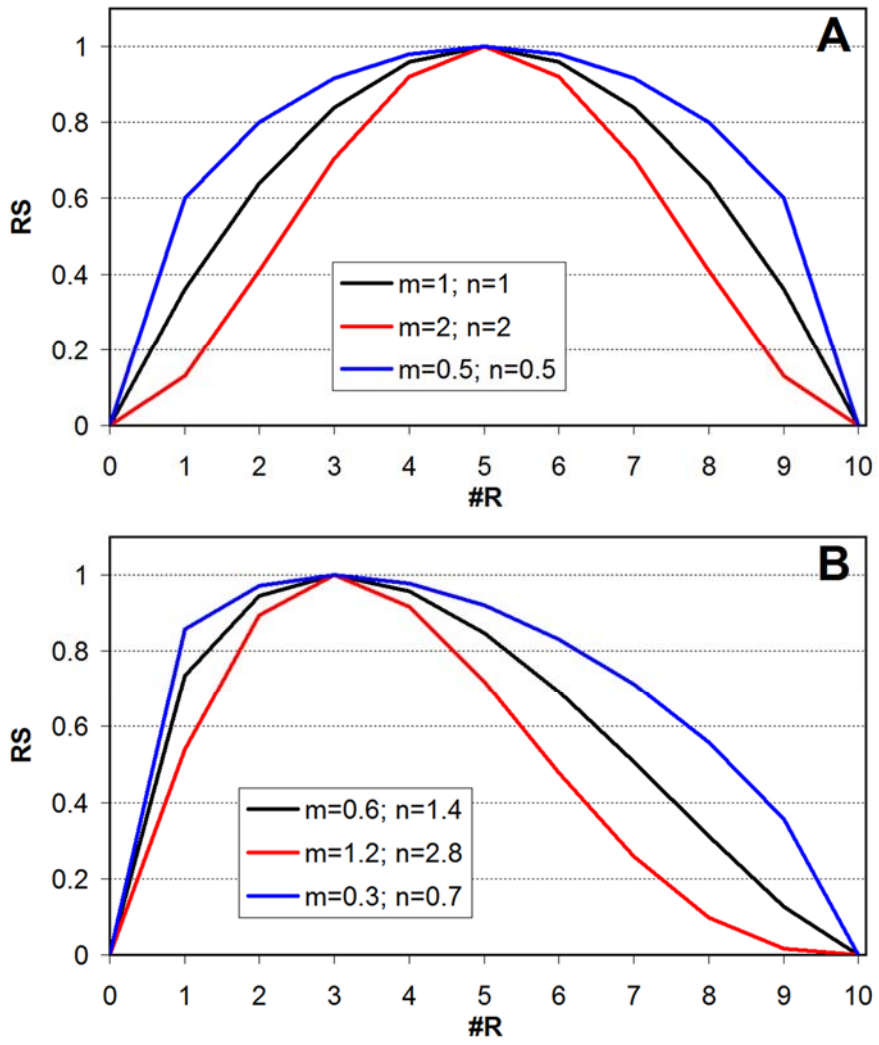

Fig. S1. Dependence of the C^mH^n product from exponents *m* and *n* for a set of model 10-residues long peptides composed only by arginine and tryptophan.
C^mH^n values were converted to relative scores (RS) by dividing C^mH^n values for the highest value obtained for each set of exponents. #R is the number of arginine residues in the peptides. The number of tryptophan residues in each peptide is = 10 - #R.

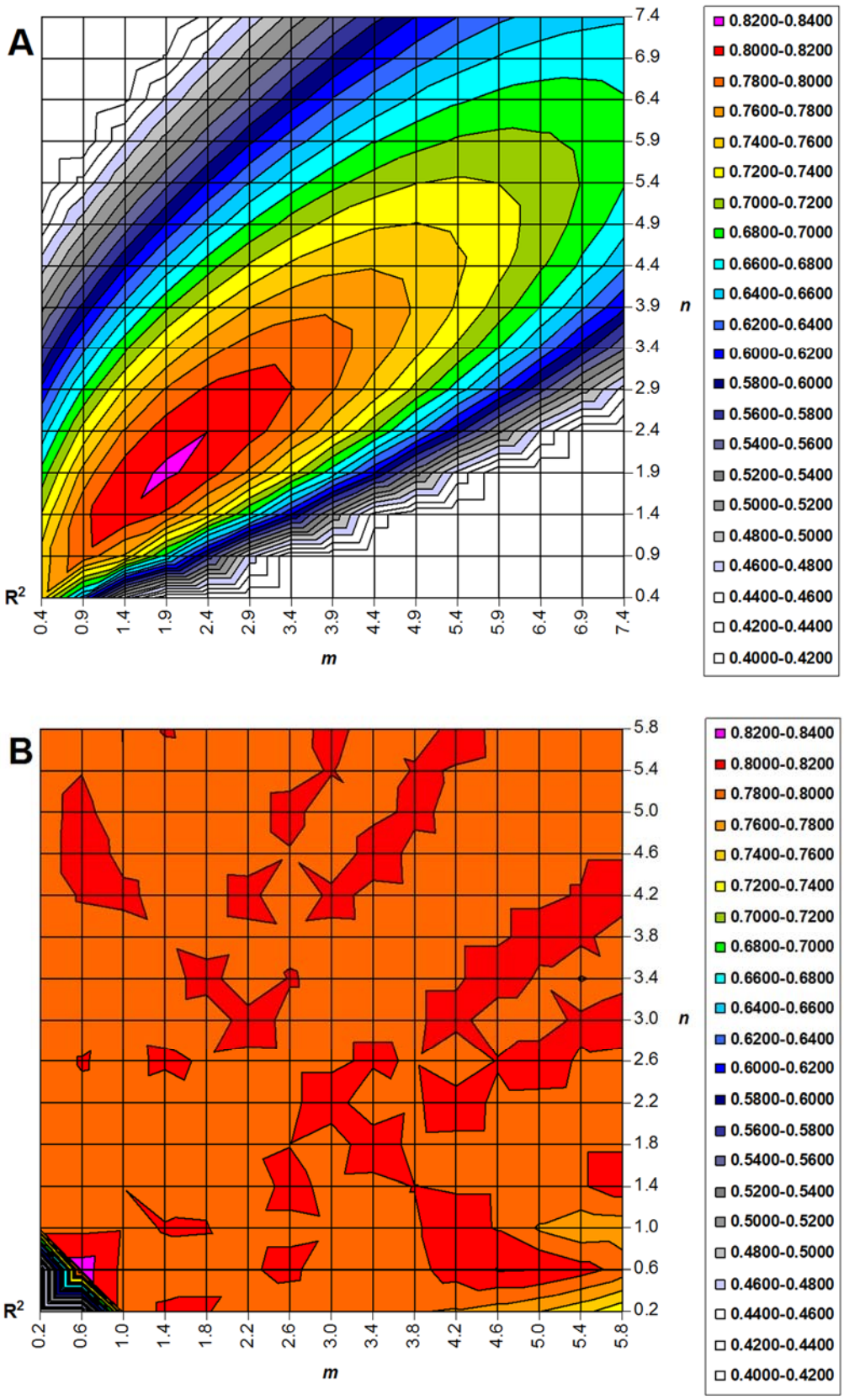

Fig. S2. Isometric plots showing the dependence from *m* and *n* of the R^2 values calculated by correlating the relative scores of the peptides of the RANDOM200 set (A) or of the $(XXYY)_n$-NH_2 set (B) to the corresponding antibacterial potency values.
RS were calculated using the Parker-Arg0 hydrophobicity scale.

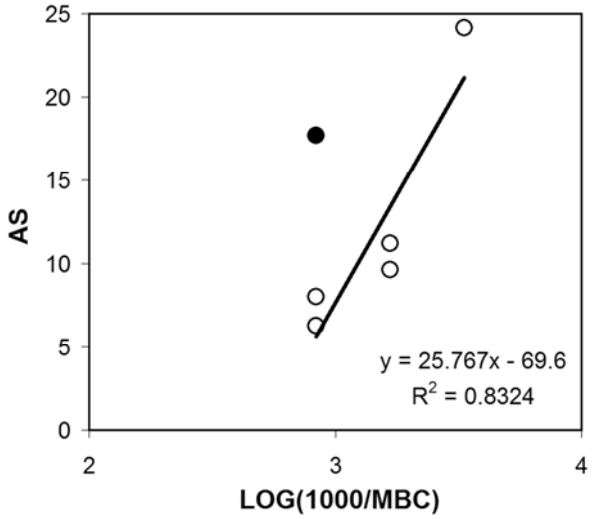

Fig. S3. Linear correlation between absolute scores and antibacterial potency values on *P. aeruginosa* of the RV-helices peptide set.
AS values were calculated using the Parker-Gly0 scale and $m = n = 1$. The least square line, the corresponding equation and the correlation coefficient are shown in the graph. The data for the 36mer peptide (black circle) were not used in the determination of the least square line.

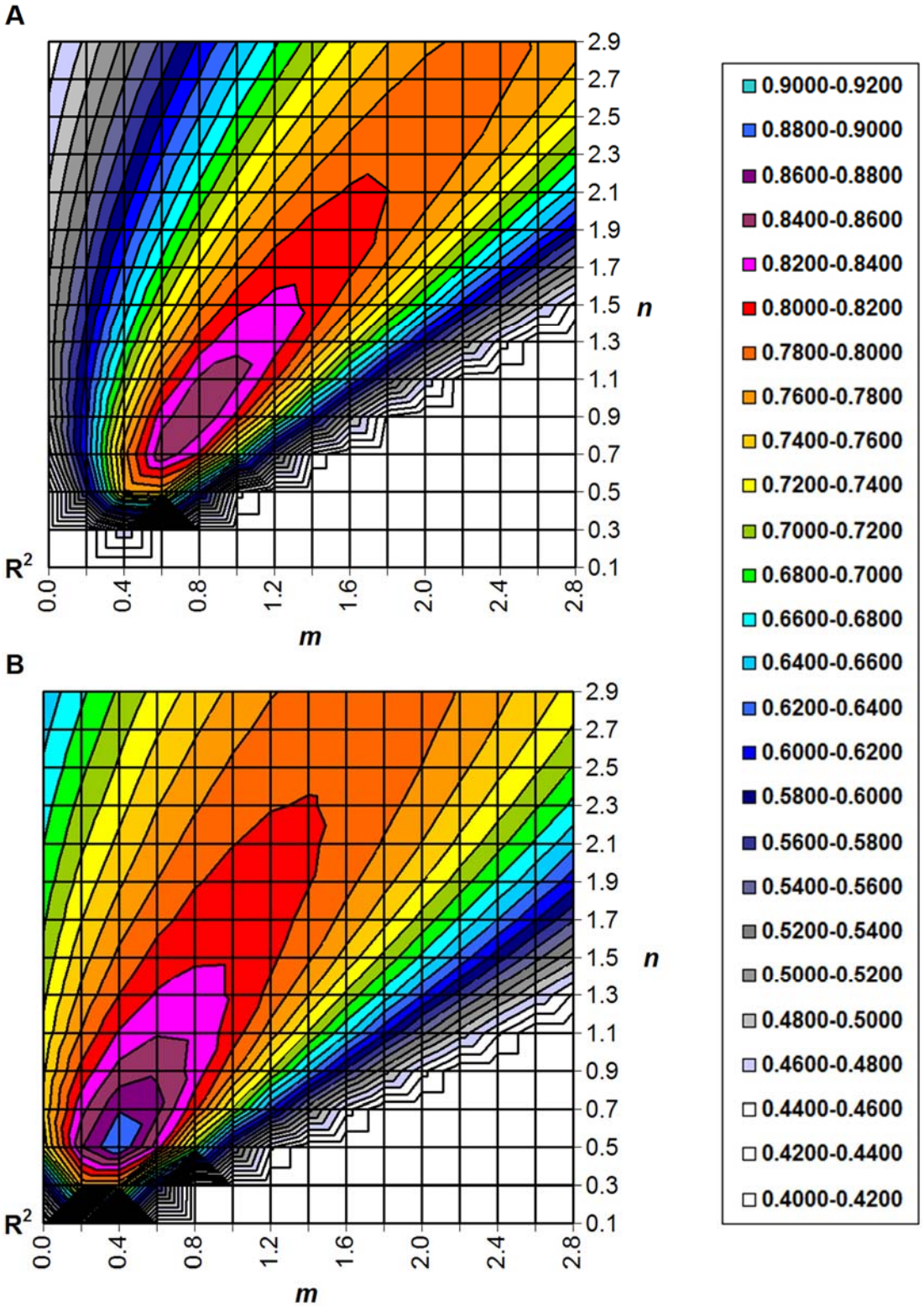

Fig. S4. Isometric plots showing the dependence from *m* and *n* of the R^2 values calculated by correlating the absolute scores of the peptides of the RANDOM19 set to their antibacterial potency values on *S. aureus* strain C623.
AS values were calculated using the Parker-Arg0 scale (A) or the Kovacs(a)-Arg0 scale (B).

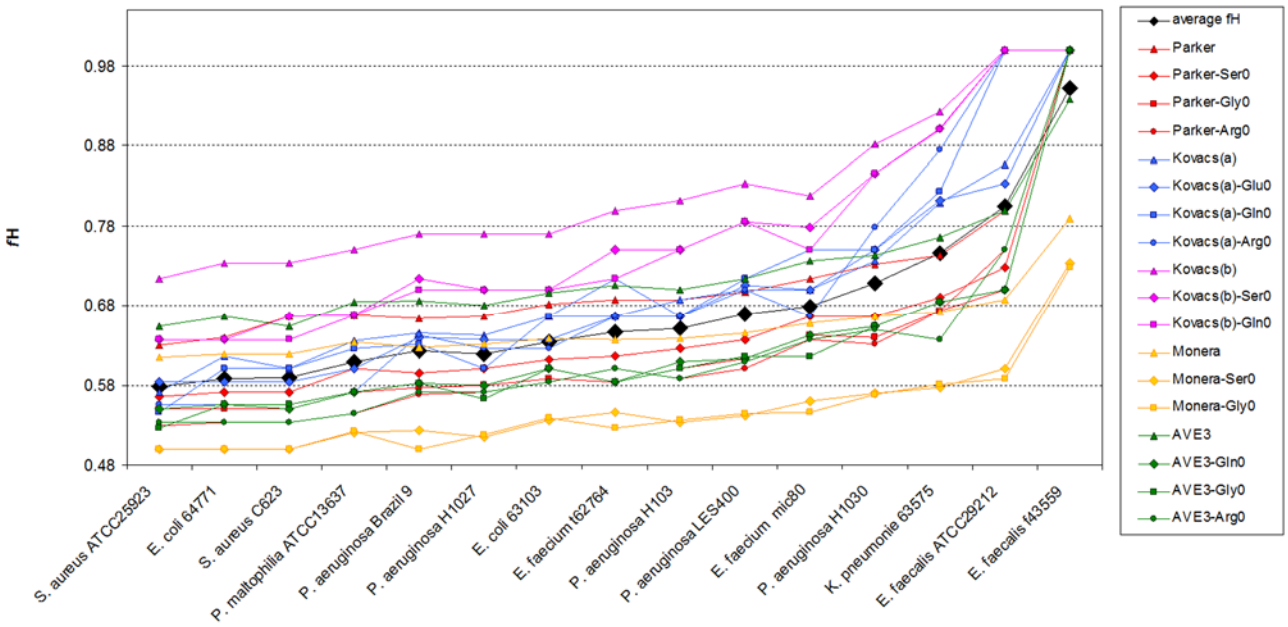

Fig. S5. Hydrophobicty scale dependence of *f*H values.
*f*H average values are shown as black diamonds. Strains are ordered on the basis of *f*H average values, from the lowest to the highest. Kovacs(a) and Monera derived scales systematically provided values higher and lower than the average, respectively. Within each set of experimental/derived scales experimental scales always provided the highest *f*H values.

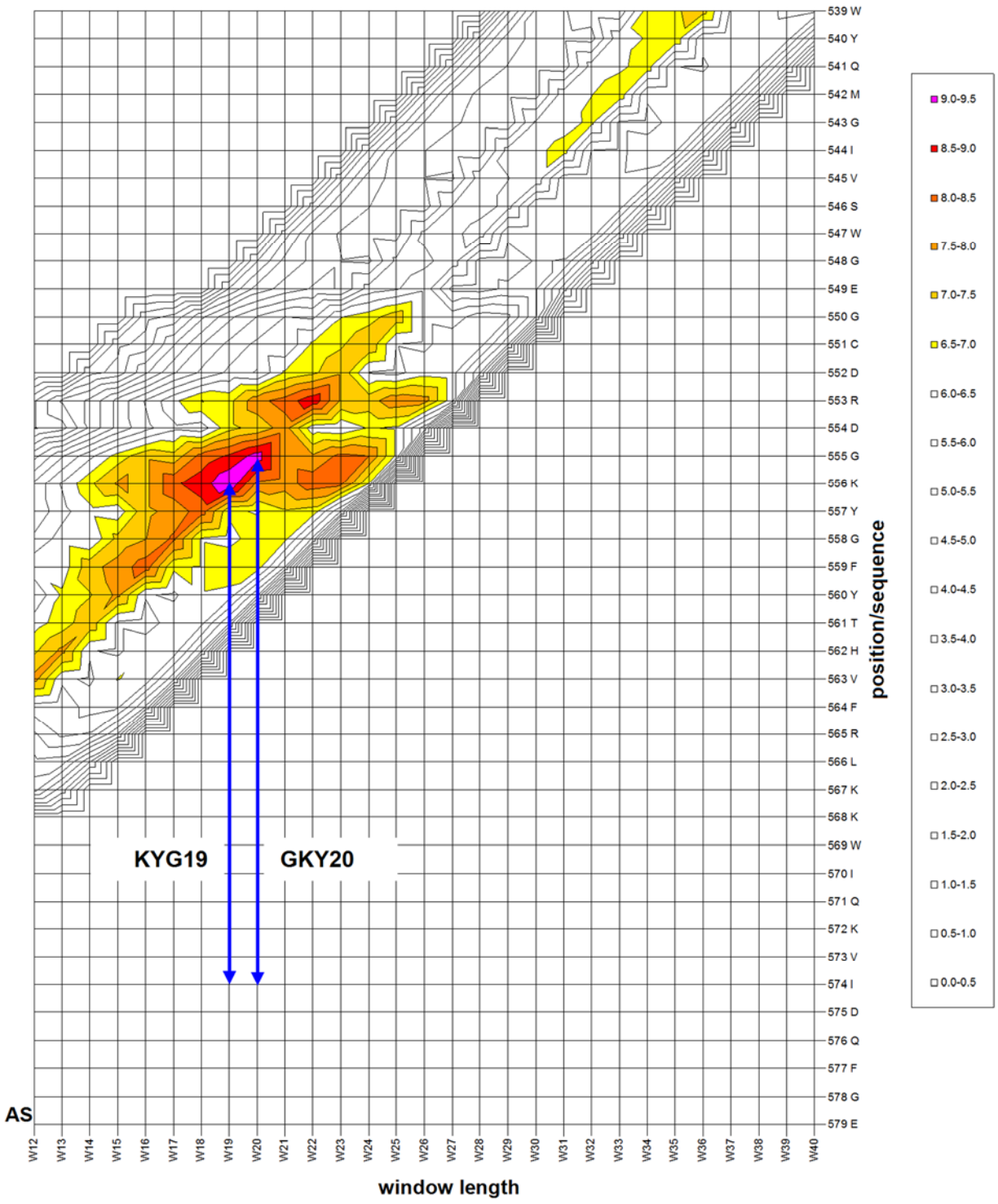

Fig. S6. Isometric plot showing AS values of peptides from 12 to 40 residues in the C-termini of human prothrombin (residues 539-579).
AS values obtained using parameters optimized for *S. aureus* C623 and Parker-Arg0 scale. Colours were used to highlight AS higher than 6.5 corresponding to MIC values lower than 200 μM.

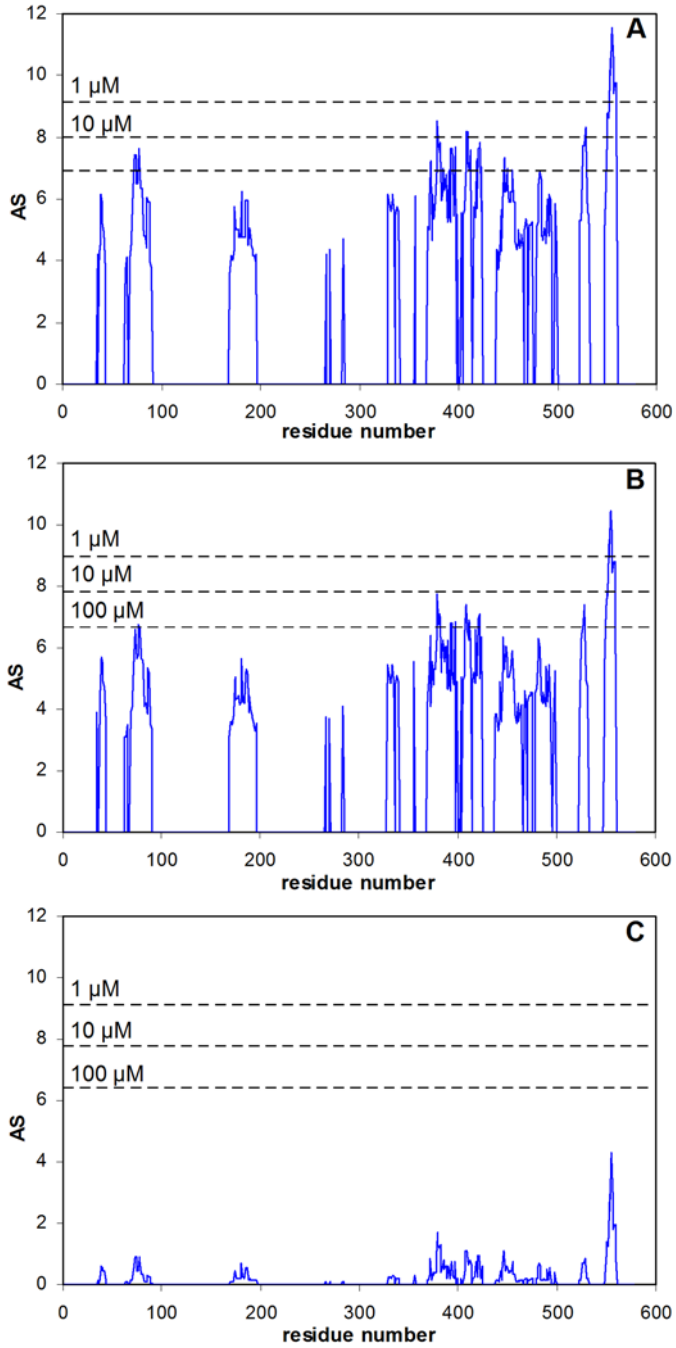

Fig. S7. Score profiles of human prothrombin (579 residues) obtained using parameters optimized for *S. aureus* C623 and Kovacs(a)-Arg0 (A), Kovacs(b)-Gln0 (B) and Monera-Gln0 (C) scales.

Profiles were obtained using a window length of 20 residues. The dotted lines indicate scores corresponding to MIC values of 100, 10 and 1 µM.

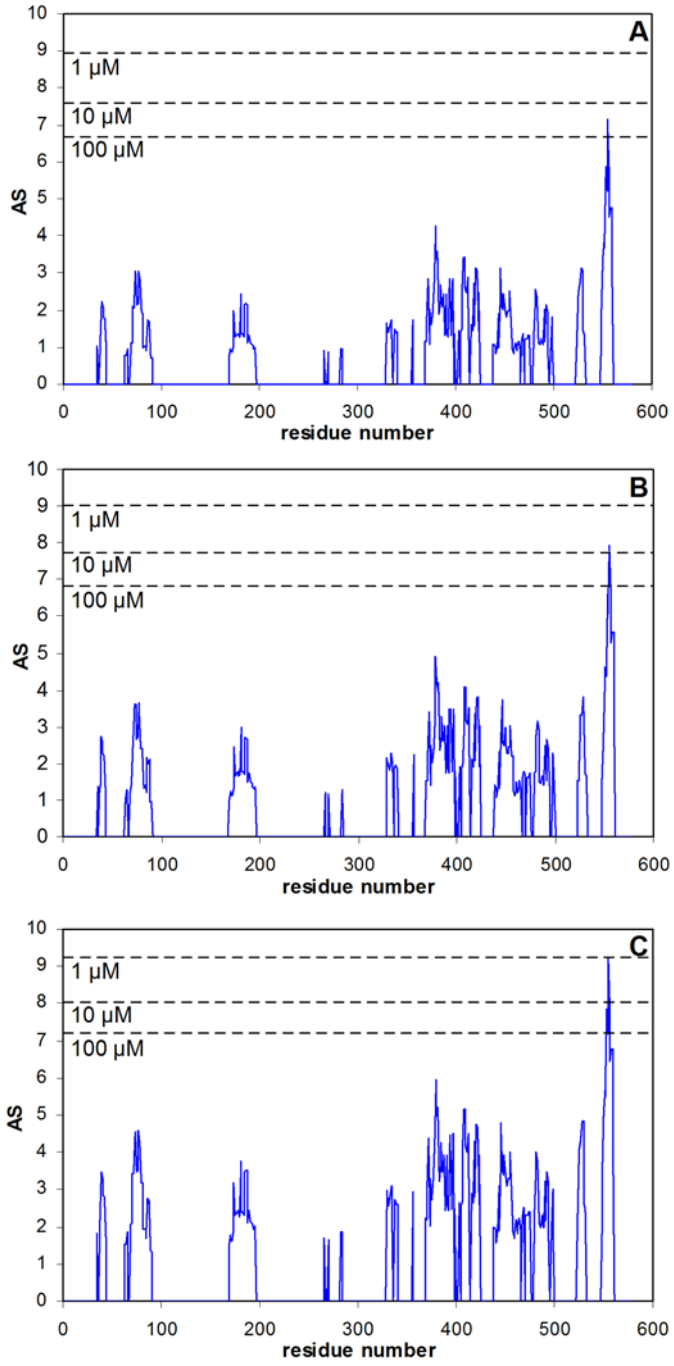

Fig. S8. Score profiles of human prothrombin (579 residues) obtained using parameters optimized for *S. aureus* C623 and AVE3-Gln0 (A), AVE3-Gly0 (B) and AVE3-Arg0 (C) scales. Profiles were obtained using a window length of 20 residues. Dotted lines indicate scores corresponding to MIC values of 100, 10 and 1 μM.

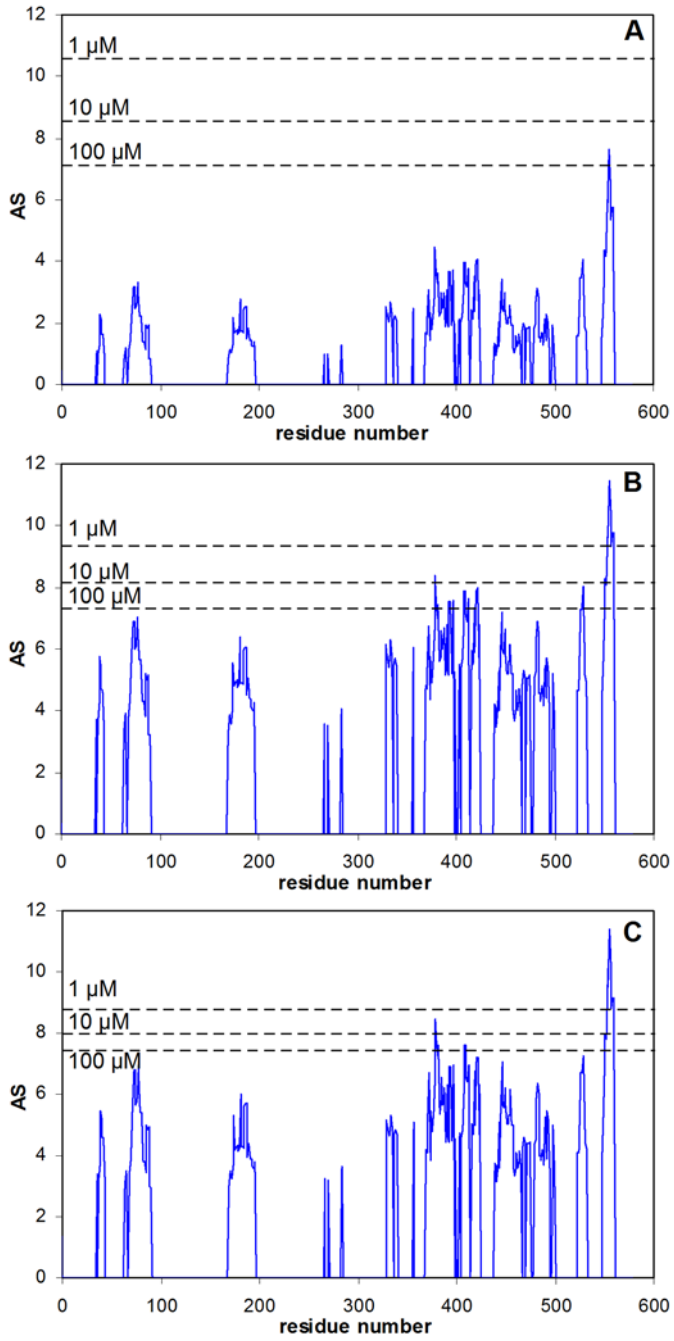

Fig. S9. Score profiles of human prothrombin (579 residues) obtained using parameters optimized for different strains.
(A) *P. aeruginosa* H1030 (*f*H = 0.63, slope = 2.03); (B) *E. faecium* mic80 (*f*H = 0.64, slope = 1.18); (C) *P. maltophilia* ATCC13637 (*f*H = 0.54, slope = 0.782). Profiles were obtained using a window length of 20 residues. Dotted lines indicate scores corresponding to MIC values of 100, 10 and 1 µM.

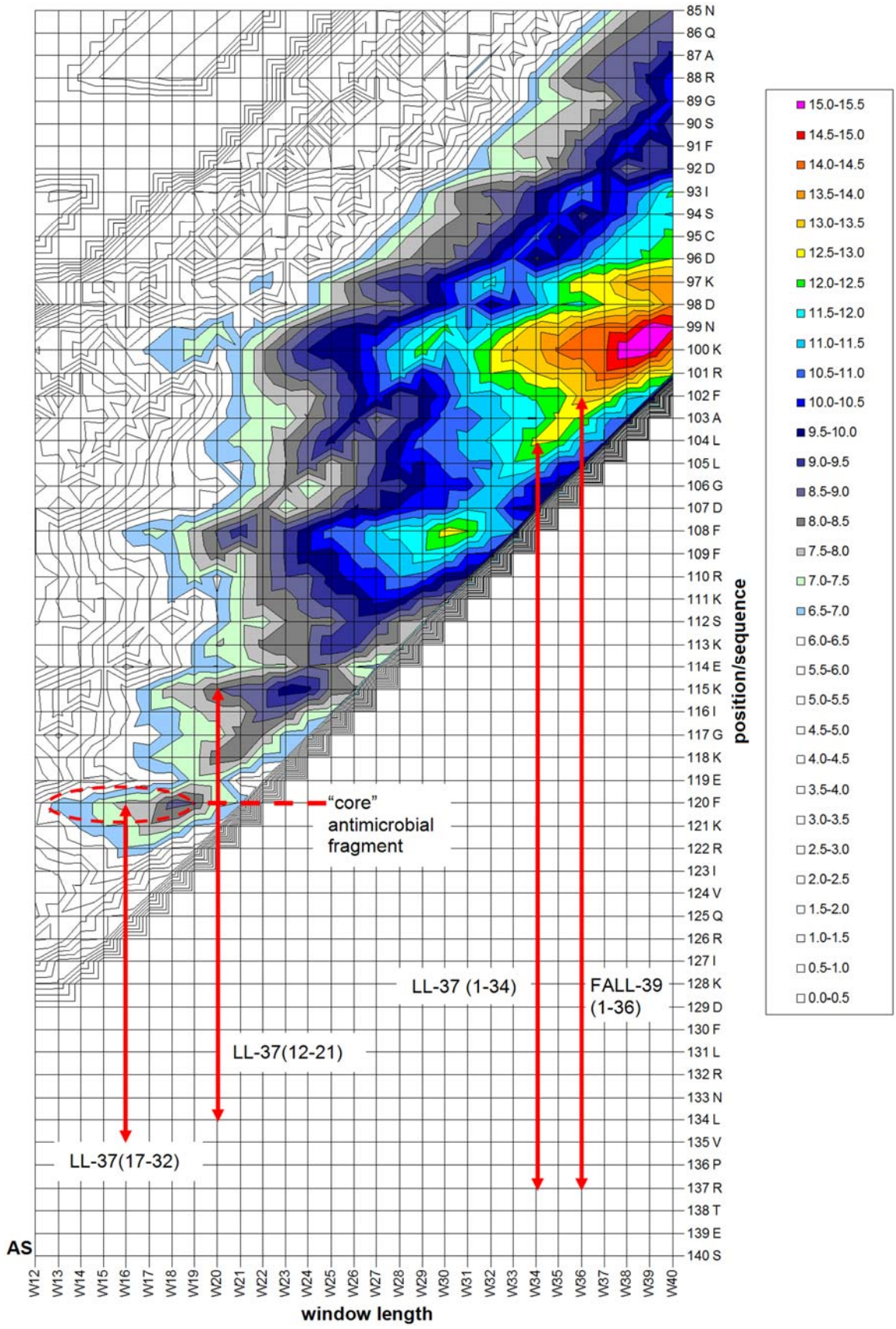

Fig. S10. Isometric plot showing AS values of peptides from 12 to 40 residues in the C-termini of hCAP-18 (residues 85-140).
AS values obtained using parameters optimized for *S. aureus* C623 and Parker-Arg0 scale. Colours were used to highlight AS higher than 6.5 corresponding to MIC values lower than 200 μM.

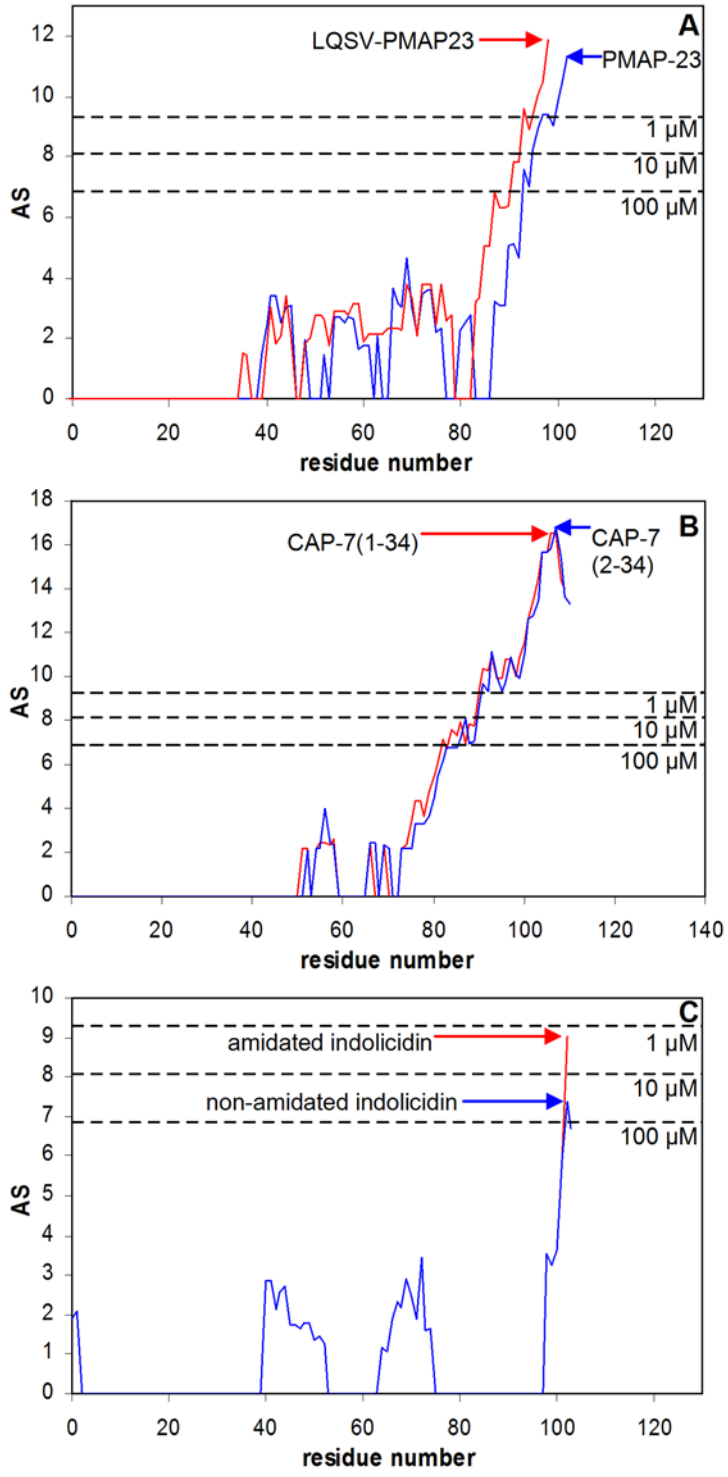

Fig. S11. Score profiles of the precursor of pig antimicrobial peptide PMAP-23 (A), of rabbit CAP18, the precursor of antimicrobial peptide CAP-7 (B), and of the precursor of bovine indolicidin (C).

AS values were obtained using parameters optimized for *S. aureus* strain C623 and Parker-Arg0 scale. Profiles were obtained using window lengths of 23 residues (blue line) and 27 residues (red line) for PMAP-23 (124 residues), of 33 residues (blue line) and 34 residues (red line) rabbit CAP18 (142 residues), of 13 residues for the precursor of bovine indolicidin (115 residues; blue and red lines correspond to scores calculated for a precursor without and with C-terminal amidation, respectively). Dotted lines indicate scores corresponding to MIC values of 100, 10 and 1 μM. In the

analysis of pig PMAP-23 (the last 23 residues of the precursor) the absolute maximum corresponds to a 27 residues peptide including PMAP-23 and four additional residues of the precursor. PMAP-23 corresponds to the maximum score obtained using a 23 residues window. In the analysis of rabbit CAP-7 (the last 37 residues of the precursor), the absolute maximum (16.7) corresponds to residues 2-34 of CAP-7, whereas the scores of fragment 1-34 and of entire CAP-7 are 16.5 and 15.6, respectively.

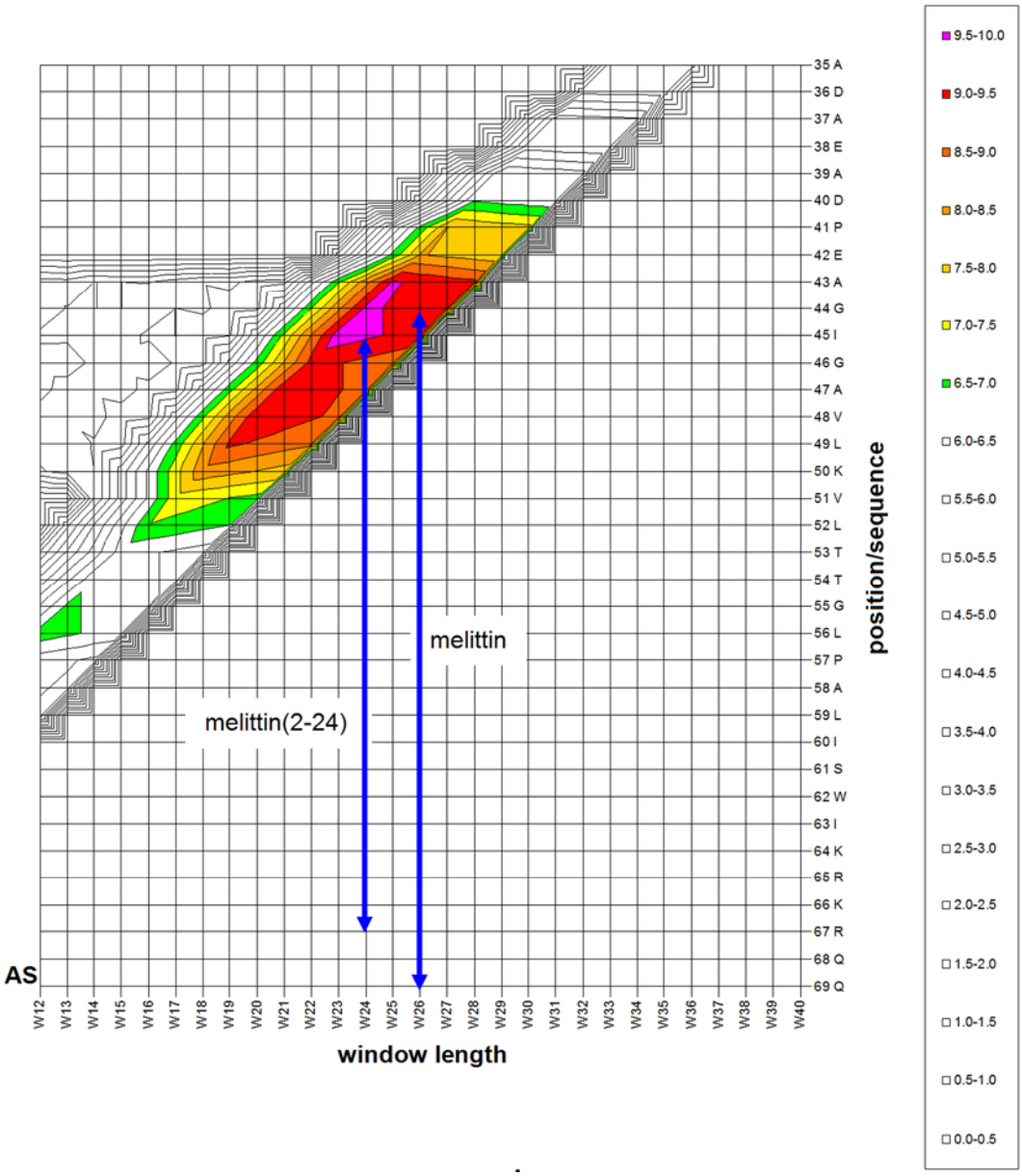

Fig. S12. Isometric plot showing AS values of peptides from 12 to 40 residues in the C-termini of the precursor of bee melittin (residues 35-69).
AS values obtained using parameters optimized for strain *S. aureus* C623 and Parker-Arg0 scale. Colours were used to highlight AS higher than 6.5 corresponding to MIC values lower than 200 μM.

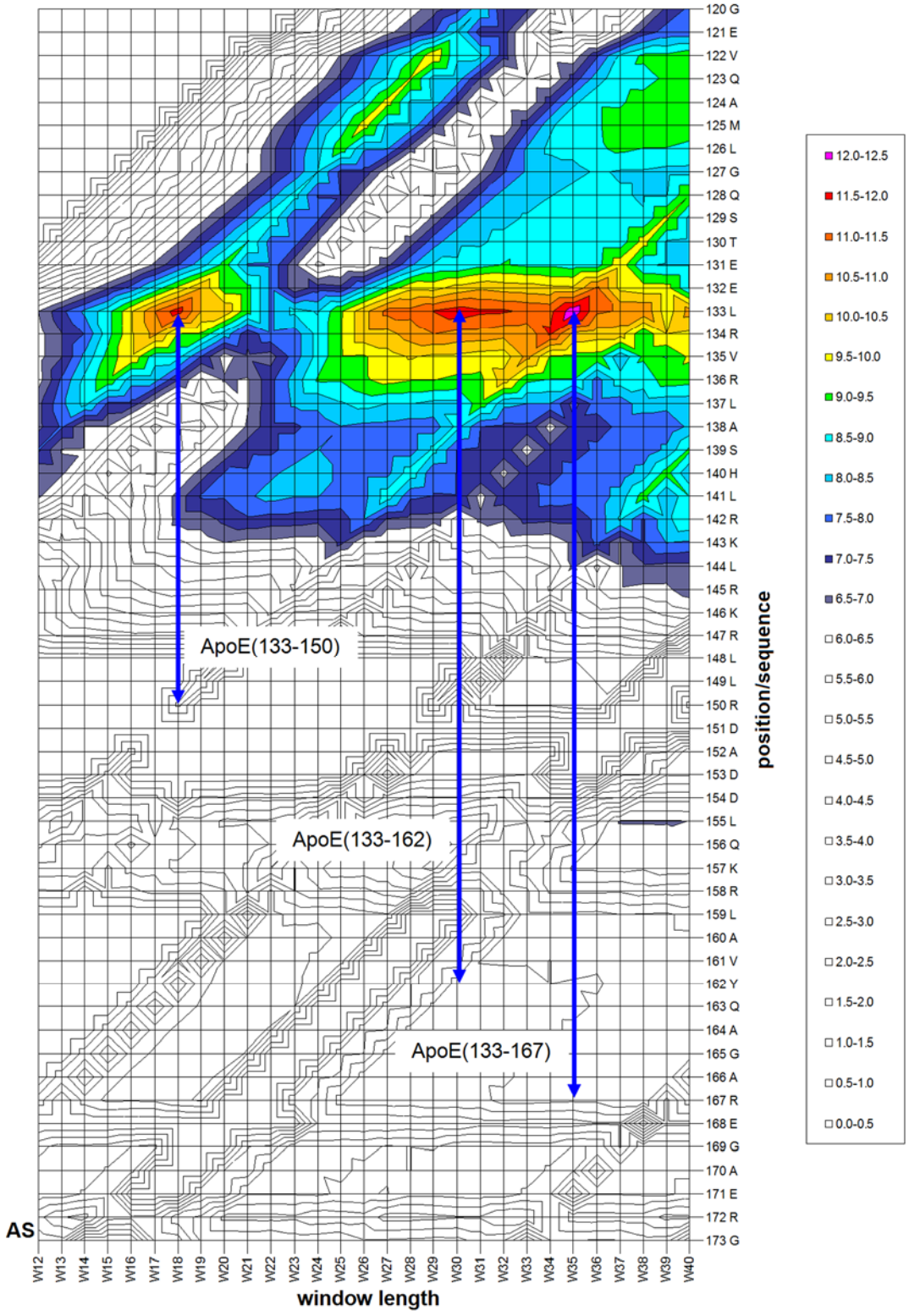

Fig. S13. Isometric plot showing AS values of peptides from 12 to 40 residues in the middle region of human apolipoprotein E (residues 120-173).
AS values obtained using parameters optimized for strain *S. aureus* C623 and Parker-Arg0 scale. Colours were used to highlight AS higher than 6.5 corresponding to MIC values lower than 200 μM.

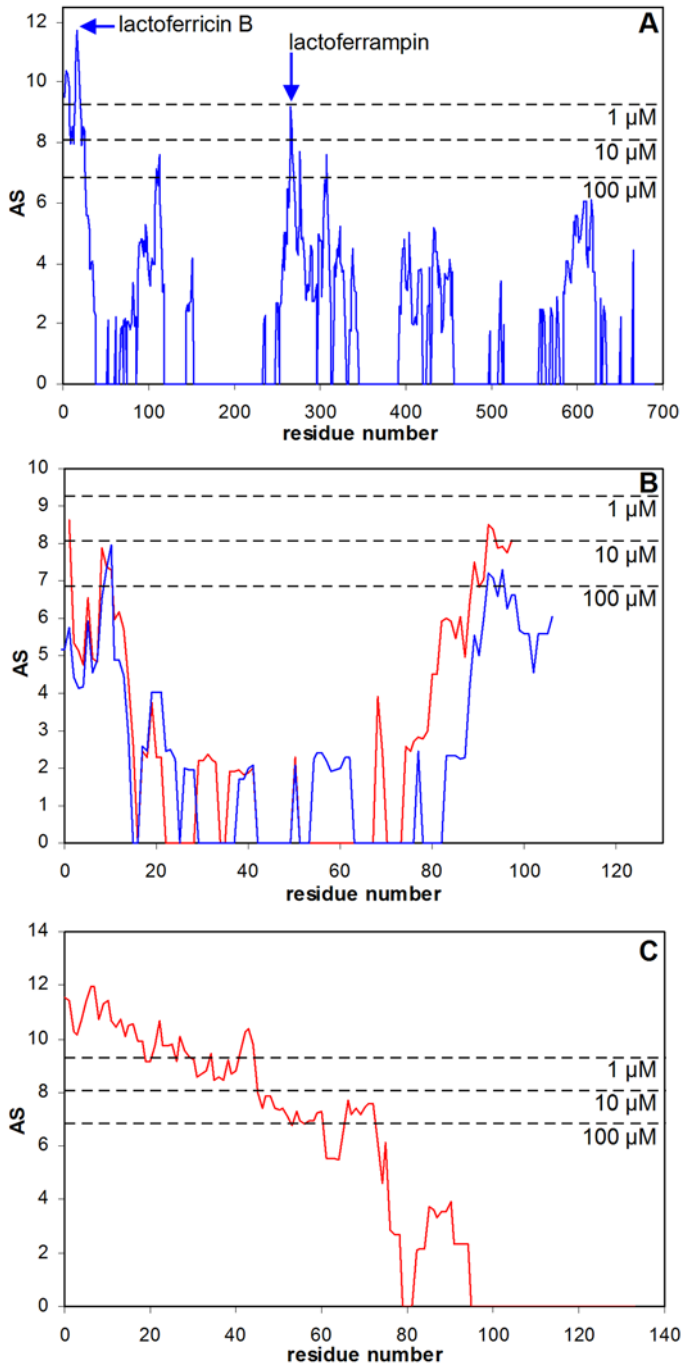

Fig. S14. Score profiles of bovine lactoferrin (A), human lysozyme C (B) and human ECP (C) obtained using parameters optimized for *S. aureus* strain C623 and Parker-Arg0 scale.
Profiles were obtained using window lengths of 25 residues for bovine lactoferrin (689 residues), of 25 residues (blue line) and 34 residues (red line) for human lysozyme C (130 residues), and of 40 residues for human ECP (133 residues). Dotted lines indicate scores corresponding to MIC values of 100, 10 and 1 μM.

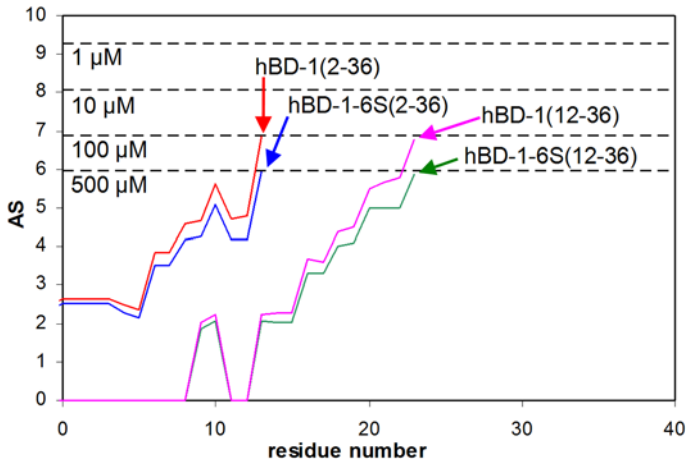

Fig. S15. Score profiles of wild type hBD-1 precursor and of variant hBD-1-6S with the six cysteine residues changed to serine.
Profiles were obtained using window lengths of 35 residues (hBD-1, red line; hBD-1-6S, blue line) and 25 residues (hBD-1, magenta line; hBD-1-6S, green line). Dotted lines indicate scores corresponding to MIC values of 500 µM, 100, 10 and 1 µM.