TABLE S1. Descriptive sensory analysis of fundamental flavors in the 14 Cheddar samples and correlations with bitterness and age.

Sample ID[1]	Bitter[2]	Sour	Salty	Sweet	Umami
T_0.2a	0.7	2.7	3.6	2.4	2.7
T_0.2b	ND	2.4	3.5	2.4	2.5
T_0.2b	ND	2.9	3.3	2.3	2.9
T_0.2d	ND	2.6	3.2	2.5	3.0
L_3.3	1.2	2.8	4.0	2.6	4.0
L_2.9	1.4	2.9	4.3	2.7	3.8
L_6.0	1.4	3.0	4.4	2.8	4.1
M_7.3	2.1	3.1	4.5	2.9	4.5
M_6.2	2.1	2.8	4.7	3.0	4.5
M_5.6	2.4	3.0	4.5	2.7	4.2
E_7.2	2.9	2.9	4.3	2.9	4.4
E_8.7a	2.9	3.4	4.9	2.9	4.0
E_5.7	3.0	3.0	4.3	2.9	4.1
E_8.7b	3.4	3.2	4.8	2.7	4.1
Descriptive statistics					
LSD[3]	0.3	0.3	0.3	0.3	0.2
Bitterness (Pearson's *r*)[4]	1.00	0.75	0.86	0.78	0.78
Age (Pearson's *r*)[4]	0.92	0.82	0.94	0.86	0.88

[1]Reference Table 1 for Sample ID definition.

[2]Data represent average values from seven panelists performing quantitative descriptive analysis on a 0–15-point universal intensity scale in duplicate (Spectrum method, Meilgaard et al., 1999; Drake et al., 2001). ND, non-detected.

[3]LSD, least significant difference ($p < 0.05$). Data were analyzed by a general linear model analysis of variance with Fisher's LSD as a post hoc test.

[4]Pearson's correlation coefficient of mean bitterness intensity and cheese age (see Table 1) to descriptive sensory results. ND values were substituted with 0.5, the panels' limit of quantification for calculating the correlation coefficients.

TABLE S2. Descriptive sensory analysis of aromatics in the 14 Cheddar samples and correlations with bitterness and age.

Sample ID[1]	Cooked[2]	Caramel	Whey	Diacetyl	Milkfat	Fruity	Sulfur	Brothy	Nutty	Catty	Cowy barny
T_0.2a	3.6	ND	2.3	1.2	3.5	ND	ND	0.7	ND	ND	ND
T_0.2b	3.7	ND	1.9	ND	3.6	ND	ND	0.7	ND	ND	ND
T_0.2c	3.7	ND	2.8	0.9	3.6	ND	ND	ND	ND	ND	ND
T_0.2d	3.8	ND	2.4	1.0	3.5	ND	ND	ND	ND	ND	ND
L_3.3	3.5	1.7	ND	ND	3.5	0.8	3.0	3.7	2.0	ND	0.8
L_2.9	3.4	1.0	ND	ND	3.5	0.6	2.4	3.4	1.1	ND	ND
L_6.0	3.0	2.5	ND	ND	3.5	1.8	2.9	3.7	2.2	1.3	ND
M_7.3	3.2	1.7	ND	ND	3.5	1.5	3.0	3.8	2.7	1.7	ND
M_6.2	3.4	1.2	ND	ND	3.5	1.5	3.2	3.9	2.2	1.0	ND
M_5.6	3.3	2.9	ND	ND	3.5	1.2	3.0	3.7	2.9	1.1	0.6
E_7.2	3.4	2.4	ND	ND	3.5	1.1	3.2	4.0	2.6	0.8	ND
E_8.7a	3.4	3.2	ND	ND	3.5	1.3	3.2	3.8	2.3	1.2	0.6
R_5.7	3.3	2.1	ND	ND	3.5	0.9	2.7	3.5	2.3	1.1	1.2
E_8.7b	3.2	3.2	ND	ND	3.5	1.0	3.2	4.0	2.4	1.3	0.6
Descriptive statistics											
LSD[3]	0.3	0.3	0.2	0.3	0.2	0.3	0.3	0.3	0.3	0.2	0.3
Bitterness (Pearson's *r*)[4]	-0.66	0.86	-0.77	-0.61	-0.53	0.54	0.82	0.81	0.85	0.69	0.39
Age (Pearson's *r*)[4]	-0.80	0.89	-0.85	-0.69	-0.56	0.79	0.92	0.90	0.92	0.83	0.18

[1]Reference Table 1. for Sample ID definition.

[2]Data represent average values from seven panelists performing quantitative descriptive analysis on a 0–15-point universal intensity scale in duplicate (Spectrum method, Meilgaard et al., 1999; Drake et al., 2001). ND, non-detected. Flavors not listed were not detected in cheeses.

[3]LSD, least significant difference ($p < 0.05$). Data were analyzed by a general linear model analysis of variance with Fisher's LSD as a post hoc test.

[4]Pearson's correlation coefficient of mean bitterness intensity and cheese age (see Table 1) to descriptive sensory results. ND values were substituted with 0.5, the panels' limit of quantification for calculating the correlation coefficients.

TABLE S3. Peptides identified in the 14 cheeses that were documented as bitter in previous literature, their standard mean difference in abundance between bitter and non-bitter groups, their linear correlation with cheese bitterness intensity, their bitterness threshold value, mean bitterness intensity and literature source.

Peptide sequence	Peptide's origin[1]	Rank order mean[2]	Standard mean difference[3]	Bitterness linear correlation (R value)[4]	Threshold value ($\mu mol \cdot L^{-1}$)[5]	Mean bitterness intensity[5] (0–15)	Literature Reference[6]
YPFPGPIPN	βA2 [60-68]	4	2.10	0.91	230	-	Toelstede & Hofmann, 2008a
YPFPGPIHNS	βA1 [60-69]	12	2.26	0.66	50	-	Toelstede & Hofmann, 2008a
YPFPGPIHN	βA1 [60-68]	16	1.45	0.76	100	-	Toelstede & Hofmann, 2008a
KPWIQPK	α_{s2} [191-197]	19	1.79	0.64	-	-	Lee et al., 1996
RPKHPIK	α_{s1} [1-7]	30	1.94	0.58	-	-	Lee et al., 1996
VLPVPQ	β [170-175]	38	1.52	0.57	310	-	Sebald et al., 2018, 2020
LVYPFPGPIHN	βA1 [58-68]	68	1.11	0.50	80	-	Toelstede & Hofmann, 2008a
YPFPGPI	β [60-66]	79	0.73	0.67	160	-	Shinoda et al., 1986a; Lemieux & Simard, 1992
EMPFPKYPVEPF	β [108-119]	101	0.74	0.51	-	NB	Karametsi et al., 2014
VYPFPGPIPN	βA2 [59-68]	118	1.11	0.40	170	-	Toelstede & Hofmann, 2008a
TDVENLHLPLPL	β [128-139]	129	0.73	0.44	-	-	Visser et al., 1975; Lemieux & Simard, 1992
MPFPKYPVEPF	β [109-119]	132	0.54	0.55	-	0.56	Karametsi et al., 2014
HLPLPLLQ	β [134-141]	143	0.60	0.48	440	-	Sebald et al., 2018, 2020
QEPVLGPVRGPFPII	β [194-208]	144	0.60	0.48	330	-	Sebald et al., 2020
YPFPGPIPNS	βA2 [60-69]	170	1.06	0.32	330	-	Toelstede & Hofmann, 2008a
TPVVVPPFLQPEVM	β [80-93]	174	0.82	0.35	>1600	-	Sebald et al., 2020
RDMPIQAFLLY	β [183-193]	199	0.75	0.32	-	-	Monnet et al., 1986; Lemieux & Simard, 1992
YQEPVLGPVRGPFPI	β [193-207]	209	0.45	0.43	-	0.56	Karametsi et al., 2014;
QEPVLGPVRGPFPI	β [194-207]	211	0.31	0.48	-	NB	Monnet et al., 1986; Karametsi et al., 2014; Lemieux & Simard, 1992
YQQKPVAL	κ [43-50]	218	0.75	0.28	500	-	Sebald et al., 2018, 2020
SLVYPFPGPIHNS	βA1 [57-69]	241	0.48	0.34	60	-	Toelstede & Hofmann, 2008a
AMAPKHKEMPFPKYPVEPF	β [101-119]	260	0.29	0.37	250	-	Sebald et al., 2020
APKHKEMPFPKYPVEPF	β [103-119]	269	0.28	0.36	-	0.36	Karametsi et al., 2014

LGPVRGPFP	β [198-206]	352	0.02	0.28	-	NB	Karametsi et al., 2014
LHLPLPLLQS	β [133-142]	368	0.13	0.17	160	-	Sebald et al., 2020
VVVPPFL	β [82-88]	373	0.50	-0.05	140	-	Shinoda et al., 1986b; Lemieux & Simard, 1992
TQTPVVVPPFLQPE	β [78-91]	399	0.13	0.09	280	-	Sebald et al., 2018, 2020
QSKVLPVPQ[7]	β [167-175]	453	0.04	-0.03	-	-	Monnet et al., 1986; Lemieux & Simard, 1992
IAKYIPI	κ [22-28]	457	-0.09	0.01	160	-	Sebald et al., 2020
LHLPLPLL	β [133-140]	477	-0.12	-0.04	110	-	Sebald et al., 2018, 2020
VLPVPQKAVPYPQ	β [170-182]	495	-0.47	0.04	340	-	Sebald et al., 2020
GPVRGPFP	β [199-206]	558	-0.70	-0.05	1180	-	Toelstede & Hofmann, 2008a
FALPQYLK	α_{s2} [174-181]	561	-0.54	-0.19	-	-	Matoba et al., 1969; Lemieux & Simard, 1992
TQTPVVVPPFL	β [78-88]	566	-0.34	-0.34	200	-	Sebald et al., 2020
VPPFLQPE	β [84-91]	567	-0.75	-0.03	>1730	-	Sebald et al., 2020
MAPKHKEMPFPKYP VEPF	β [102-119]	571	-0.55	-0.21	90	0.9	Karametsi et al., 2014; Sebald et al., 2018, 2020
QEPVLGPVRGPFPIIV	β [194-209]	582	-0.56	-0.25	-	-	Gordon & Speck, 1965; Lemieux & Simard, 1992
ERYLGYLEQ	α_{s1} [89-97]	610	-0.66	-0.28	460	-	Sebald et al., 2020
IPPLTQTPVVVPP	β [74-86]	632	-0.86	-0.22	>6,000	-	Toelstede & Hofmann, 2008b
RPKHPIKHQGLPQ	α_{s1} [1-13]	648	-0.80	-0.34	-	-	Lee et al., 1996
APFPEVFG	α_{s1} [26-33]	652	-0.64	-0.42	-	-	Matoba et al., 1970; Lemieux & Simard, 1992
SITRINK	β [22-28]	664	-0.92	-0.29	>6,000	-	Toelstede & Hofmann, 2008a
RPKHPIKHQ	α_{s1} [1-9]	669	-0.65	-0.45	-	-	Broadbent et al., 1998, 2002
EPVLGPVRGPFP	β [195-206]	674	-1.06	-0.22	-	NB	Karametsi et al., 2014
PVLGPVRGPFP	β [196-206]	676	-1.06	-0.22	-	NB	Karametsi et al., 2014
PVRGPFPIIV	β [200-209]	685	-0.76	-0.46	4	-	Shinoda et al., 1985
APFPEVF	α_{s1} [26-32]	700	-0.78	-0.51	-	-	Richard & Creamer, 1973; Lemieux & Simard, 1992
NLHLPLPLLQS	β [132-142]	703	-0.88	-0.47	180	-	Sebald et al., 2020
YQEPVLGPVRGPFP	β [193-206]	730	-1.03	-0.44	-	-	Karametsi et al., 2014; Visser et al., 1975, 1983; Lemieux & Simard, 1992
KAVPYPQ	β [176-182]	766	-0.98	-0.58	-	-	Monnet et al., 1986; Lemieux & Simard, 1992
VAPFPEVFGKE	α_{s1} [25-35]	769	-1.02	-0.57	570	-	Sebald et al., 2018, 2020

KVLPVPQKAVPYPQ	β [169-182]	776	-1.09	-0.56	140	-	Sebald et al., 2018, 2020
GPVRGPFPIIV	β [199-209]	809	-1.33	-0.55	-	4.56	Karametsi et al., 2014
YLGYLEQLLR	α_{s1} [91-100]	810	-1.23	-0.58	-	-	Hill and Van Leeuwen, 1974; Lemieux & Simard, 1992
QEPVLGPVRGPFP	β [194-206]	842	-1.82	-0.60	-	NB	Karametsi et al., 2014
VFGKEKVNEL	α_{s1} [31-40]	862	-1.53	-0.77	110	-	Sebald et al., 2018, 2020

[1]Casein variants (bovine origin) are α_{s1}-, α_{s2}-, β- and κ-casein. βA1 is the A1 variant of β-casein in which position 67 is Pro. βA2 is the A2 variant of β-casein in which position 67 is His.

[2]Ranked mean of the ascending order of average standard mean difference and R-values for the bitterness linear correlation.

[3]Standard mean difference calculated in accordance with Cohen's d value formula.

[4]R-value, correlation of cheese mean bitterness score (see Table 1) to each peptide's normalized abundance.

[5]Reference literature sources for information on sensory analysis methodology.

[6]Full literature references are found in the following article: Kuhfeld, R., A. Zeynep, D. Dallas, 2022. A comprehensive database of cheese-derived bitter peptides and analysis of their physical properties[Manuscript in preparation].).

[7]The dotted line distinguishes peptides according to their standard mean difference, with positive values located above the line and negative values situated below it.