

Supporting information for “Identifying sequential residue patterns in bitter and umami peptides”

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Primary structures

Here we have written out the complete original and coarse-grained primary structures of two bitter proteins mentioned in the main text (see the subsection *Selecting the minimal peptide pattern*). The coarse-grained residues are denoted as follows: ‘H’ for hydrophobic, ‘P’ for polar and hydrophilic, ‘+’ for positively charged, and ‘-’ for negatively charged (see main text for details).

- Patatin-T5

FASTA entry

```
>sp|P15478|PATT5_SOLTU Patatin-T5 OS=Solanum tuberosum OX=4113 PE=1 SV=1
MATTNSFTILIFMILATTSSTFATLGEMVTVLSIDGGGIKGIIPATILEFLEGQLQEVDN
NTDARLADYFDVIGGTSTGGLLTAMITTPNETNRPFAAAKDIVPFYFEHGPKIFQSSGSI
FGPKYDGKYLQVLQEKLGETRVHQALTEVAISSFDIKTNKPVIFTKSNLAKSPELDAKM
YDICYSTAAAPTFFPPHYFATNTSNGDKYEFNLVDGAVATVDDPALLSISVATKLAQVDP
KFASIKSLNYKQMLLLSLGTGTTSEFDKTYAEETAKWGTARWMLVIQKMTSAASSYMTD
YYLSTAFQALDSQNNYLRVQENALTGTTTELDDASEANMQLLVQVGEDLLKKS SVSKDNPE
TYEEALKRFAKLLSDRKKLRANKASY
```

Coarse-grained sequence

```
HHPPPPHPPHHHHHHHHPPPPPHHPHP-HHPHHPH-PPPH+PHHPHPHH-HH-PPHP-H-P
PP-H+HH-PH-HHPPPPPPHHPHHHPPPP-PP+PHHHH+-HHPHPH-+PP+HHPPPPPH
HPP+P-P+PHHPHP-+HP-P+H+PHHP-HHHPPH-H+PP+PHHHP+PHH+PP-H-H+H
P-HHPPPHHPPHHP+PHHPPPPPP-+P-HPHH-PHHHPH--PHHHPHPHP+HHPH-P
+HHPH+HPP+PHHHHPHPPPPPP-H-+PPH--PH+PPH+PHHHHP+HPPHPPHP-
PPHPPHHPHH-PPPPH+HP-PHPPPPPP-H--HP-HHPHHPHP--HH++PHP+-PP-
PP--HH++HH+HHP-+++H+HP+HPP
```

- Legumin A

FASTA entry

```
>sp|P02857|LEGA_PEA Legumin A OS=Pisum sativum OX=3888 GN=LEGA PE=1 SV=1
MAKLLALSLSFCFLLLGGCFALREQPQQNECQLERLDALEPDNRIESEGLIETWNPNNK
QFRCAGVALSRATLQRNALRRPYYSNAPQEIFIQQNGYFGMVFPGCPETFEEPQESEQG
EGRRYRDRHQKVNRFREGDIIAVPTGIVFWMYNDQDTPVIAVSLTDIRSSNNQLDQMPRR
FYLAGNHEQEFLQYQHQQGGKQEQENEGNNIFSGFKRDYLEDAFNVNRHIVDRLQGRNED
EEKGAIVKVKGGLSIIISPPEKQARHQGRSRQEEDEDEEKQPRHQGRSRQEEEEDEDEERQ
PRHQRRRGEEEEEDKKERGGSQKGSRRQDNGLEETVCTAKLRLNIGSSSPDIYNPEA
GRIKTVTSLDLPVLRWLKLSAEHGS LHKNAMFVPHYNLNANSIIYALKGRARLQVVNCNG
NTVFDGELEAGRALTVPQNYA VAAKSLSDRFSYVAFKTNDRAGIARLAGTSSVINNLPLD
VVAATFNLRNEARQLKSNPFPKFLVPARESEN RASA
```

Coarse-grained sequence

```
HH+HHHHHPHPPHHHHHPHPPHHH+-PPPPP-HPH-+H-HH-P-P+H-P-PPHH-PPPPP+
PH+HHPHHPH+HPHP+PHH++PPPPHPP-HHHPPPPPPHPPHHHPHP-PH--PP-P-PP
-P++P+-++P+HP+H+-P-HHHHPPHHHPHP-P-PPHHHPHP-H+PPPPH-PHP++
HPHHP+-P-HHPPP+PPP+P-P-P-PPHHPH++-PH--HHPHP++HH+HPP+P--
--P+PHHH+H+PPHPHPP+-PH++P+PP+P-----+PP++P+PP+P-----+P
P++P+++P-----++-+PPPP+P+P++PP-PPH--PHHPH+H+HPHPPPPP-HPPP-H
P+H+PHPPH-HPHH+PH+HPH-+PPH++PHHHHP+PPHPHPPHHPHH+P+H+HPHHPHP
PPHH-P-H-HP+HHPHPPPHHHH+PHP-+HPPHHH+PP-+HPHH+HHPHPPHHPHPH-
HHHHPHPHP+P-H+PH+PPPH+HHHPH+-P-P+HPH
```

Disputes regarding some umami peptides

A review by Zhang *et al.*¹ points to some disputes in the community regarding the umami taste of the following peptides: AE, DA, DD, DE, DL, ED, EE, EL, EK, ES, EV, KG, AEA, DES, EEE, GDG, VEV, and KGDEESLA. The objection primarily comes from van den Oord and van Wassenaar,² who, in 1997, found that an eight-member expert panel could not detect umami taste in those peptides. However, note that almost all of the mentioned peptides are rich in glutamic or aspartic acids (E or D), and multiple studies—using modern techniques such as molecular sensory approaches and *in-silico* methods—have now reported umami peptides that are rich in aspartic or glutamic acids.^{3,4} Consequently, it is unclear why these short peptides made almost entirely of acidic residues would lack umami taste. Further, from a more molecular point of view, their umami taste seems logical. A single E (or D) interacts with the appropriate amino acids receptor proteins T1R1/T1R3. The listed di- and tri-peptides, lacking sufficient steric hindrance, should interact similarly with the umami receptor protein—especially when the E (or D) appears at one of the ends of the peptide. These

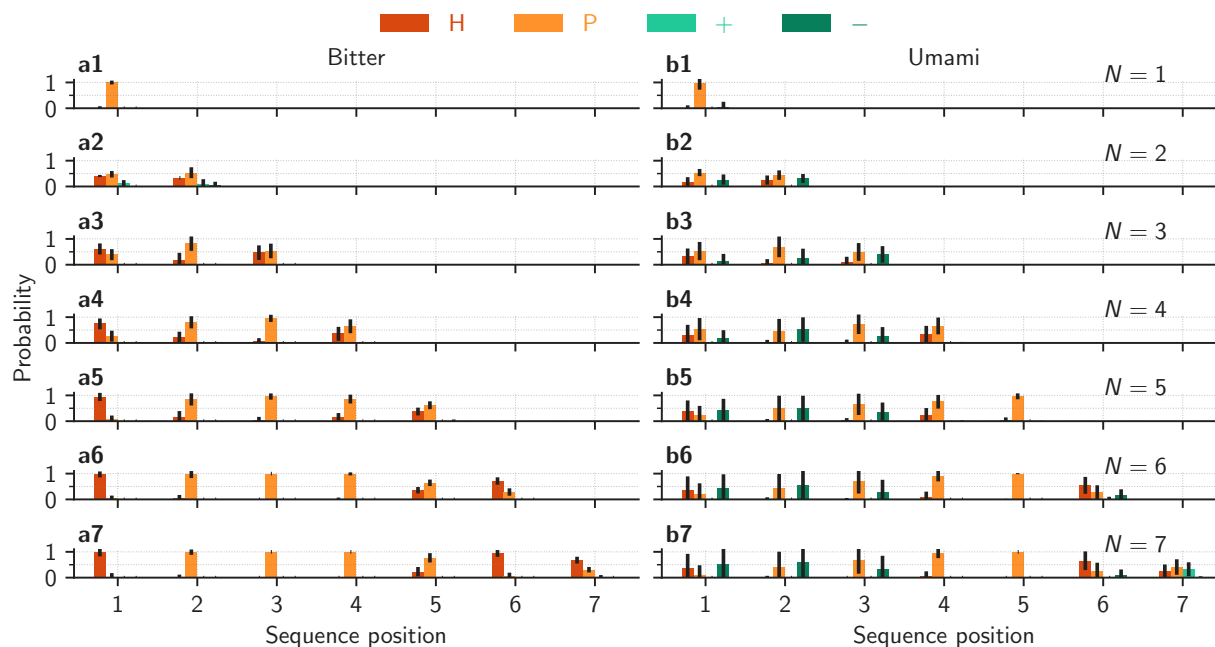


Figure S1: Predicted bitter and umami patterns after removing the disputed umami peptides. See SI text for discussion.

considerations led us to keep these short peptides in our database—which was compiled from published resources.^{5–7}

For completeness, we reanalyzed the umami peptides after removing the disputed ones. In comparison to the short umami patterns shown in the main text (Fig. 3b1–b3), the new short umami patterns have more polar residues than negative residues (panels b1–b3, Fig. S1). This is expected since the majority of the removed umami peptides are di- or tri-peptides with negatively-charged acidic residues, and polar residues are the second most abundant residue type after negative residues for umami peptides (Fig. 2c,e, main text). However, the longer patterns—especially the predicted $N = 5$ umami pattern ‘--PPP’—remained robust, though the prediction uncertainties (standard deviations computed over 300 training sets) increased. To conclude, we believe that the peptide taste community and the industry will benefit from a rigorous reassessment of the umami potentials of these disputed peptides using *both* expert panel and objective modern methods.⁸

References

- (1) Zhang, Y.; Venkitasamy, C.; Pan, Z.; Liu, W.; Zhao, L. Novel umami ingredients: Umami peptides and their taste. *Journal of Food Science* **2017**, *82*, 16–23.
- (2) van den Oord, A. H.; van Wassenaar, P. D. Umami peptides: assessment of their alleged taste properties. *Zeitschrift für Lebensmitteluntersuchung und-Forschung A* **1997**, *205*, 125–130.
- (3) Zhu, W.; Luan, H.; Bu, Y.; Li, X.; Li, J.; Zhang, Y. Identification, taste characterization

- and molecular docking study of novel umami peptides from the Chinese anchovy sauce. *Journal of the Science of Food and Agriculture* **2021**, *101*, 3140–3155.
- (4) Chen, W.; Li, W.; Wu, D.; Zhang, Z.; Chen, H.; Zhang, J.; Wang, C.; Wu, T.; Yang, Y. Characterization of novel umami-active peptides from *Stropharia rugoso-annulata* mushroom and in silico study on action mechanism. *Journal of Food Composition and Analysis* **2022**, *110*, 104530.
 - (5) Charoenkwan, P.; Yana, J.; Nantasenamat, C.; Hasan, M. M.; Shoombuatong, W. iUmami-SCM: A Novel Sequence-Based Predictor for Prediction and Analysis of Umami Peptides Using a Scoring Card Method with Propensity Scores of Dipeptides. *Journal of Chemical Information and Modeling* **2020**, *60*, 6666–6678.
 - (6) Shiyang, R.; Liping, S.; Xiaodong, S.; Jinlun, H.; Yongliang, Z. Novel umami peptides from tilapia lower jaw and molecular docking to the taste receptor T1R1/T1R3. *Food Chemistry* **2021**, *362*, 130249.
 - (7) Liu, Z.; Zhu, Y.; Wang, W.; Zhou, X.; Chen, G.; Liu, Y. Seven novel umami peptides from *Takifugu rubripes* and their taste characteristics. *Food Chemistry* **2020**, *330*, 127204.
 - (8) Smyth, H.; Cozzolino, D. Instrumental methods (spectroscopy, electronic nose, and tongue) as tools to predict taste and aroma in beverages: advantages and limitations. *Chemical reviews* **2013**, *113*, 1429–1440.