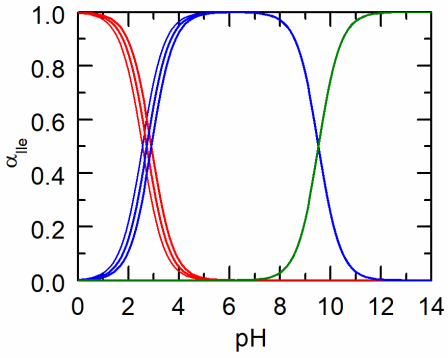
4. Species distribution diagram

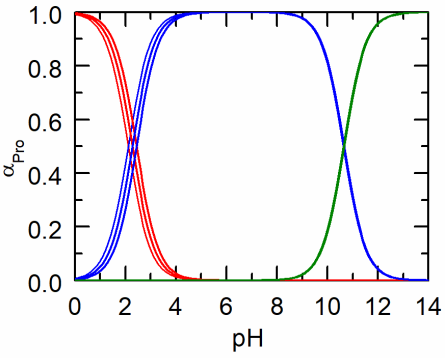


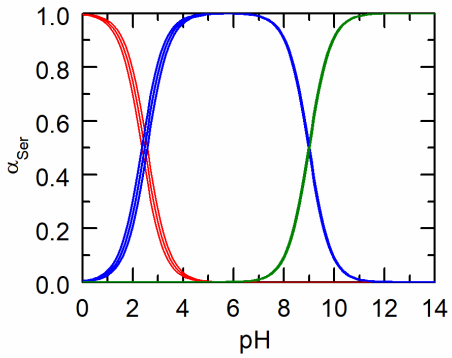








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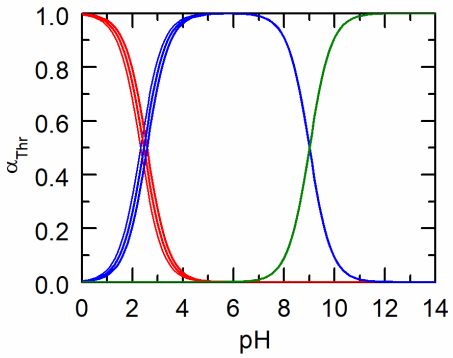
0.6
0.4
0.2
0.0
α_{Ser}
0 2 4 6 8 10 12 14
pH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α_{Thr}
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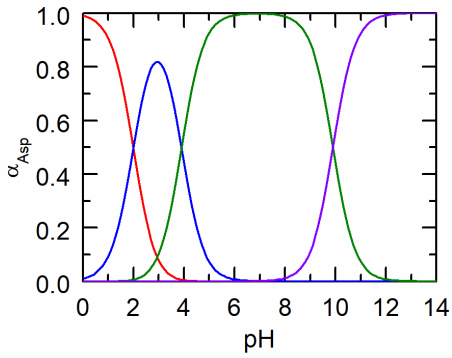
pH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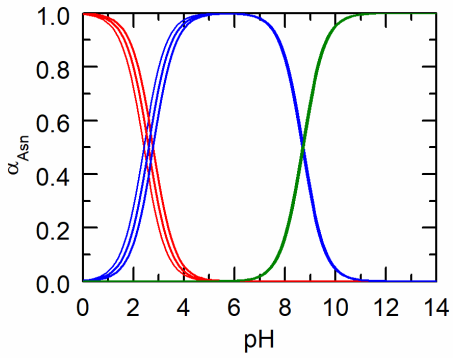
pH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0.0
α_{Asn}
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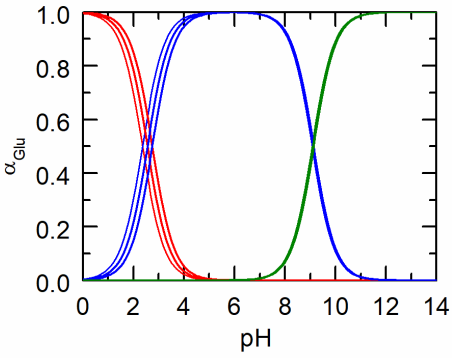
pH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α_{Glu}
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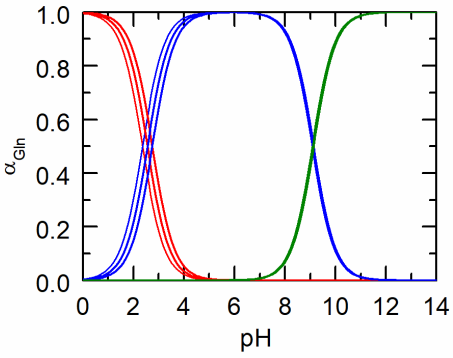
pH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0.2
0.0
α_{Gln}
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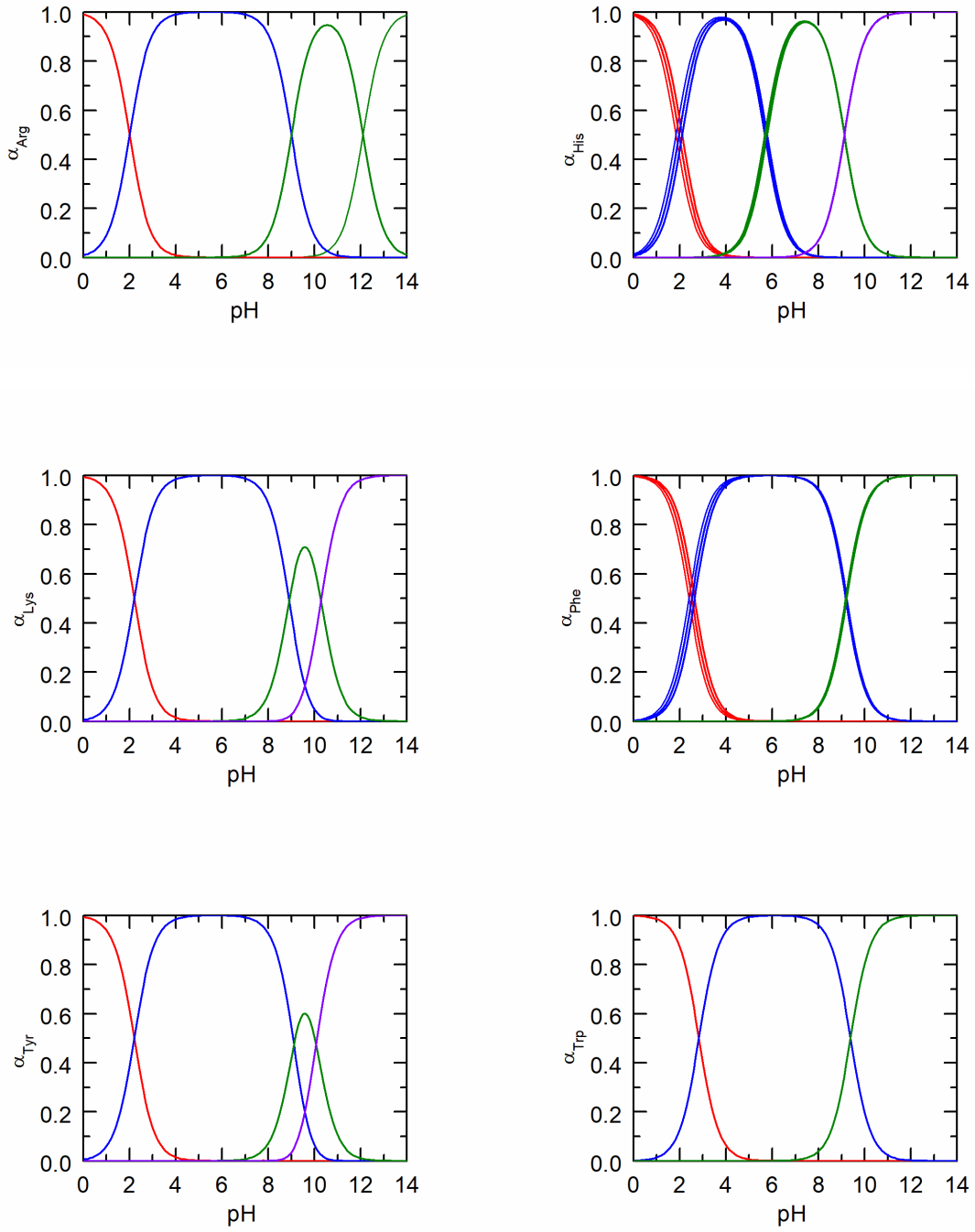
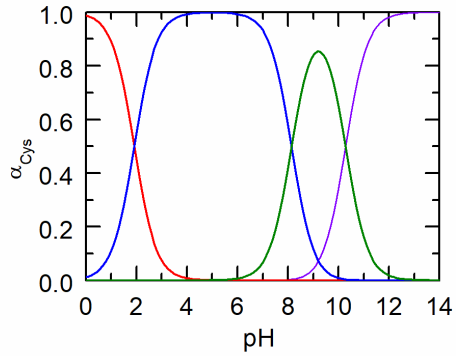
pH

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0.6
0.4
0.2
0.0
α_{Cys}
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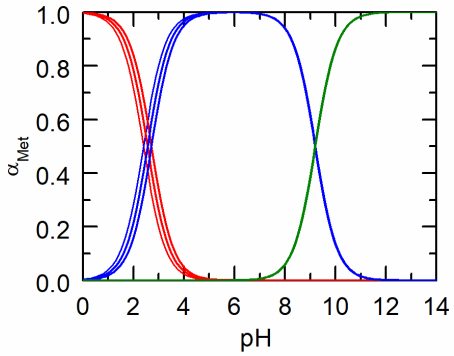
pH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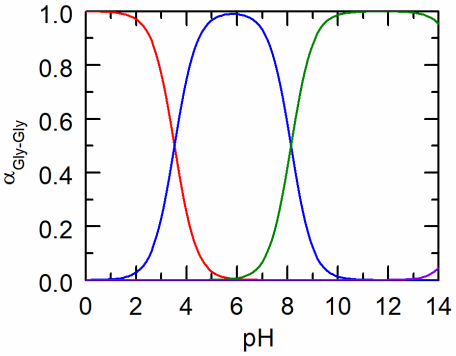
0.6
0.4
0.2
0.0
α_{Met}
0 2 4 6 8 10 12 14
pH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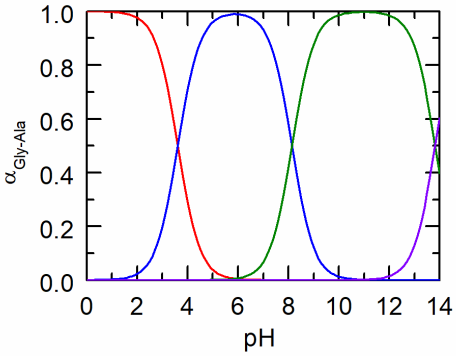
0.2
0.0
$\alpha_{Gly\text{-}Gly}$
0 2 4 6 8 10 12 14
pH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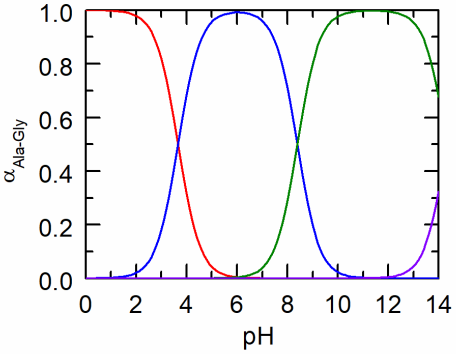
pH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0.6
0.4
0.2
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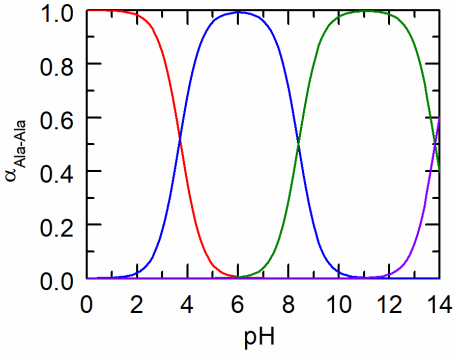
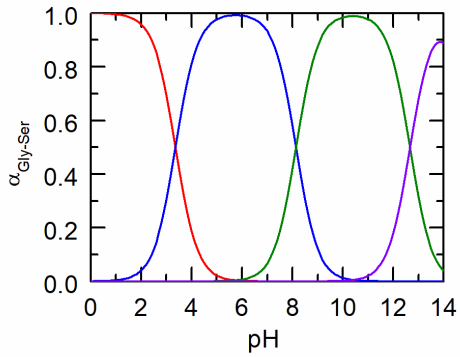
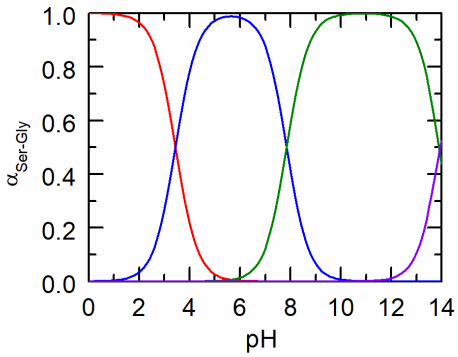
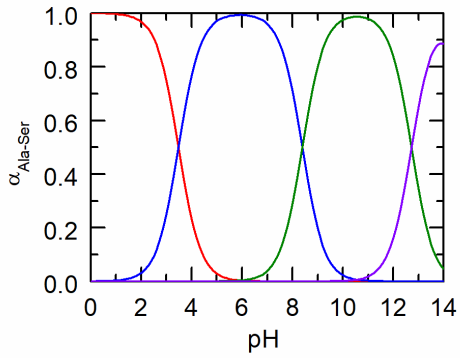
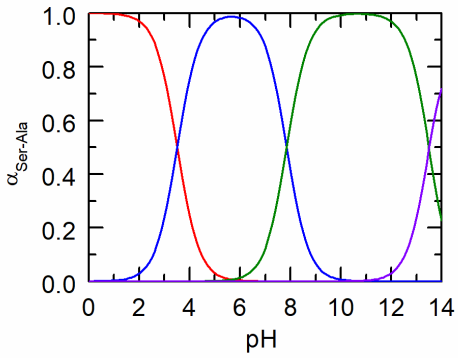
0 2 4 6 8 10 12 14
pH

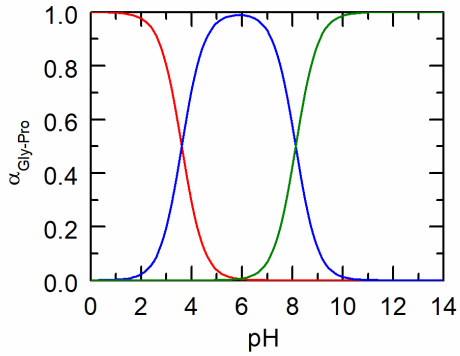

1.0
0.8
0.6
0.4
0.2
0.0
$\alpha_{Ala\text{-}Ala}$
0 2 4 6 8 10 12 14
pH

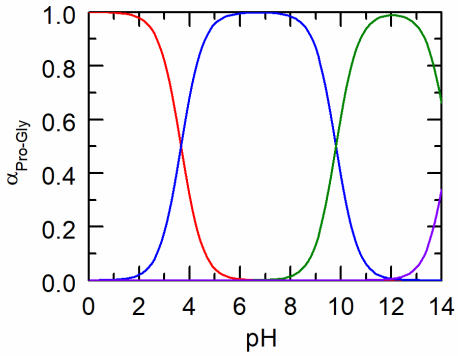


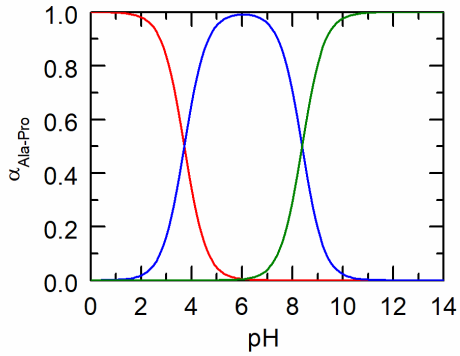








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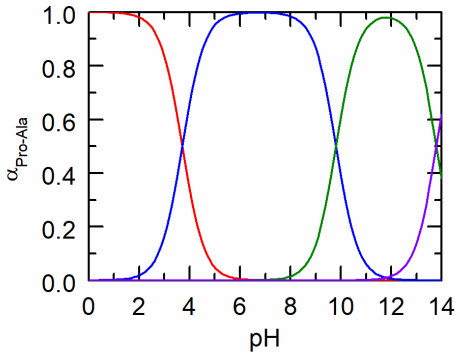
0.2
0.0
$\alpha_{Ala\text{-}Pro}$
0 2 4 6 8 10 12 14
pH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0.0
$\alpha_{Pro\text{-}Ala}$
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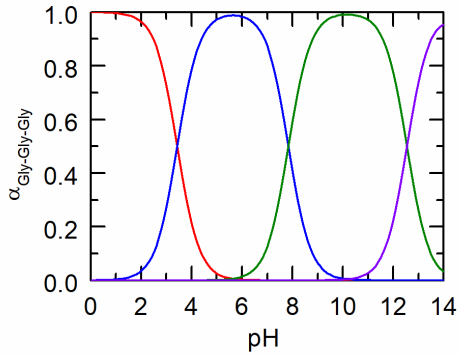
pH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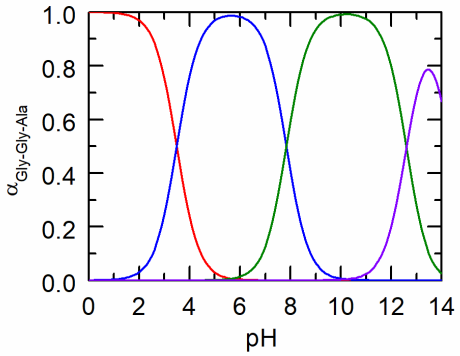
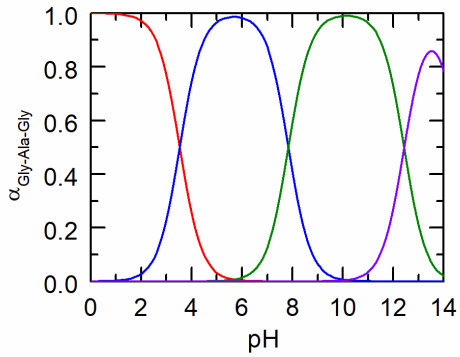
0.8
0.6
0.4
0.2
0.0
$\alpha_{Gly\text{-}Gly\text{-}Gly}$
0 2 4 6 8 10 12 14
pH


1.0
0.8
0.6
0.4
0.2
0.0
$\alpha_{Gly\text{-}Gly\text{-}Ala}$
0 2 4 6 8 10 12 14
pH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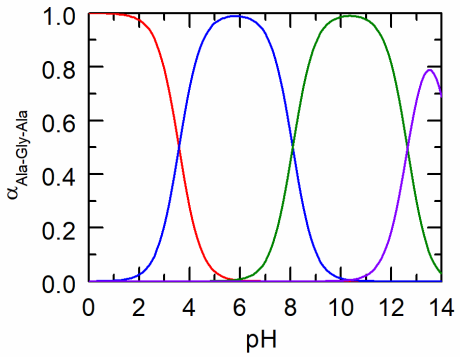
0.8
0.6
0.4
0.2
0.0
$\alpha_{Gly\text{-}Ala\text{-}Gly}$
0 2 4 6 8 10 12 14
pH


1.0
0.8
0.6
0.4
0.2
0.0
$\alpha_{Ala\text{-}Gly\text{-}Ala}$
0 2 4 6 8 10 12 14
pH

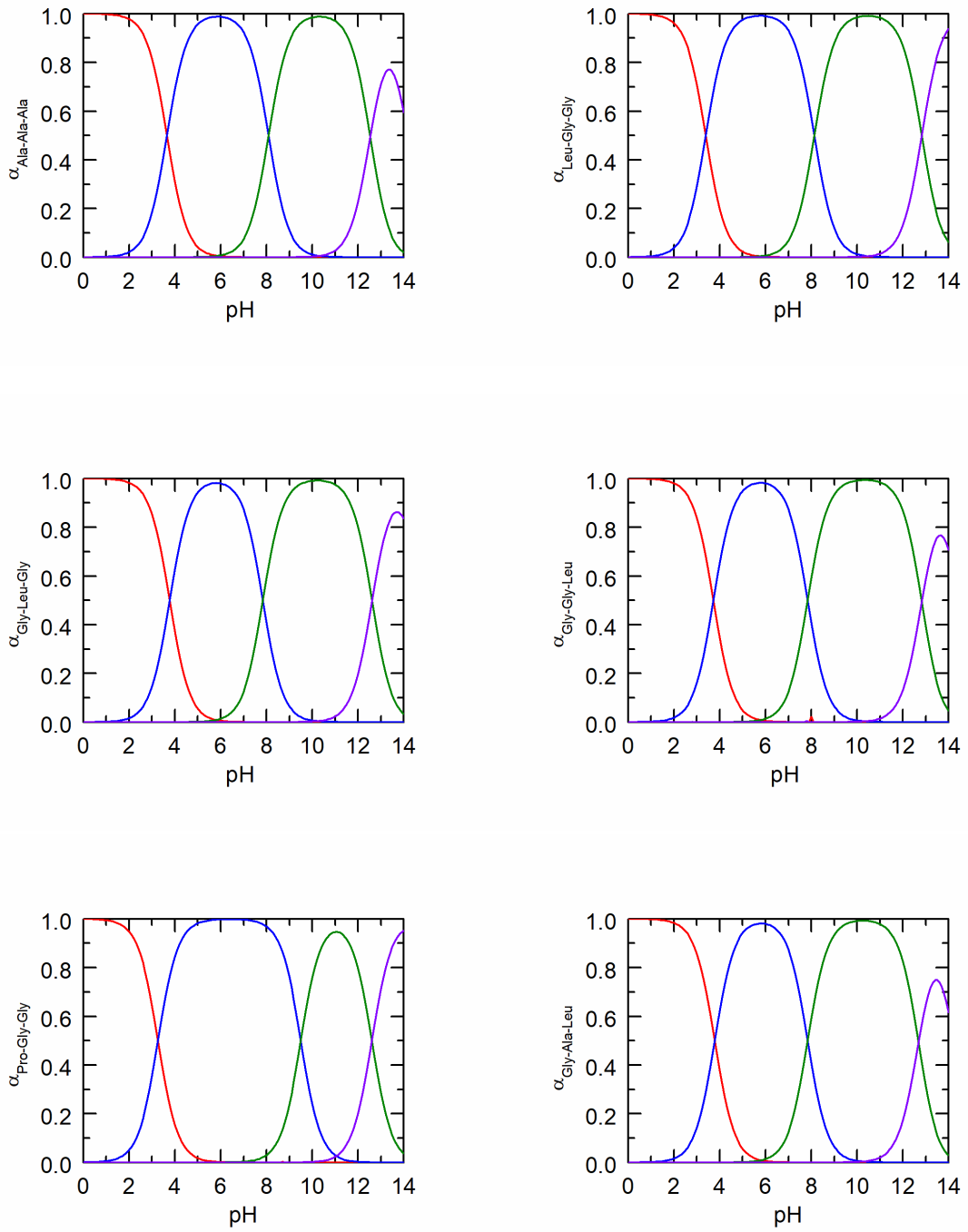


Figure S1 The pH distribution of peptides species in aqueous solution. Lines represent the contribution of species: positive net charged specie (red), zero net charge specie (blue), one negative net charged specie (green), species with double negative charge (violet).

5. PC-SAFT parameters

Table S4 PC-SAFT pure-component parameters and binary interaction parameters k_{ij} according to Equation (7). (1) amino acid/peptide, (2) water, (3) 2-propanol). The ARD values between the PC-SAFT modelled solubility and the experimental solubility data in aqueous solutions with 2-propanol are listed in the last column.

	m_i^{seg}	σ_i / Å	σ_i/k_B / K	ε^{AiBi}/k_B / K	κ^{AiBi}	N	k_{12} / 10^{-2}	k_{13} / 10^{-2}	k_{23} / 10^{-2}	ARD / %
H_2O	1.2047	[a]	353.94	2425.67	0.045	1/1	-	-	-4.4	-
2-propanol[d]	3.0929	3.209	208.42	2253.90	0.025	1/1	-	-	-4.4	-
Gly[c]	4.850	2.327	216.960	2598.060	0.039	1/1	-5.85[c]	+15.50	-	1.43
Ala[c]	5.465	2.522	287.590	3176.600	0.082	1/1	-6.12[c]	+3.75	-	8.50
Val[b]	7.485	2.589	306.410	3183.800	0.039	1/1	-7.57[b]	-3.15	-	14.88
Leu[b]	8.304	2.700	330.000	3600.000	0.020	1/1	-6.39[b]	-4.86	-	9.74
Ile[b]	8.241	2.586	281.884	2207.529	0.001	1/1	-8.75[b]	-2.47	-	5.21
Pro[b]	6.981	2.548	289.720	5527.750	0.036	1/1	-6.99[b]	-	-	-
Ser[b]	7.024	2.284	236.920	2671.930	0.039	2/1	-2.57[b]	-	-	-
Thr[b]	6.329	2.606	325.370	2519.410	0.039	2/1	-2.78[b]	+4.58	-	9.33
Asp[d]	5.827	2.522	287.625	2544.234	0.041	2/1	+1.45[d]	+17.63	-	10.01
Asn[b]	3.000	3.367	280.000	3265.670	0.044	1/2	+0.00[b]	-	-	-
Glu[d]	6.831	2.560	227.192	2544.234	0.041	2/1	-4.45[d]	+15.74	-	8.25
Gln[d]	9.289	2.360	273.555	2637.341	0.020	1/2	-5.18[d]	+1.70	-	10.04
Arg[b]	9.908	2.657	349.710	2555.450	0.039	1/3	-1.45[b]	-1.55	-	7.37
His[d]	9.088	2.473	281.954	2640.981	0.078	1/2	-3.89[d]	+3.86	-	10.72
Lys[b]	11.673	2.378	301.210	3787.310	0.033	1/2	-7.07[b]	-	-	-
Phe[d]	9.310	2.690	391.827	3206.094	0.010	1/1	-5.18[d]	-8.57	-	2.79
Tyr[b]	8.139	2.280	289.370	2500.000	0.040	2/1	$+2.27 \cdot 10^{-4}$	+3.87	-	4.35
Trp[d]	10.577	2.825	260.641	2563.249	0.024	1/2	-7.68	-0.22	-	13.64
Cys[b]	7.739	2.384	322.910	1964.000	0.010	1/2	-2.35	-	-	-
Met[b]	16.026	2.150	220.370	1964.000	0.010	1/2	-1.43	-	-	-
Gly-Gly	7.337	2.327	216.959	2598.060	0.039	1/1	-8.04	+13.00	-	10.84
Gly-Ala	9.154	2.445	257.126	2946.760	0.065	1/1	-7.60	+2.67	-	4.82
Ala-Gly	9.206	2.423	249.314	2883.420	0.060	1/1	-8.13	+2.67	-	12.53
Ala-Ala	9.824	2.522	287.587	3176.595	0.082	1/1	-7.27	-2.00	-	1.15
Gly-Ser	9.353	2.417	229.568	2645.475	0.039	2/1	-5.94	+9.20	-	6.56
Ser-Gly	10.671	2.304	227.583	2638.186	0.039	2/1	-7.50	+4.06	-	10.23
Ala-Ser	9.583	2.537	256.471	2878.429	0.056	2/1	-6.35	-0.10	-	4.79
Ser-Ala	11.290	2.403	261.026	2924.261	0.060	2/1	-7.30	+5.31	-	25.64
Gly-Pro	10.671	2.474	262.800	4539.860	0.037	1/1	-8.49	-	-	-
Pro-Gly	-	-	-	-	-	-	-	-	-	-
Ala-Pro	-	-	-	-	-	-	-	-	-	-
Pro-Ala	11.352	2.536	288.708	4415.543	0.058	1/1	-6.48	-0.20	-	8.61
Gly-Gly-Gly	10.156	2.410	216.959	2598.061	0.039	1/1	-7.48	+11.70	-	3.58
Gly-Gly-Ala	12.754	2.412	245.150	2848.850	0.058	1/1	-9.50	+1.65	-	7.25
Gly-Ala-Gly	9.474	52.645		2800.426	0.054	1/1	-9.01	+9.00	-	1.49
Ala-Gly-Ala				-	-	-	-		-	-
Ala-Ala-Ala	-	-	-	-	-	-	-		-	-
Leu-Gly-Gly	15.697	2.501	263.725	3064.420	0.030	1/1	-9.08	-3.70	-	2.91
Gly-Leu-Gly	13.725	2.612	263.270	3060.300	0.030	1/1	-7.16	+0.32	-	1.61
Gly-Gly-Leu	12.222	2.758	262.250	3100.484	0.020	1/1	-7.05	+5.00	-	4.56
Gly-Ala-Leu	16.350	2.567	289.303	3259.600	0.041	1/1	-7.01	-1.00	-	1.29

[a] Temperature-dependent segment diameter σ = 2.7927+10.11 exp(-0.01775T)-1.417 exp(-0.01146T), [b]pure-component parameters from Held et al.[3], [c]pure-component parameters from Chua et al.[4], [d]pure-component parameters from this work, [e]pure-component parameters from Gross and Sadowski[5]

6. Melting properties

Table S5 Melting properties used in PC-SAFT: melting temperature T_{0i}^{SL}, melting enthalpy Δh_{0i}^{SL} and the slope ($a_{c_{poi}}^{L}$, $a_{c_{poi}}^{S}$) and interception ($b_{c_{poi}}^{L}$, $b_{c_{poi}}^{S}$) of the heat capacity of liquid and solid, and difference in the heat capacity at melting temperature $\Delta c_{p0i}^{SL}(T_{0i}^{SL})$.

Amino acid / peptide	T_{0i}^{SL} / *K*	Δh_{0i}^{SL} / *kJ·mol⁻¹*	$a_{c_{poi}}^{L}$ / *J·mol⁻¹·K⁻²*	$b_{c_{poi}}^{L}$ / *J·mol⁻¹·K⁻¹*	$a_{c_{poi}}^{S}$ / *J·mol⁻¹·K⁻²*	$b_{c_{poi}}^{S}$ / *J·mol⁻¹·K⁻¹*	$\Delta c_{p0i}^{SL}(T_{0i}^{SL})$ / *J·mol⁻¹·K⁻¹*
Gly	*569*	*24.96*	*0.225*	*62.681*	*0.266*	*21.033*	*18.59*
Ala	*608*	*25.99*	*0.267*	*64.148*	*0.324*	*24.225*	*5.26*
Val	*529*	*46.72*	*0.351*	*106.488*	*0.453*	*32.573*	*20.00*
Leu	*518*	*49.09*	*0.525*	*71.622*	*0.577*	*24.322*	*10.15*
Ile	*595*	*47.11*	*0.459*	*87.228*	*0.512*	*35.624*	*20.39*
Pro	-	-	-	-	-	-	-
Ser[c]	*519*	*32.98*	*0.267*	*121.318*	*0.346*	*31.028*	*49.38*
Thr	*587*	*36.64*	*0.379*	*125.276*	*0.406*	*47.019*	*62.18*
Asp	*610*	*35.73*	*0.176*	*213.341*	*0.397*	*37.182*	*41.37*
Asn	-	-	-	-	-	-	-
Glu	*566*	*48.24*	*0.321*	*147.115*	*0.481*	*32.014*	*24.33*
Gln	*589*	*51.96*	*0.474*	*129.528*	*0.500*	*34.849*	*79.19*
Arg	*558*	*28.64*	*0.326*	*265.689*	*0.690*	*27.698*	*34.83*
His	*619*	*56.01*	*0.507*	*152.902*	*0.537*	*21.854*	*112.80*
Lys	-	-	-	-	-	-	-
Phe	*579*	*60.66*	*0.496*	*280.823*	*0.635*	*15.731*	*184.37*
Tyr	*678*	*49.77*	*0.664*	*93.511*	*0.681*	*19.229*	*62.74*
Trp	*620*	*65.55*	*0.351*	*289.570*	*0.758*	*15.771*	*21.82*
Cys	-	-	-	-	-	-	-
Met	-	-	-	-	-	-	-
Gly-Gly	*593*	*42.18*	*0.256*	*185.660*	*0.415*	*41.175*	*50.469*
Gly-Ala	*551*	*38.38*	*0.253*	*219.937*	*0.474*	*44.123*	*54.219*
Ala-Gly	*611*	*47.03*	*0.357*	*169.339*	*0.475*	*41.054*	*55.956*
Ala-Ala	*606*	*41.44*	*0.396*	*175.923*	*0.503*	*49.918*	*60.971*
Gly-Ser	*530*	*47.12*	*0.323*	*222.766*	*0.546*	*38.543*	*65.630*
Ser-Gly	*553*	*66.37*	*0.293*	*247.192*	*0.564*	*37.212*	*60.533*
Ala-Ser	*556*	*46.65*	*0.396*	*217.162*	*0.641*	*33.400*	*47.609*
Ser-Ala	*609*	*79.03*	*0.328*	*254.405*	*0.585*	*44.293*	*53.470*
Gly-Pro	*541*	*25.06*	*0.604*	*96.144*	*0.658*	*31.474*	*35.794*
Pro-Gly[d]	-	-	-	-	-	-	-
Ala-Pro[e]	-	-	-	-	-	-	-
Pro-Ala	*624*	*41.93*	*0.525*	*135.934*	*0.631*	*47.121*	*22.582*
Gly-Gly-Gly	*594*	*52.64*	*0.418*	*244.477*	*0.630*	*48.568*	*70.058*
Gly-Gly-Ala	*592*	*70.15*	*0.503*	*223.719*	*0.675*	*57.131*	*64.940*
Gly-Ala-Gly	*623*	*60.03*	*0.528*	*223.619*	*0.675*	*55.335*	*77.284*
Ala-Gly-Ala[d]	-	-	-	-	-	-	-
Ala-Ala-Ala[d]	-	-	-	-	-	-	-
Leu-Gly-Gly	*530*	*73.03*	*0.390*	*428.149*	*0.885*	*55.252*	*159.252*
Gly-Leu-Gly	*545*	*65.43*	*0.797*	*251.747*	*0.888*	*63.721*	*138.565*
Gly-Gly-Leu	*521*	*59.63*	*0.621*	*409.351*	*1.028*	*37.967*	*110.302*
Gly-Ala-Leu	*578*	*77.06*	*0.576*	*394.529*	*0.946*	*69.079*	*111.494*

7. Solubility data and pH values

Table S6 Solubility w^{sat}_{Solute} (and $w^{sat}_{Solute,pH=7}$) of amino acids and peptides in aqueous-2-propanol saturated unbuffered (and shifted to pH = 7 using Henderson Hasselbalch eq. Table S3) solutions at T = 298.15 K and p = 1 atm, pH values of saturated solutions under study (uncertainties represents the standard deviations of multiple measurements, isoelectric point (pI) from the platform Chemicalize® and literature for amino acids by Dey et al.[6]. Additionally information about a crystal structure change using PXRD and the PC-SAFT modeled activity coefficients are given.

Solute	w_{H2O} / $g \cdot g^{-1}$	$w_{2-prop.}$ / $g \cdot g^{-1}$	w^{sat}_{Solute} / $g \cdot g^{-1}$	pH^{sat}	pI[6]	$w^{sat}_{Solute,pH=7}$ / $g \cdot g^{-1}$	PXRD transitions	γ^{L}
Gly	1.000	0.000	0.2019 ± 0.0020	6.32 ± 0.04	5.97		Polymorphs	0.306
	0.900	0.100	0.1366 ± 0.0018	5.8 ± 0.01				
	0.802	0.198	0.0885 ± 0.0021	6.23 ± 0.01				
	0.703	0.297	0.0587 ± 0.002	6.26 ± 0.01				
Ala	1.000	0.000	0.1415 ± 0.0015	6.33 ± 0.02	6.00			0.236
	0.900	0.100	0.0987 ± 0.0010	6.31 ± 0.03				0.312
	0.800	0.200	0.0649 ± 0.0010	6.29 ± 0.03				0.474
	0.700	0.300	0.0457 ± 0.0016	6.39 ± 0.03				0.730
Val	1.000	0.000	0.0553 ± 0.0006	6.08 ± 0.07	5.96			0.060
	0.900	0.100	0.0401 ± 0.0004	6.10 ± 0.03				0.073
	0.800	0.200	0.0258 ± 0.0014	6.22 ± 0.05				0.104
	0.701	0.299	0.0193 ± 0.0017	6.32 ± 0.07				0.155
Leu	1.000	0.000	0.0237 ± 0.0003	5.68 ± 0.15	5.98			0.130
	0.900	0.100	0.0184 ± 0.0005	5.56 ± 0.04				0.140
	0.800	0.200	0.0133 ± 0.0010	5.69 ± 0.04				0.175
	0.700	0.300	0.0095 ± 0.0013	5.89 ± 0.01				0.240
Ile	1.000	0.000	0.0329 ± 0.0003	6.22 ± 0.14	6.02			0.043
	0.900	0.100	0.0248 ± 0.0004	5.78 ± 0.51				0.052
	0.800	0.200	0.0175 ± 0.0003	6.24 ± 0.03				0.070
	0.701	0.299	0.0149 ± 0.0009	6.34 ± 0.73				0.102
Pro	1.000	0.000	0.6365 ± 0.0154	7.26 ± 0.07	6.30		Monohydrate	
	0.900	0.100	0.5481 ± 0.0183	7.43 ± 0.01				
	0.800	0.200	0.5047 ± 0.0047	7.39 ± 0.01				
	0.701	0.299	0.4510 ± 0.0040	7.38 ± 0.01				
Ser	1.000	0.000	0.2867 ± 0.0123	6.01 ± 0.02	5.68		Monohydrate	
	0.900	0.100	0.2128 ± 0.0027	5.93 ± 0.01				
	0.801	0.199	0.1365 ± 0.0013	5.98 ± 0.01				
	0.702	0.298	0.0865 ± 0.0006	6.06 ± 0.01				
Thr	1.000	0.000	0.0894 ± 0.0008	5.87 ± 0.01	5.60			0.465
	0.900	0.100	0.0559 ± 0.0006	5.72 ± 0.04				0.667
	0.800	0.200	0.0339 ± 0.0006	5.82 ± 0.04				1.121
	0.700	0.300	0.0214 ± 0.0004	5.90 ± 0.04				1.892
Asp	1.000	0.000	0.0057 ± 0.0002	3.05 ± 0.01	2.77			5.819
	0.900	0.100	0.0027 ± 0.0005	3.09 ± 0.03				9.098
	0.800	0.200	0.0016 ± 0.0001	3.26 ± 0.03				16.215
	0.700	0.300	0.0009 ± 0.0001	3.44 ± 0.05				28.003
Asn	1.000	0.000	0.0267 ± 0.0016	5.13 ± 0.05	5.41		Monohydrate	
	0.900	0.100	0.0139 ± 0.0009	5.12 ± 0.03				
	0.800	0.200	0.0083 ± 0.0002	5.25 ± 0.03				
	0.700	0.300	0.0049 ± 0.0004	5.35 ± 0.04				
Glu	1.000	0.000	0.0088 ± 0.0003	3.28 ± 0.04	3.22			0.324
	0.900	0.100	0.0049 ± 0.0001	3.33 ± 0.03				0.481
	0.800	0.200	0.0030 ± 0.0001	3.49 ± 0.03				0.820
	0.700	0.300	0.0021 ± 0.0001	3.70 ± 0.03				1.380
Gln	1.000	0.000	0.0405 ± 0.0002	5.01 ± 0.04	5.65			0.114
	0.900	0.100	0.0260 ± 0.0004	4.31 ± 0.06				0.156
	0.800	0.200	0.0163 ± 0.0005	4.48 ± 0.03				0.248
	0.700	0.300	0.0105 ± 0.0004	4.67 ± 0.03				0.403
Arg	1.000	0.000	0.1639 ± 0.0034	11.45 ± 0.02	10.8			0.967
	0.900	0.100	0.1437 ± 0.0112	11.34 ± 0.04				1.017
	0.800	0.200	0.1108 ± 0.0093	11.40 ± 0.04				1.258
	0.700	0.300	0.0883 ± 0.0035	11.46 ± 0.04				1.729
His	1.000	0.000	0.0414 ± 0.0003	7.75 ± 0.05	7.59			0.205
	0.900	0.100	0.0266 ± 0.0003	7.65 ± 0.03				0.278
	0.800	0.200	0.0172 ± 0.0004	7.62 ± 0.04				0.441
	0.700	0.300	0.0113 ± 0.0003	7.57 ± 0.03				0.720
Lys	1.000	0.000	0.5197 ± 0.1256	10.66 ± 0.10	9.74			
	0.900	0.100	0.6294 ± 0.0278	10.51 ± 0.05				
	0.800	0.200	0.5907 ± 0.0110	10.49 ± 0.04				
	0.700	0.300	0.6177 ± 0.0189	10.26 ± 0.06				
Phe	1.000	0.000	0.0291 ± 0.0007	5.99 ± 0.20	5.48			1.750
	0.900	0.100	0.0216 ± 0.0001	5.64 ± 0.04				1.935

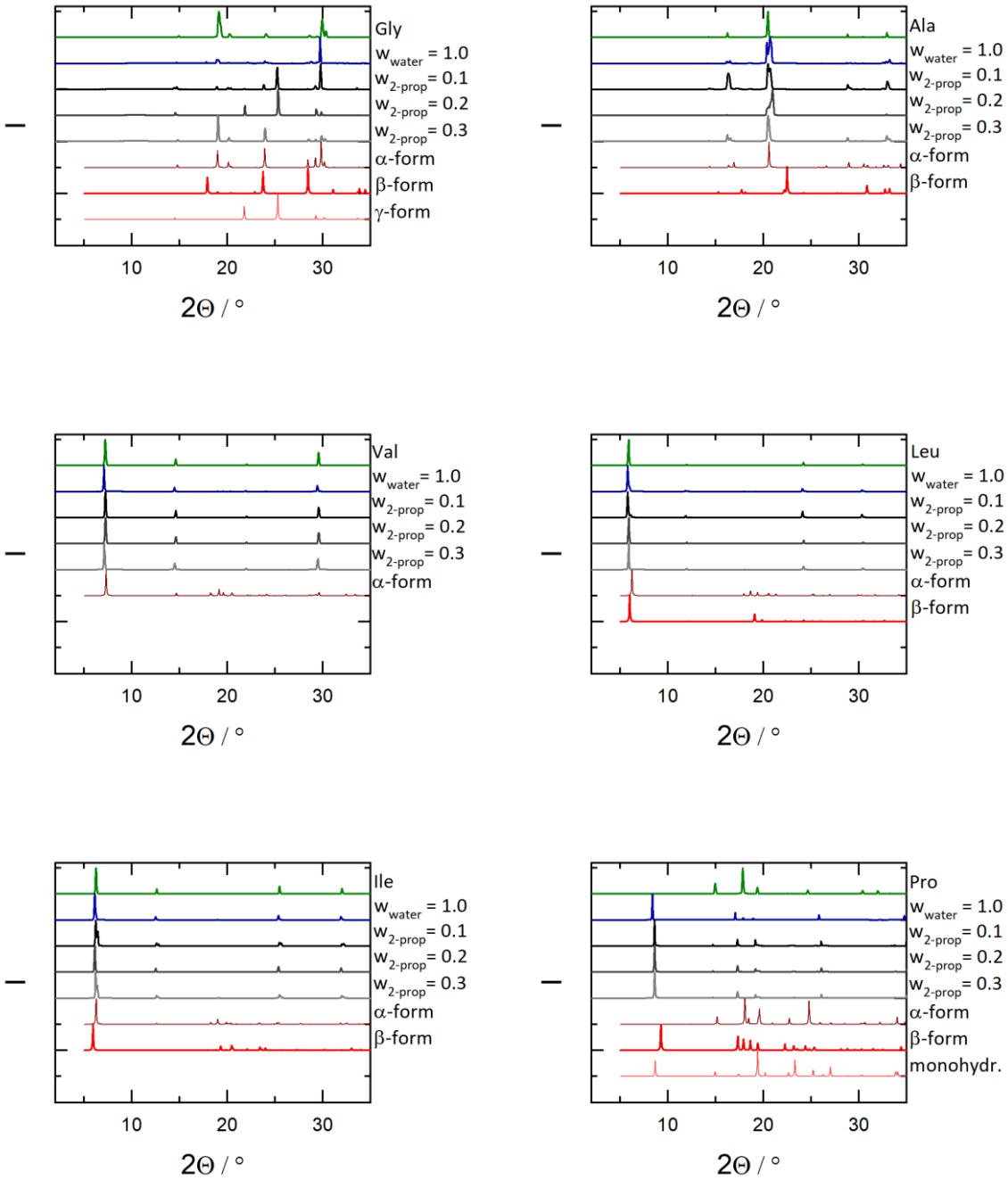
	0.800	0.200	0.0167 ± 0.0004	5.97 ± 0.49				2.569
	0.700	0.300	0.0163 ± 0.0007	5.75 ± 0.03				3.784
Tyr	1.000	0.000	0.0006 ± 0.0001	5.77 ± 0.34	5.66			11.158
	0.900	0.100	0.000444 ± 0.000016	6.44 ± 0.04				11.582
	0.800	0.200	0.000354 ± 0.000013	5.99 ± 0.04				13.605
	0.700	0.300	0.000243 ± 0.000026	5.91 ± 0.05				17.208
Trp	1.000	0.000	0.0138 ± 0.0001	5.08 ± 0.11	5.89			0.021
	0.900	0.100	0.0095 ± 0.0029	5.85 ± 0.04				0.017
	0.800	0.200	0.0123 ± 0.0021	5.41 ± 0.04				0.016
	0.700	0.300	0.0129 ± 0.0007	5.15 ± 0.04				0.019
Cys	1.000	0.000	0.0813b	5.14 ± 0.03	5.74		Polymorph	
	0.900	0.100	0.0951 ± 0.0010	5.20 ± 0.05				
	0.800	0.200	0.0605 ± 0.0006	5.31 ± 0.04				
	0.700	0.300	0.0414 ± 0.0005	5.42 ± 0.03				
Met[a]	1.000	0.000	0.0536 ± 0.0014	5.91 ± 0.03	5.07			
	0.900	0.100	0.0329 ± 0.0060	6.00 ± 0.05				
	0.800	0.200	0.0298 ± 0.0054	6.00 ± 0.03				
	0.700	0.300	0.0198 ± 0.0006	6.00 ± 0.05				
Gly-Gly	1.000	0.000	0.1948 ± 0.0040	5.85 ± 0.01	5.83	0.2048 ± 0.0040		0.075
	0.900	0.100	0.0944 ± 0.0195	5.79 ± 0.01		0.1004 ± 0.0195		0.139
	0.801	0.199	0.0587 ± 0.0008	5.83 ± 0.01		0.0624 ± 0.0008		0.308
	0.702	0.298	0.0319 ± 0.0005	5.88 ± 0.01		0.0339 ± 0.0005		0.615
Gly-Ala	1.000	0.000	0.4019 ± 0.0040	6.08 ± 0.02	5.88	0.4172 ± 0.0040		0.086
	0.901	0.099	0.3501 ± 0.0026	6.07 ± 0.01		0.3728 ± 0.0026		0.099
	0.800	0.200	0.2791 ± 0.0011	6.10 ± 0.01		0.2967 ± 0.0011		0.131
	0.703	0.297	0.2133 ± 0.0021	6.14 ± 0.01		0.2265 ± 0.0021		0.200
Ala-Gly	1.000	0.000	0.1745 ± 0.0010	5.85 ± 0.07	6.03	0.1792 ± 0.0010		0.037
	0.901	0.099	0.1213 ± 0.0002	5.85 ± 0.03		0.1252 ± 0.0002		0.052
	0.800	0.200	0.0709 ± 0.0016	5.90 ± 0.01		0.0732 ± 0.0016		0.087
	0.701	0.299	0.0427 ± 0.0008	5.91 ± 0.08		0.0441 ± 0.0008		0.150
Ala-Ala	1.000	0.000	0.2895 ± 0.0100	5.77 ± 0.02	6.06	0.2959 ± 0.0200		0.080
	0.901	0.099	0.2780 ± 0.0021	5.87 ± 0.02		0.2869 ± 0.0021		0.091
	0.801	0.199	0.2126 ± 0.0017	5.91 ± 0.01		0.2195 ± 0.0017		0.119
	0.704	0.296	0.1594 ± 0.0015	6.04 ± 0.01		0.1646 ± 0.0015		0.171
Gly-Ser	1.000	0.000	0.2894 ± 0.0110	5.73 ± 0.03	5.75	0.3029 ± 0.0110		0.044
	0.900	0.100	0.2115 ± 0.0046	5.73 ± 0.01		0.2255 ± 0.0046		0.063
	0.803	0.197	0.1157 ± 0.0026	5.64 ± 0.01		0.1232 ± 0.0026		0.122
	0.703	0.297	0.0644 ± 0.0081	5.69 ± 0.01		0.0686 ± 0.0081		0.239
Ser-Gly	1.000	0.000	0.0430 ± 0.0010	5.14 ± 0.01	5.65	0.0478 ± 0.0010		0.010
	0.900	0.100	0.0286 ± 0.0003	5.20 ± 0.01		0.0320 ± 0.0003		0.014
	0.800	0.200	0.0162 ± 0.0002	5.26 ± 0.01		0.0182 ± 0.0002		0.023
	0.700	0.300	0.0106 ± 0.0005	5.38 ± 0.01		0.0119 ± 0.0005		0.039
Ala-Ser	1.000	0.000	0.3325 ± 0.0130	5.70 ± 0.01	5.94	0.3401 ± 0.0130		0.026
	0.900	0.100	0.3366 ± 0.0019	5.66 ± 0.03		0.3482 ± 0.0019		0.027
	0.800	0.200	0.3134 ± 0.0375	5.68 ± 0.03		0.3242 ± 0.0375		0.030
	0.700	0.300	0.2097 ± 0.0274	5.75 ± 0.04		0.2169 ± 0.0274		0.035
Ser-Ala	1.000	0.000	0.0046 ± 0.0010	5.09 ± 0.01	5.68	0.0051 ± 0.0010		0.005
	0.900	0.100	0.0024 ± 0.0006	5.10 ± 0.01		0.0027 ± 0.0006		0.010
	0.800	0.200	0.0005 ± 0.0002	5.11 ± 0.09		0.0006 ± 0.0002		0.025
	0.700	0.300	0.0003 ± 0.0003	5.24 ± 0.01		0.0005 ± 0.0003		0.060
Gly-Pro	1.000	0.000	0.6638 ± 0.1240	6.88 ± 0.01	5.87	0.6682 ± 0.1240		0.184
	0.900	0.100	0.5475 ± 0.0153	6.74 ± 0.01		0.5675 ± 0.0153	Polymorph	
	0.804	0.196	0.5182 ± 0.0053	6.80 ± 0.01		0.5338 ± 0.0053		
	0.700	0.300	0.5012 ± 0.0152	6.84 ± 0.01		0.5135 ± 0.0152		
Pro-Gly	1.000	0.000	0.1941 ± 0.0080	6.02 ± 0.01	6.74	0.1937 ± 0.0080	Monohydrate	
	0.900	0.100	0.1560 ± 0.0021	6.05 ± 0.01		0.1557 ± 0.0021		
	0.802	0.198	0.0987 ± 0.0067	6.08 ± 0.01		0.0985 ± 0.0067		
	0.701	0.299	0.0691 ± 0.0029	6.14 ± 0.01		0.0690 ± 0.0029		
Ala-Pro	1.000	0.000	0.5141 ± 0.0150	6.39 ± 0.01	6.05	0.5221 ± 0.0150	Polymorph	
	0.900	0.100	0.5342 ± 0.0078	6.36 ± 0.05		0.5523 ± 0.0078		
	0.800	0.200	0.4898 ± 0.0159	6.42 ± 0.04		0.5057 ± 0.0159		
	0.700	0.300	0.4733 ± 0.0077	6.46 ± 0.03		0.4882 ± 0.0077		
Pro-Ala	1.000	0.000	0.0518 ± 0.0010	6.03 ± 0.01	6.76	0.0516 ± 0.0010		0.123
	0.900	0.100	0.0377 ± 0.0008	5.90 ± 0.03		0.0376 ± 0.0008		0.155
	0.800	0.200	0.0210 ± 0.0008	6.00 ± 0.04		0.0209 ± 0.0008		0.238
	0.700	0.300	0.0132 ± 0.0008	6.11 ± 0.03		0.0131 ± 0.0008		0.393
Gly-Gly-Gly	1.000	0.000	0.0612 ± 0.0010	5.65 ± 0.02	5.64	0.0688 ± 0.0010		0.128
	0.900	0.100	0.0308 ± 0.0008	5.69 ± 0.03		0.0348 ± 0.0008		0.206
	0.800	0.200	0.0144 ± 0.0005	5.74 ± 0.03		0.0162 ± 0.0005		0.377
	0.700	0.300	0.0072 ± 0.0009	5.83 ± 0.03		0.0082 ± 0.0009		0.673
Gly-Gly-Ala	1.000	0.000	0.0448 ± 0.0010	5.43 ± 0.02	5.67	0.0503 ± 0.0010		0.004
	0.900	0.100	0.0254 ± 0.0006	5.50 ± 0.03		0.0287 ± 0.0006		0.006
	0.800	0.200	0.0122 ± 0.0002	5.56 ± 0.04		0.0137 ± 0.0015		0.013

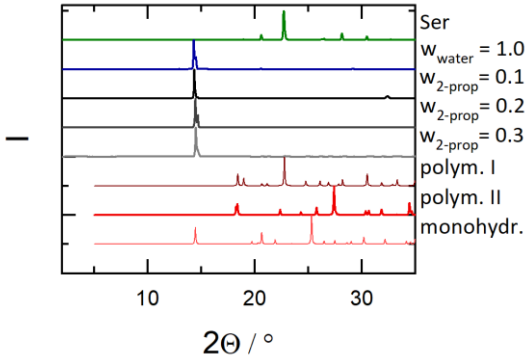
	0.700	*0.300*	*0.0068 ± 0.0001*	*5.69 ± 0.04*		*0.0077 ± 0.0016*		*0.027*
Gly-Ala-Gly	*1.000*	*0.000*	*0.0491 ± 0.0010*	*4.65 ± 0.01*	*5.69*	*0.0520 ± 0.0010*		*0.042*
	0.900	*0.100*	*0.0265 ± 0.0002*	*4.70 ± 0.04*		*0.0284 ± 0.0002*		*0.073*
	0.800	*0.200*	*0.0129 ± 0.0007*	*4.73 ± 0.04*		*0.0139 ± 0.0007*		*0.158*
	0.700	*0.300*	*0.0068 ± 0.0003*	*4.86 ± 0.05*		*0.0074 ± 0.0003*		*0.339*
Ala-Gly-Ala	*1.000*	*0.000*	*0.4059 ± 0.0010*	*5.86 ± 0.02*	*5.84*	*0.4232 ± 0.0010*	*Monohydrate*	
	0.900	*0.100*	*0.3563 ± 0.0013*	*5.91 ± 0.02*		*0.3822 ± 0.0013*		
	0.800	*0.200*	*0.2775 ± 0.0806*	*5.94 ± 0.01*		*0.2974 ± 0.0806*		
	0.700	*0.300*	*0.2107 ± 0.0390*	*5.95 ± 0.01*		*0.2256 ± 0.0390*		
Ala-Ala-Ala	*1.000*	*0.000*	*0.0946 ± 0.0040*	*5.51 ± 0.01*	*5.87*	*0.1002 ± 0.0040*	*Hemihydrate*	
	0.900	*0.100*	*0.0947 ± 0.0019*	*5.15 ± 0.04*		*0.1017 ± 0.0019*		
	0.800	*0.200*	*0.0584 ± 0.0030*	*5.41 ± 0.04*		*0.0632 ± 0.0030*		
	0.700	*0.300*	*0.0328 ± 0.0015*	*5.46 ± 0.04*		*0.0355 ± 0.0015*		
Leu-Gly-Gly	*1.000*	*0.000*	*0.2812 ± 0.0030*	*5.42 ± 0.02*	*5.76*	*0.2940 ± 0.0030*		*0.004*
	0.900	*0.100*	*0.2470 ± 0.0127*	*5.51 ± 0.04*		*0.2632 ± 0.0127*		*0.004*
	0.800	*0.200*	*0.2181 ± 0.0037*	*5.55 ± 0.04*		*0.2325 ± 0.0030*		*0.005*
	0.700	*0.300*	*0.1650 ± 0.0031*	*5.64 ± 0.04*		*0.1760 ± 0.0019*		*0.006*
Gly-Leu-Gly	*1.000*	*0.000*	*0.0625 ± 0.0013*	*5.34 ± 0.01*	*5.81*	*0.0693 ± 0.0010*		*0.070*
	0.900	*0.100*	*0.0561 ± 0.0105*	*5.56 ± 0.09*		*0.0630 ± 0.0105*		*0.072*
	0.800	*0.200*	*0.0460 ± 0.0072*	*5.62 ± 0.06*		*0.0517 ± 0.0072*		*0.092*
	0.700	*0.300*	*0.0252 ± 0.0044*	*5.73 ± 0.06*		*0.0283 ± 0.0044*		*0.136*
Gly-Gly-Leu	*1.000*	*0.000*	*0.1676 ± 0.0040*	*5.71 ± 0.01*	*5.77*	*0.1866 ± 0.0040*		*0.186*
	0.900	*0.100*	*0.1176 ± 0.0016*	*5.75 ± 0.03*		*0.1325 ± 0.0016*		*0.231*
	0.800	*0.200*	*0.0798 ± 0.0021*	*5.87 ± 0.04*		*0.0899 ± 0.0021*		*0.366*
	0.720	*0.280*	*0.0680 ± 0.0019*	*6.01 ± 0.04*		*0.0764 ± 0.0019*		*0.649*
Gly-Ala-Leu	*1.000*	*0.000*	*0.0141 ± 0.0010*	*5.89 ± 0.01*	*5.81*	*0.0158 ± 0.0010*		*0.041*
	1.000	*0.000*	*0.0096 ± 0.0008*	*5.92 ± 0.02*		*0.0108 ± 0.0008*		*0.056*
	0.900	*0.100*	*0.0068 ± 0.0006*	*5.94 ± 0.02*		*0.0076 ± 0.0006*		*0.102*
	0.800	*0.200*	*0.0028 ± 0.0019*	*5.97 ± 0.01*		*0.0032 ± 0.0019*		*0.208*

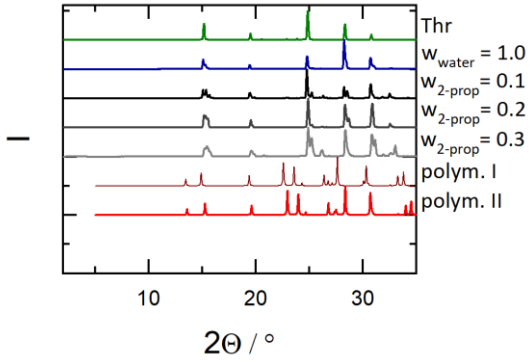
[a] For Met no experimental determined melting properties was possible to measure using FSC, [b] solubility data measured from previous work[7], [c] solubility data measured from previous work[8], [d] Bowden,2018[9]

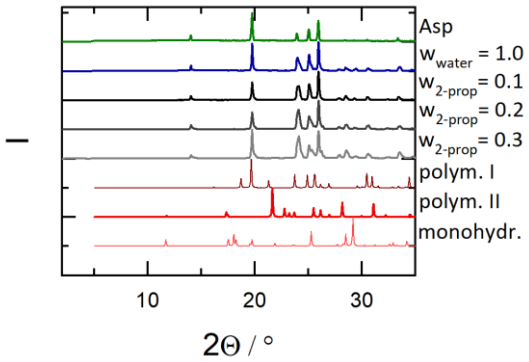
8. Diffractograms

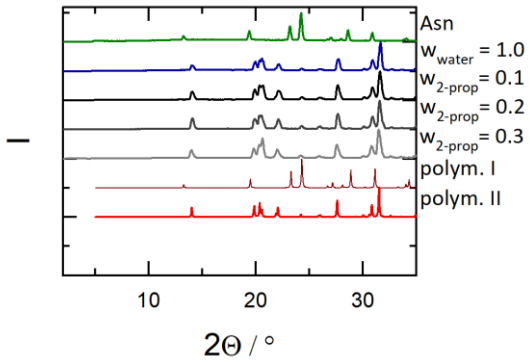
PXRD measurements of pure amino acids and the amino acids in solid phase equilibrated with saturated solution




Ser
w_{water} = 1.0
$w_{2\text{-}prop}$ = 0.1
$w_{2\text{-}prop}$ = 0.2
$w_{2\text{-}prop}$ = 0.3
polym. I
polym. II
monohydr.
10
20
30
2Θ / °


Thr
w_{water} = 1.0
$w_{2\text{-}prop}$ = 0.1
$w_{2\text{-}prop}$ = 0.2
$w_{2\text{-}prop}$ = 0.3
polym. I
polym. II
10
20
30
2Θ / °


Asp
w_{water} = 1.0
$w_{2\text{-}prop}$ = 0.1
$w_{2\text{-}prop}$ = 0.2
$w_{2\text{-}prop}$ = 0.3
polym. I
polym. II
monohydr.
10
20
30
2Θ / °


Asn
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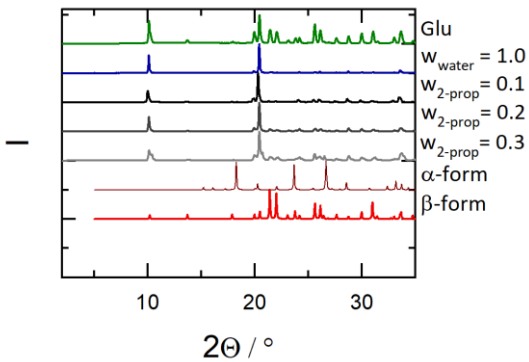
$w_{2\text{-}prop}$ = 0.2
$w_{2\text{-}prop}$ = 0.3
polym. I
polym. II
10
20
30
2Θ / °


Glu
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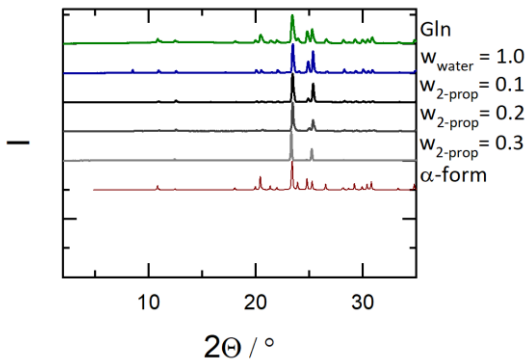
$w_{2\text{-}prop}$ = 0.3
α-form
β-form
10
20
30
2Θ / °


Gln
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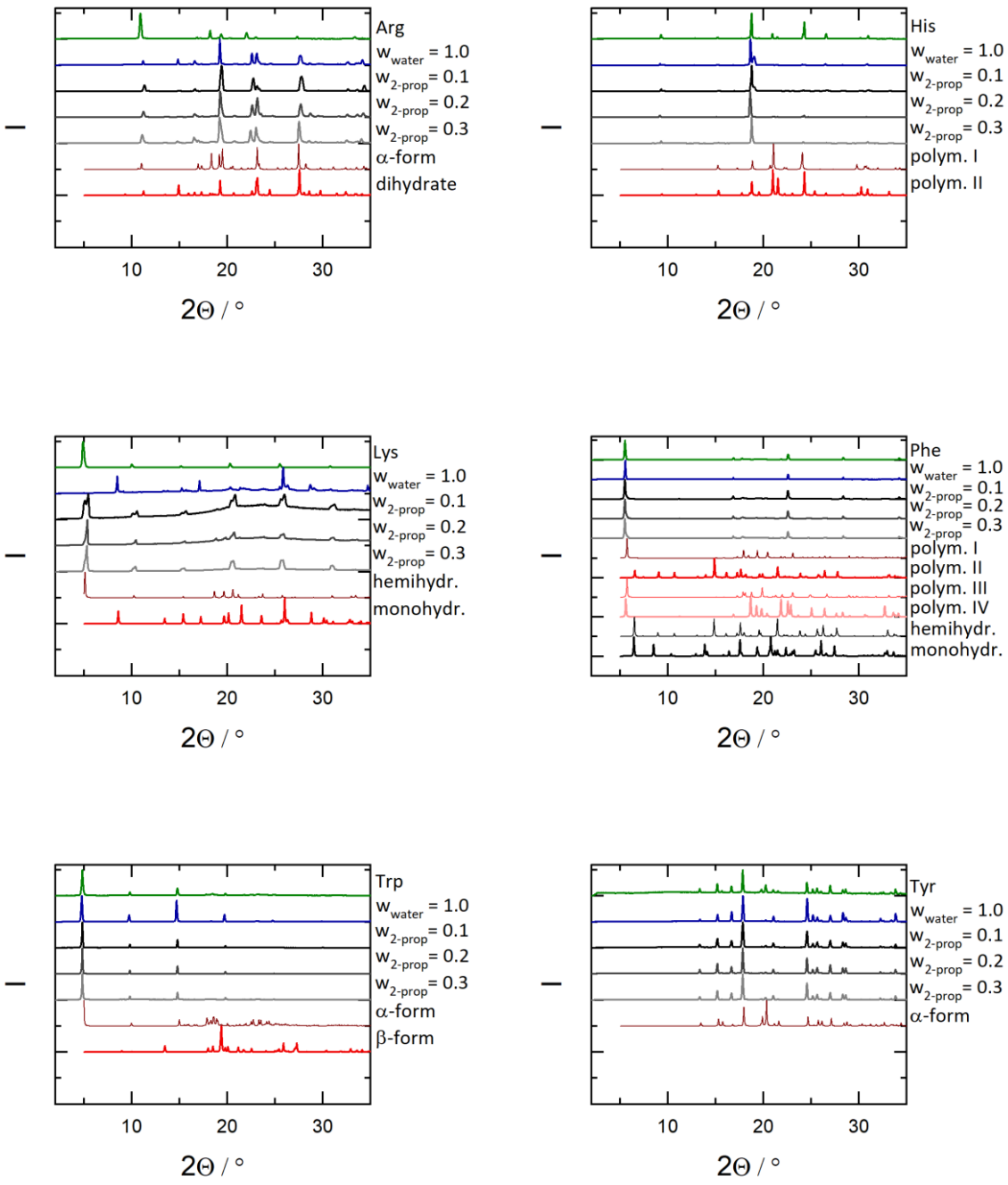
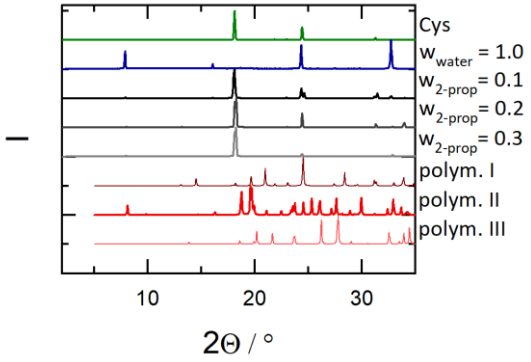
$w_{2\text{-}prop}$ = 0.3
α-form
10
20
30
2Θ / °




Cys
w_{water} = 1.0
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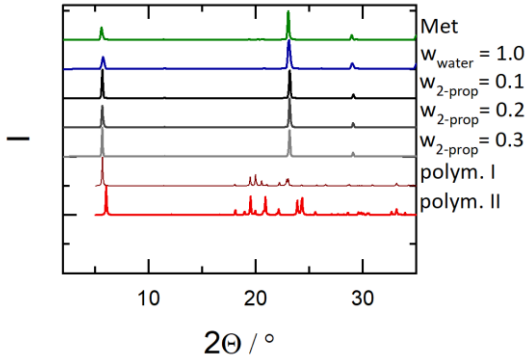
$w_{2\text{-}prop}$ = 0.2
$w_{2\text{-}prop}$ = 0.3
polym. I
polym. II
polym. III
I
10
20
30
2Θ / °


Met
w_{water} = 1.0
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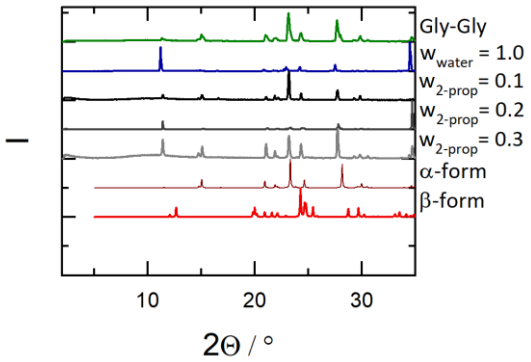
$w_{2\text{-}prop}$ = 0.2
$w_{2\text{-}prop}$ = 0.3
polym. I
polym. II
I
10
20
30
2Θ / °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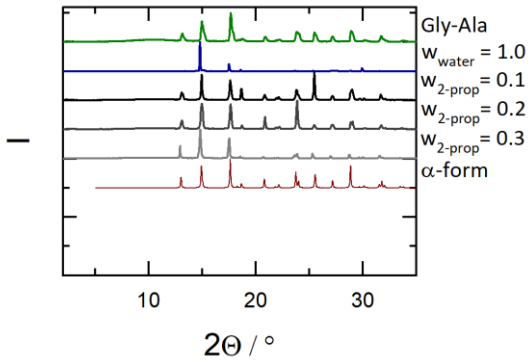
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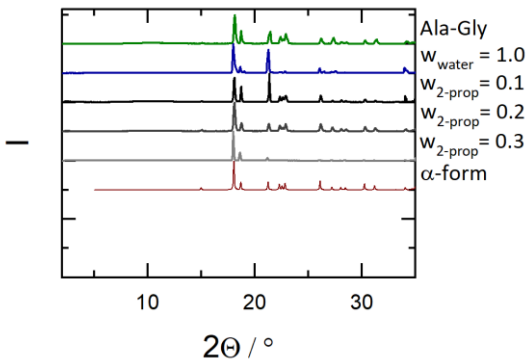
2Θ / °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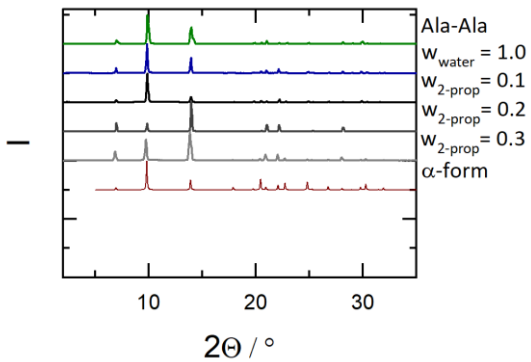
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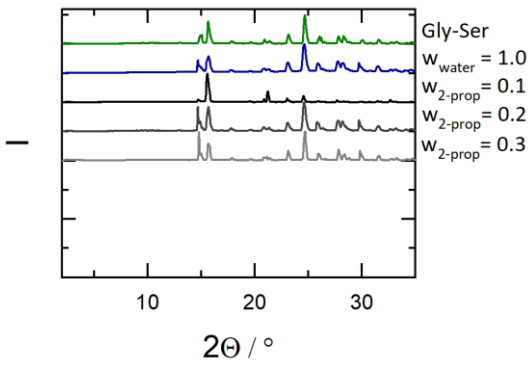

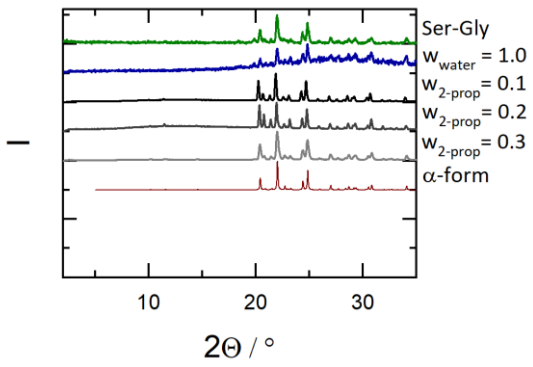

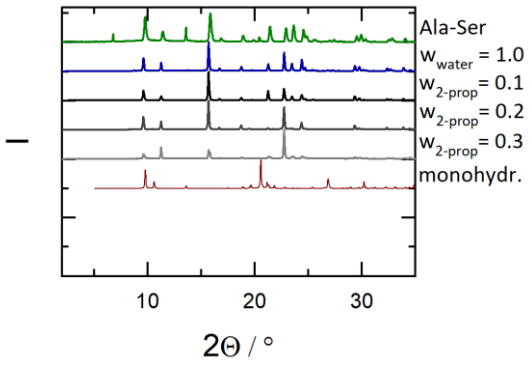

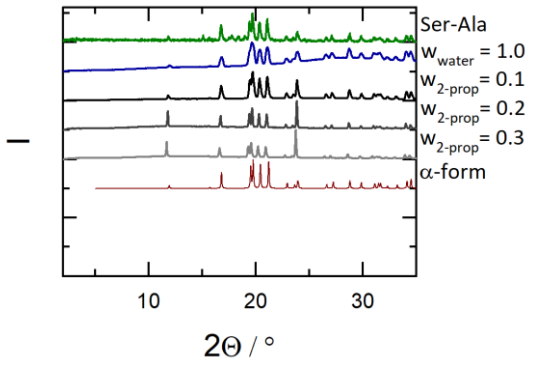

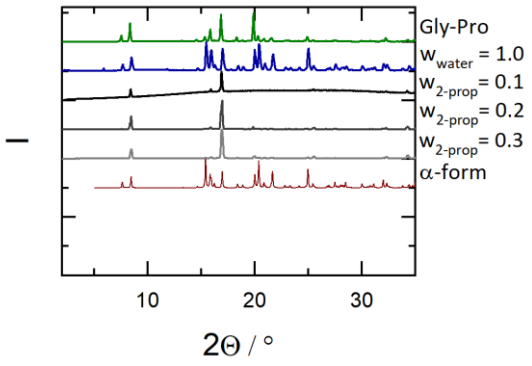

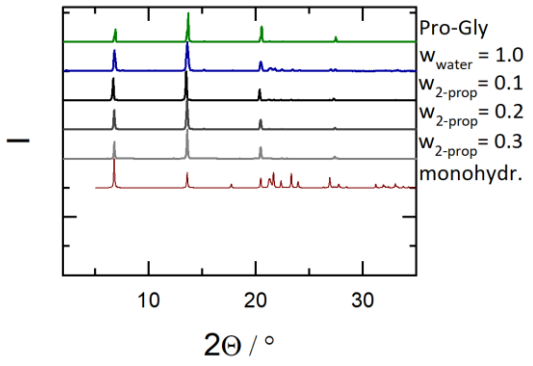

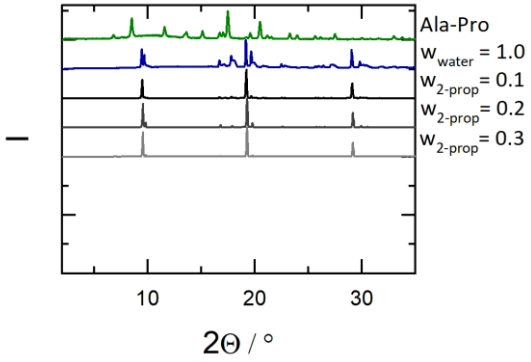
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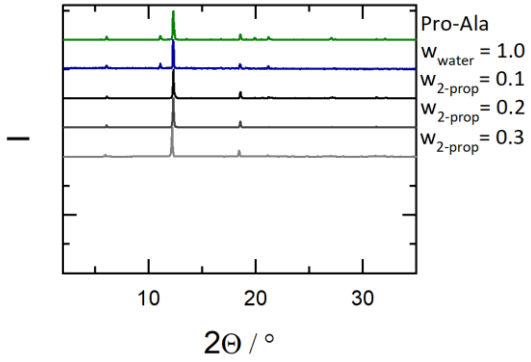
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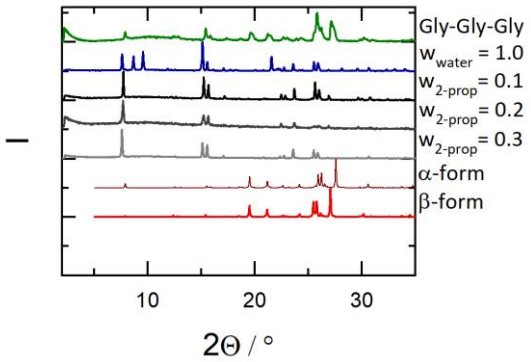
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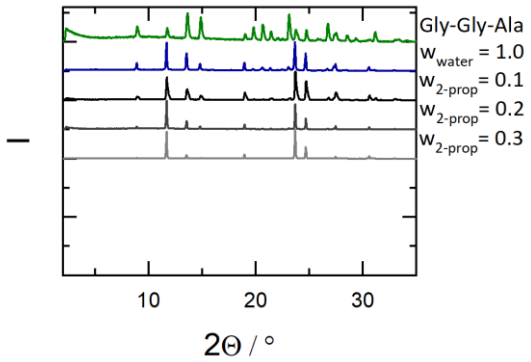
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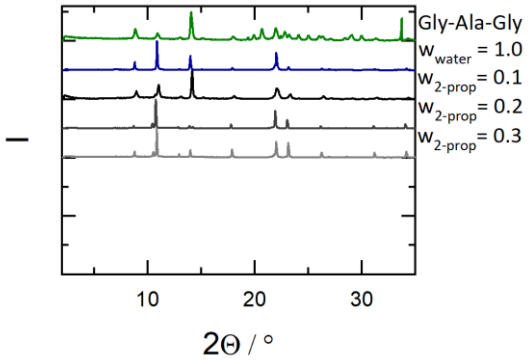
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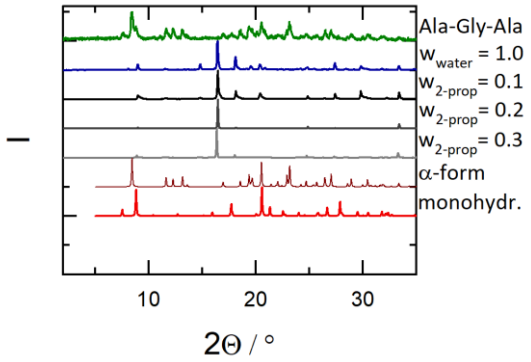
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α-form
monohydr.
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2Θ / °

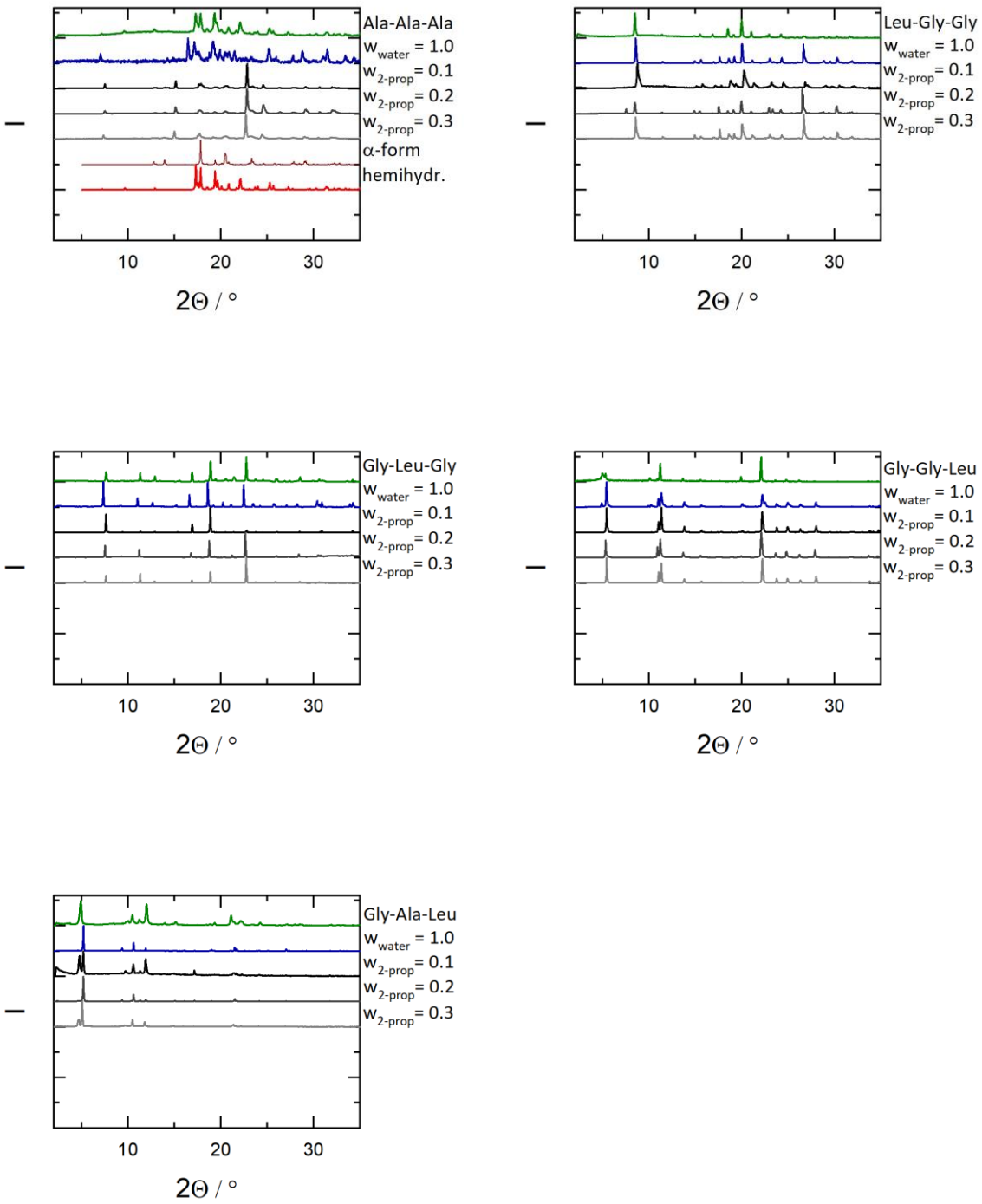

Figure S2: PXRD diffractograms of amino acids and peptides. Green line: pure component; blue line: solid phase of the supersaturated solution containing pure water; black line: solid phase of the supersaturated solution containing a 2-propanol fraction of 10 wt%; dark grey line: solid phase of the supersaturated solution containing a 2-propanol fraction of 20 wt%; light grey line: solid phase of the supersaturated solution containing a 2-propanol fraction of 30 wt%; red lines: diffractograms from Cambridge Crystallographic Data Centre (CCDC).

9. g^E models vs. PC-SAFT

In the current work, the solubility of 15 proteinogenic amino acids and 18 peptides in water and in water+-2-propanol was modeled using different g^E models (Wilson, NRTL, UNIQUAC) in comparison with PC-SAFT. As an example only the results for the amino acid Glu is shown:.

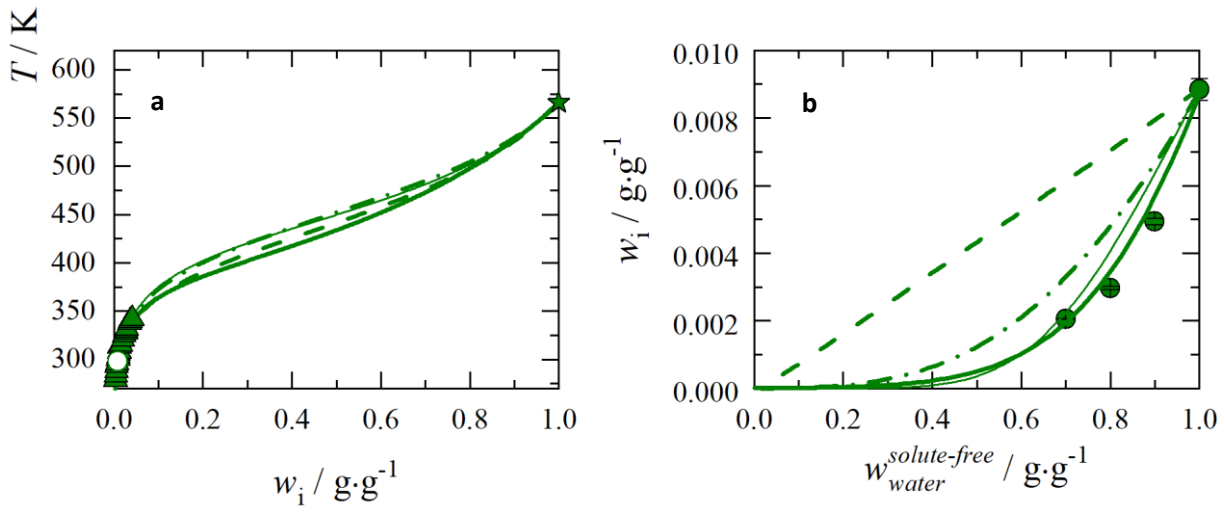

Figure S3: (a) The temperature-dependent solubilities of Glu at p = 1atm. ○: represent the own solubility measurement, literature solubility data ▲: Matsuo[10] and ★: melting temperature of Glu. (b) The Glu solubility dependent on the 2-propanol weight fraction at T = 298.15 K and p = 1 atm in unbuffered solutions pH = pI in a pseudo-binary plot. ●represents the own solubility measurements. On the x-axis the solute-free weight fraction of water for aqueous 2-propanol solutions is shown. On the y-axis the solubility in the ternary system of the amino acid is shown. Lines are modeling results using PC-SAFT (thick solid lines), Wilson (dashed lines), NRTL (dashed-dotted lines), UNIQUAC (thin solid lines).

The binary parameters between component (1) and water (2) were fitted to aqueous solubility data shown in Figure S3 (a). The binary parameters between water (2) and 2-propanol (3) were separately fitted to vapor-liquid data and shown in Table S7. In a last step the binary parameters of component (1) and 2-propanol (3) were fitted to aqueous solubility data with 2-propanol contributions shown in Figure S3 (b).

Table S7 *Modeling parameters with Wilson, NRTL and UNIQUAC of binary and ternary systems with Glu as component (1) + water (2) + 2-propanol (3). For Wilson, NRTL and UNIQUAC the binary parameters were simultaneously fitted to the experimental determined activity coefficients. The ARD values including all the number of experimental points (NP) and the corresponding literature solubility data were determined for temperature-dependent solubility in binary mixtures (second column); for ternary systems ARD includes only data at* $T = 298.15\ K$*, but the mass fraction of 2-propanol in water varies.*

	Binary mixture component(1)+water(2)				Ternary mixture component(1)+water(2)+2-propanol(3)					
Wilson	$\Delta\lambda_{12}$ / $J \cdot mol^{-1}$	$\Delta\lambda_{21}$ / $J \cdot mol^{-1}$	NP/[Lit.]	ARD / %	$\Delta\lambda_{13}$ / $J \cdot mol^{-1}$	$\Delta\lambda_{31}$ / $J \cdot mol^{-1}$	$\Delta\lambda_{23}$ / $J \cdot mol^{-1}$	$\Delta\lambda_{32}$ / $J \cdot mol^{-1}$	NP/[Lit.]	ARD / %
	-672.28	-1562.59	23/[10]	12.73	25000.00	25000.00	7567.00	1265.58	3/[11]	100.42
NRTL	Δg_{12} / $J \cdot mol^{-1}$	Δg_{21} / $J \cdot mol^{-1}$	NP/[Lit.]	ARD / %	Δg_{13} / $J \cdot mol^{-1}$	Δg_{31} / $J \cdot mol^{-1}$	Δg_{23} / $J \cdot mol^{-1}$	Δg_{32} / $J \cdot mol^{-1}$	NP/[Lit.]	ARD / %
	-4914.93	6075.15	23/[10]	5.80	14969.02	14618.02	8463.11	-344.29	3/[11]	39.83
UNIQUAC	Δu_{12} / $J \cdot mol^{-1}$	Δu_{21} / $J \cdot mol^{-1}$	NP/[Lit.]	ARD / %	Δu_{13} / $J \cdot mol^{-1}$	Δu_{31} / $J \cdot mol^{-1}$	Δu_{23} / $J \cdot mol^{-1}$	Δu_{32} / $J \cdot mol^{-1}$	NP/[Lit.]	ARD / %
	-1432.46	559.12	23/[10]	8.59	20000.00	20000.00	1145.06	841.15	3/[11]	23.51

For binary mixtures (component + water) the modeling performance of all g^E models as well as PC-SAFT are in good agreement with the experimental data of Glu. For ternary mixtures the modeling performances differ. The Wilson model shown qualitatively good results but not quantitatively. Additionally the fit of binary parameters between component (1) and 2-propanol (3) was set to a maximum value of 25000 J mol^{-1}. On the one hand higher values don't lead to significantly better results and on the other hand higher values would not be physically reasonable. The NRTL model shows better results compared to the Wilson model. Here the lowest ARD values could be determined but the modeling results are still not in a good agreement with the experimental solubility data. The UNIQUAC model shows also better results comparing to NRTL. But as applied already in the Wilson model, the binary parameters between component (1) and 2-propanol (3) was also set to a maximum value of 20000 J mol^{-1}.

Glu is only one example shown here. The overall mean ARD of all amino acids and peptides in binary and ternary mixtures are listed in Table S8.

Table S8 Average relative deviation (ARD) between modeling results and experimental solubility of amino acids and peptides for g^E models (Wilson, NRTL, UNIQUAC) and PC-SAFT.

	Component(1)+water(2)		Component(1)+water(2)+2-propanol(3)	
Model	*Amino acids* ARD / %	*Peptides* ARD / %	*Amino acids* ARD / %	*Peptides* ARD / %
Wilson	19.71	6.95	50.15	118.42
NRTL	18.61	6.78	28.61	56.30
UNIQUAC	15.00	8.10	28.27	33.74
PC-SAFT	5.63	5.69	7.80	7.31

The accuracy of the experimental uncertainty was determined to be about RMSD = 3%. It can be clearly seen that the PC-SAFT modeling shows a better modeling performance with less binary parameters (k_{13}). To summarize, PC-SAFT is recommended for modeling solubility of biomolecules such as amino acids and peptides in broad temperature ranges and/or upon co-solvent addition. In contrast, among the g^E models only UNIQUAC allowed a reasonable modeling result while Wilson and NRTL is not recommended for modeling the systems under study. It would be interesting to prove or disprove this finding also for other systems in the future.

10. References

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