

## **ELECTRONIC SUPPORTING INFORMATION**

# **Peptide Structure and Silver Ion Affinity: Influence on the Formation of $\alpha$ -Helices upon Metal Binding**

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## Experimental methods

### Solid-Phase Peptide Synthesis

The majority of the peptides used in this study were obtained from Bachem SA (purities  $\geq$  95%). The remaining peptides (M1-B2, M15-B2, M16-B2, M17-B2, M18-B2, and M19-B2,) were synthesized using SPPS (Solid-Phase Peptide Synthesis) on a Rink-Amide resin (ChemMatrix, loading 0.42-0.47 mmol/g) with a Biotage Initiator+ Alstra automated peptide synthesizer, following a procedure reported in the literature.<sup>1</sup>

### Electrospray ionization mass spectrometry

The ESI-MS (Bruker Esquire HCT) in positive ion mode was performed on the six undecapeptides synthesized in-house, immediately following the purification process. This procedure was conducted to verify the identity of the undecapeptide obtained (Fig. S11-S18).

### Determination of peptide concentrations

Approximately 1 mg of each lyophilized peptide was dissolved in 700  $\mu$ L of bidistilled H<sub>2</sub>O, and the concentrations were determined by UV-Vis spectroscopy (Perkin Elmer Lambda 25) and the Beer-Lambert law:  $A_\lambda = \varepsilon_\lambda cl$ , where  $A$  is the absorbance,  $\varepsilon_\lambda$  is the molar extinction coefficient at wavelength  $\lambda$ ,  $c$  is the concentration, and  $l$  is the length of the cuvette (1 cm in this research). The molar extinction coefficient at 205 nm ( $\varepsilon_{205}$ ) of each peptide was determined by using the formula of Anthis *et al.*:<sup>2</sup>

$$\varepsilon_{205} = \sum (\varepsilon_i n_i) + \varepsilon_{bb}(r - 1),$$

where for each amino acid  $i$ ,  $\varepsilon_i$  is the molar extinction coefficient of the amino acid side chain (from Goldfarb *et al.*)<sup>3</sup>,  $n_i$  is the number of occurrences of that amino acid in the peptide sequence,  $\varepsilon_{bb}$  is the molar extinction coefficient for a single backbone peptide bond, and  $r$  is the number of amino acid residues in the peptide sequence. In the case of HEWM probe, the exact concentration was determined from the molar extinction coefficient at 280 nm ( $\varepsilon_{280} = 5540 \text{ M}^{-1}\cdot\text{cm}^{-1}$ ).<sup>4</sup>

## Determination of Ag<sup>+</sup>/peptide secondary structure

As previously reported, the study of the secondary structure was investigated using a circular dichroism (CD) spectrometer (Applied Photophysics Chirascan V100).<sup>1</sup> CD spectra (Fig S20-S27) were recorded at 25°C by adding increasing amounts of AgNO<sub>3</sub> (silver nitrate, Fisher Chemical ≥99.9%) dissolved in bidistilled H<sub>2</sub>O, ranging from 0 to 20 equivalents.

### DichroWeb analysis server

The screenshot displays the DichroWeb server interface. At the top left is the logo, and at the top right is a 'Server Status' box indicating 'Current Service Info : No reported problems. Since'. Below the logo is a link to a 'CD BOOK'. The main form is divided into several sections: 'Registration' with fields for 'UserID' and 'IDpassword'; 'Input File Details' with 'Protein name' (B2 - 1eq.) and 'File location' (Choose File B2 - 1eq.txt); 'About the Data File' with 'File Format' (FREE), 'Input Units' (delta epsilon), 'Initial Wavelength' (310), 'Final Wavelength' (190), 'Wavelength Step' (1.0), and 'Lowest nm datapoint' (180); 'Choice of Methods' with 'Analysis Programme' (CDSSTR) and 'Reference Set' (Set 7); 'Advanced Options' with 'Optional Scaling Factor' (1.0); and 'Output Options' with 'Output Units' (delta epsilon). A 'submit' button is at the bottom right. A 'SERVICE INFORMATION' box at the bottom left shows 'No reported problems. Since 09 Dec 2019'. Other buttons include 'RESET THE FORM' and 'Check the server load (new window)'.

**Fig. S1** Example of data input interface of the DichroWeb server,<sup>5-7</sup> used for the CD analysis of HQAMAEHRRM (B2) titrated with 1 equivalent Ag<sup>+</sup>. The ASCII-format CD data file (B2 – 1eq.txt), containing ellipticity values in  $\Delta\epsilon$  [ $M^{-1}\cdot cm^{-1}$ ], is uploaded under the “Input File Details” section. The following key experimental parameters are provided: wavelength range (310-190 nm), and the step size (1.0 nm). The minimum wavelength employed for analysis is set to 180 nm. In the “Choice of Methods” section, the CDSSTR algorithm is selected with reference dataset Set 7, which has been optimized for the 190-240 nm range. The output units are maintained at a consistent level in order to ensure precise and reliable measurements. These settings enable precise estimation of the secondary structure composition from CD spectrum.

## Determination of Ag<sup>+</sup>/peptide binding constants

In accordance with previously reported methodologies, the silver binding constants ( $\log(K_{b-1/b-2})$ ) of each peptide were determined using a fluorescence spectrometer (Perkin Elmer LS 50 B).<sup>1</sup> Each peptide was subjected to three titrations at two different concentrations ( $1 \cdot 10^{-5}$  M and  $2 \cdot 10^{-5}$  M) employing a competition titration strategy with HEWM probe (1 equivalent). The experiments were conducted in MOPS (3-(N-morpholino)propansulfonic acid, Alfa Aesar  $\geq 99\%$ ) buffer (20 equivalents, pH 7.4-7.5) by addition of AgNO<sub>3</sub> (silver nitrate, Fisher Chemical  $\geq 99.9\%$ ) solution in bidistilled H<sub>2</sub>O (0 to 5.5 equivalents) at 25°C (Fig S28-S71).

## Dynafit coding

```
[task]
  task = fit
  data = equilibria
[mechanism] ; "M" = metal, "P" = peptide, "P*" = labelled peptide
  M + P* <=> MP* : Kd1   dissoc
  M + P <=> MP : Kd2   dissoc
  MP + M <=> MMP : Kd3   dissoc
  MMP + M <=> MMMP : Kd4   dissoc
  MMMP + M <=> MMMMP : Kd5   dissoc
[constants]
  Kd1 = 3.79e-7
  Kd2 = 1.2e-07 ??
  Kd3 = 1.2e-07 ??
  Kd4 = 1.2e-07 ??
  Kd5 = 1.2e-07 ??
[responses]
  P* = 38681.00 ?, MP* = 1.98E+04 ?
[data]
  variable M, P, P*
  plot titration ;

  set 1

[output]
  directory ./data/output/fit
[settings]
[Output]
  XAxisLabel = [Metal], M
  YAxisLabel = Fluorescence, A.U.
;
[set:1]
M, M          P, M          P*, M          Fluorescence
0             0.019684583   0.023902309   924.5653
0.004016787  0.019668848   0.023883203   884.17
0.008027157  0.019653138   0.023864127   838.31
0.016028708  0.019621793   0.023826066   771.92
0.024004777  0.019590548   0.023788126   699.07
0.035921366  0.019543867   0.023731443   599.06
0.0477813    0.019497408   0.023675029   523.98
0.063507109  0.019435805   0.023600226   480.35
0.086910377  0.019344126   0.023488904   469.29
0.117773438  0.019223226   0.023342099   464.84
0.155813953  0.019074208   0.023161152   459.76
0.193269231  0.018927484   0.02298299    455.89
[end]
;
;
```

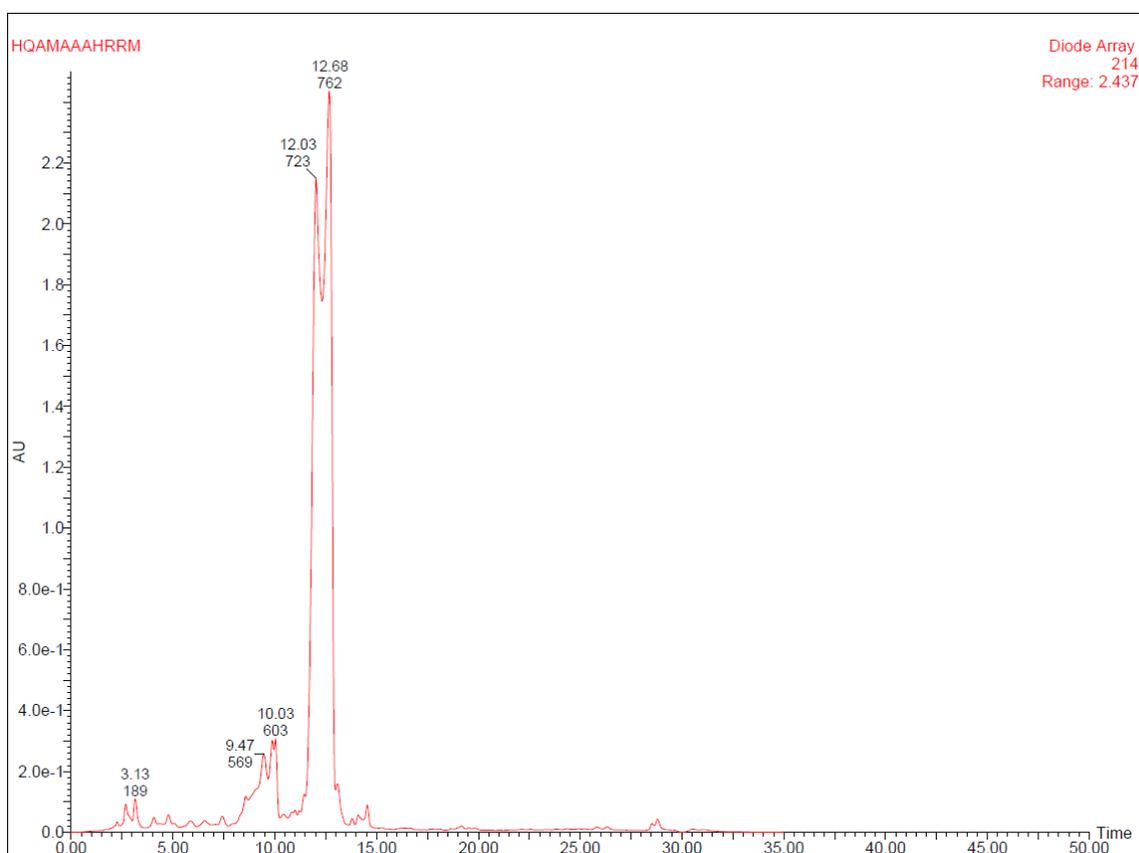
**Fig. S2** Example of Dynafit code used to determine the binding constants for the competition titration between HQAMAEHRRM (B2) and HEWM, both at  $2 \cdot 10^{-5}$  M. *M* represents the metal ion (Ag<sup>+</sup>), *P* represents the peptide (B2), *P\** represents the probe (HEWM). The dissociation constant of the probe ( $K_{d1}$ ) was previously determined by Chabert *et al.*<sup>8-10</sup>

## Experimental data

### HPLC: Retention times of undecapeptides

**Table S1** Retention time [min] of the synthesized peptide using semi-preparative reverse phase HPLC with a linear gradient from 95% to 70% of A in B, at a flow rate of 5 mL/min for 25 min, where A is a solution of 0.1% TFA in H<sub>2</sub>O, and B is a solution of 0.1% TFA in ACN.

Model	Retention time [min]	Model	Retention time [min]
HQAMAAHRRM	12.68	MKKMAEAHQH	9.80
MQAMAEHRRM	14.93	HQQHAAHQH	2.87
HQAMAEAMRRM	17.98	MKKMAAAMKKM	15.53
MKKMAEAMKKM	18.98	MKKMAAAHQH	2.43



**Fig. S3** HPLC chromatogram of HQAMAAHRRM (M1-B2)

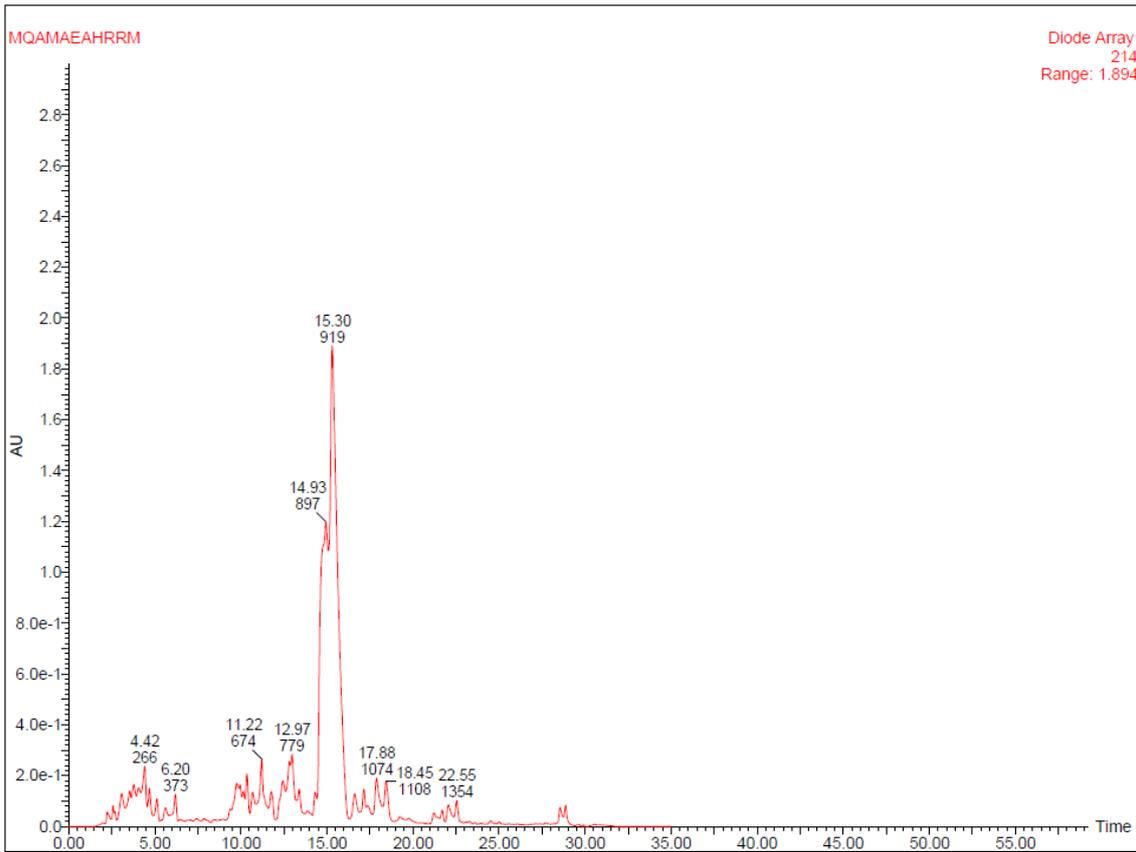


Fig. S4 HPLC chromatogram of MQAMAEHRRM (M11-B2)

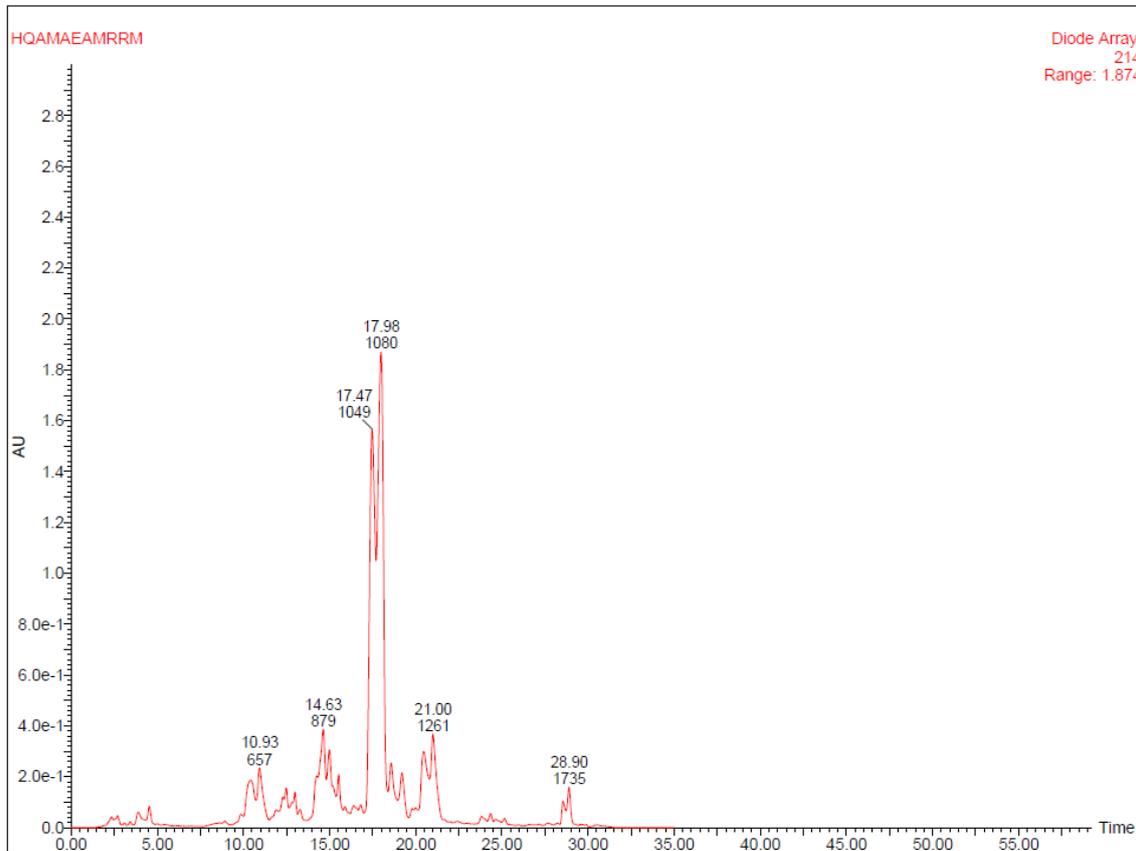


Fig. S5 HPLC chromatogram of HQAMAEAMRRM (M13-B2)

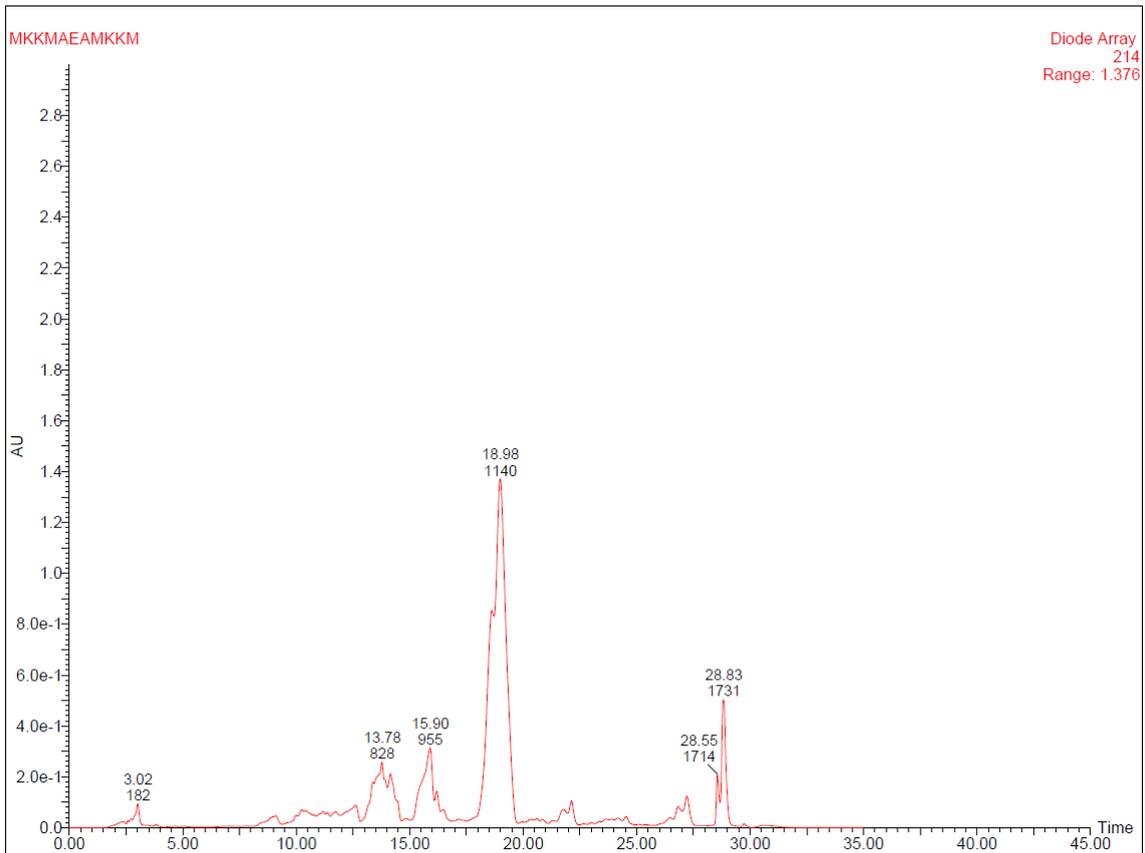


Fig. S6 HPLC chromatogram of MKKMAEAMKKM (M17-B2)

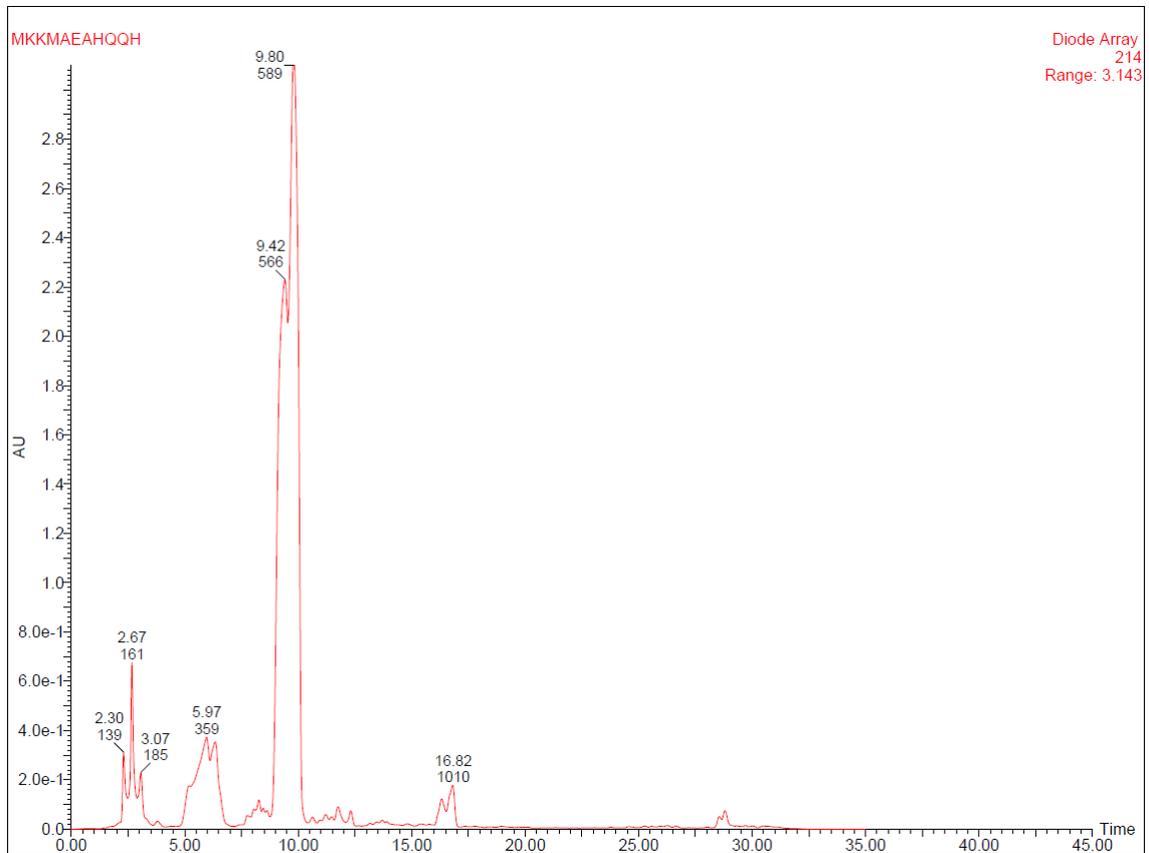


Fig. S7 HPLC chromatogram of MKKMAEAHQQH (M18-B2)

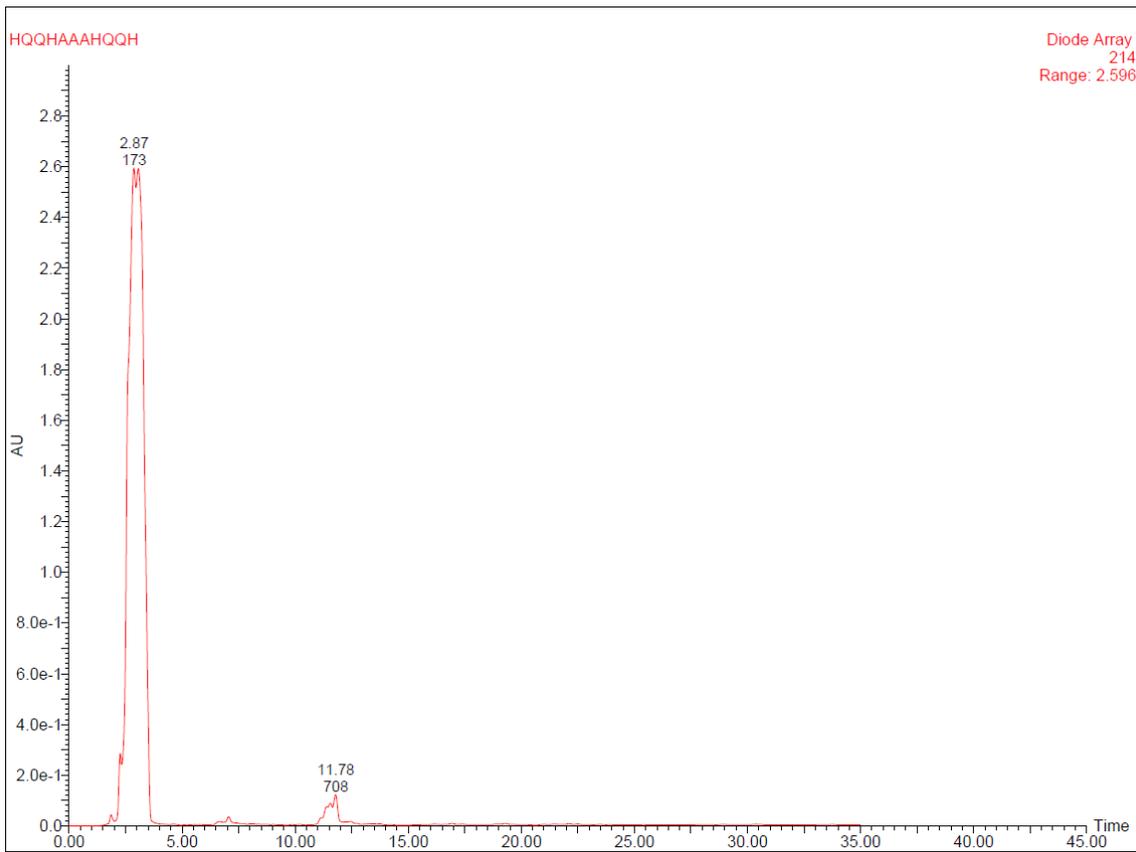


Fig. S8 HPLC chromatogram of HQQHAAAHQQH (M19-B2)

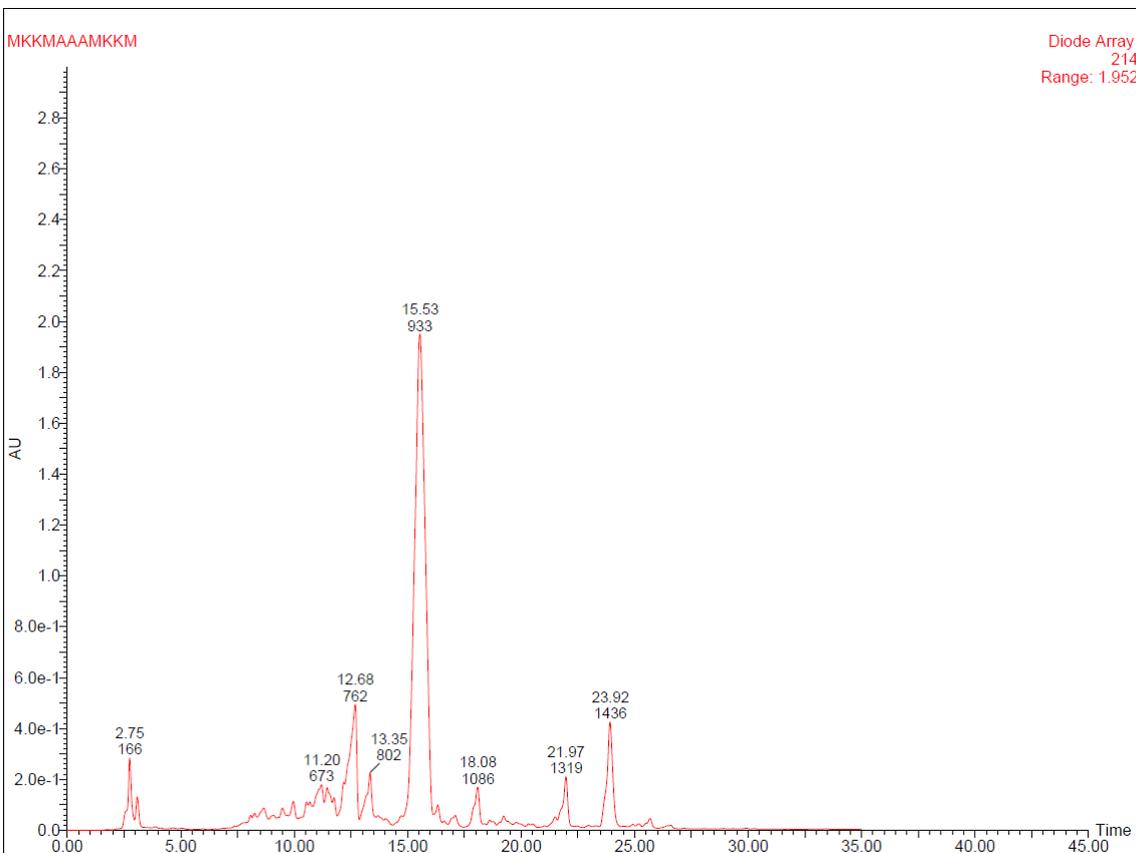
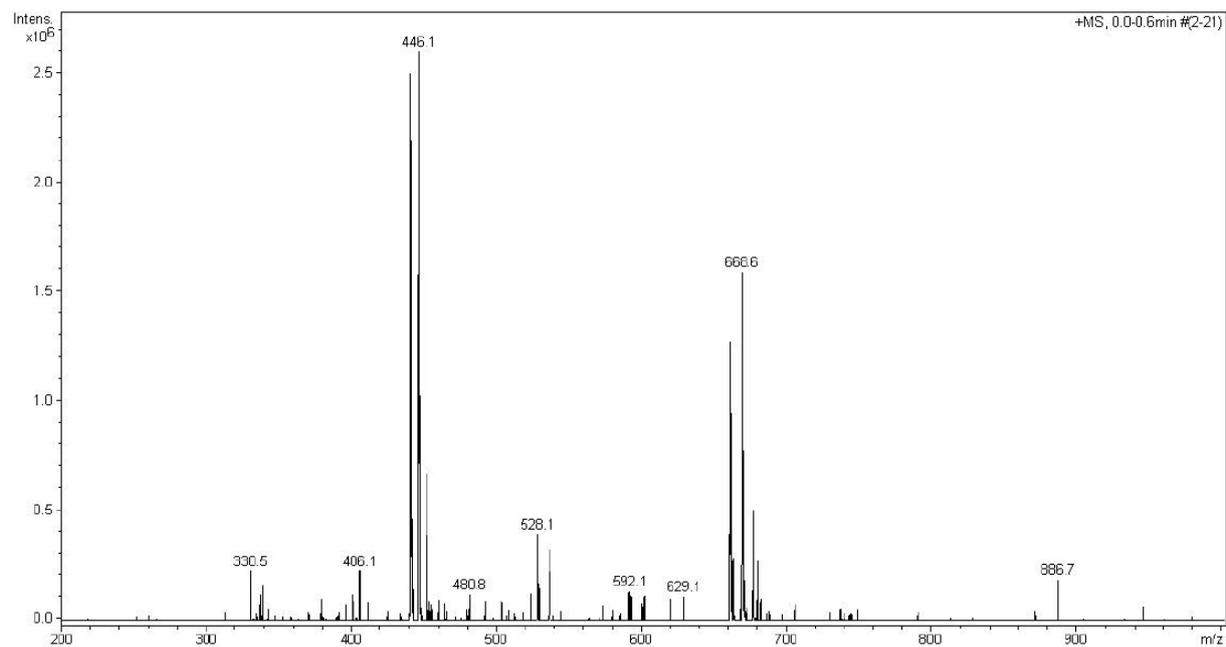


Fig. S9 HPLC chromatogram of MKKMAAAMKKM (M20-B2)

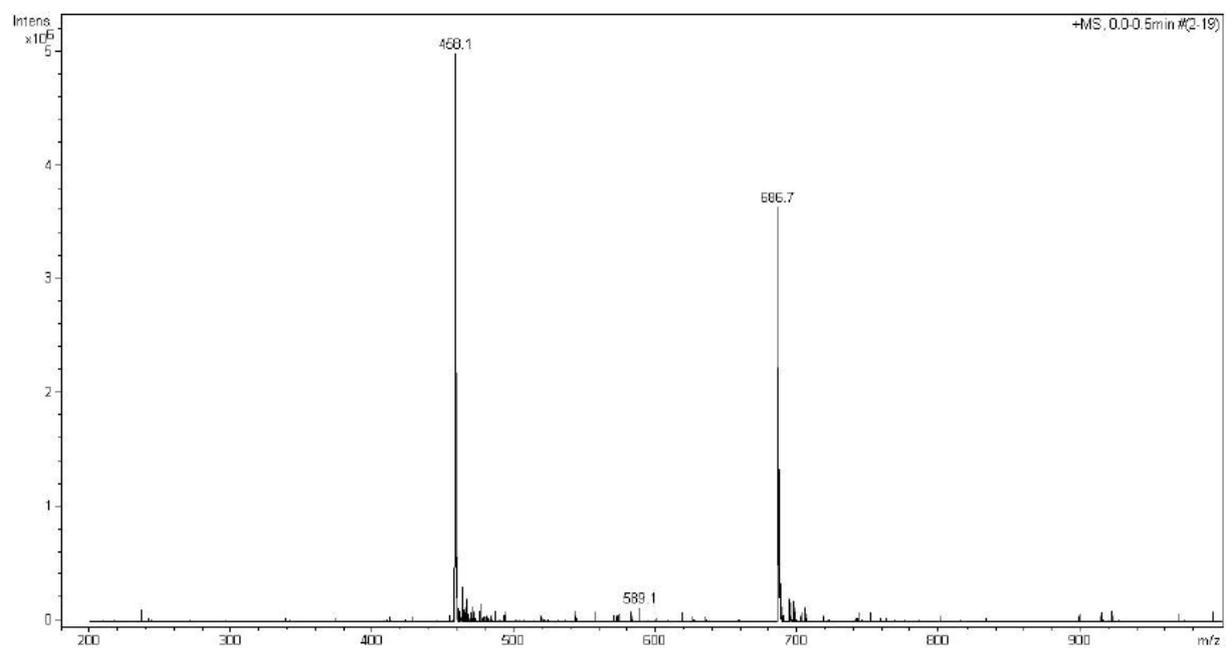


**Fig. S10** HPLC chromatogram of MKKMAAAHQH (M21-B2)

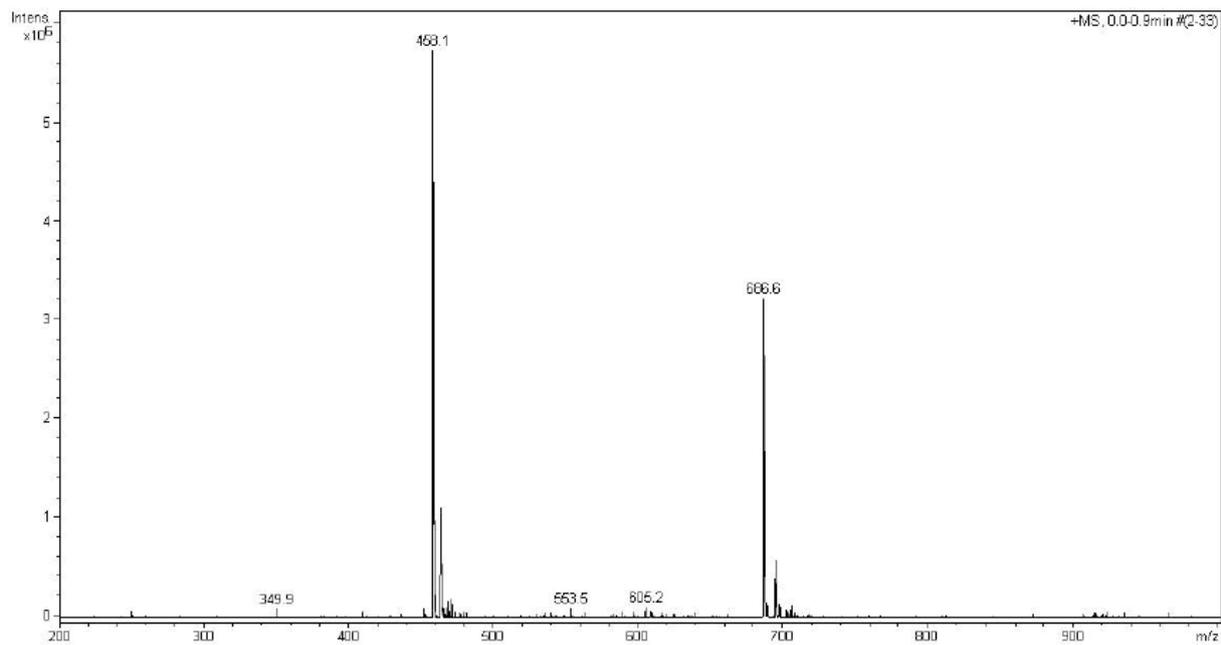
## Electrospray ionization mass spectrometry



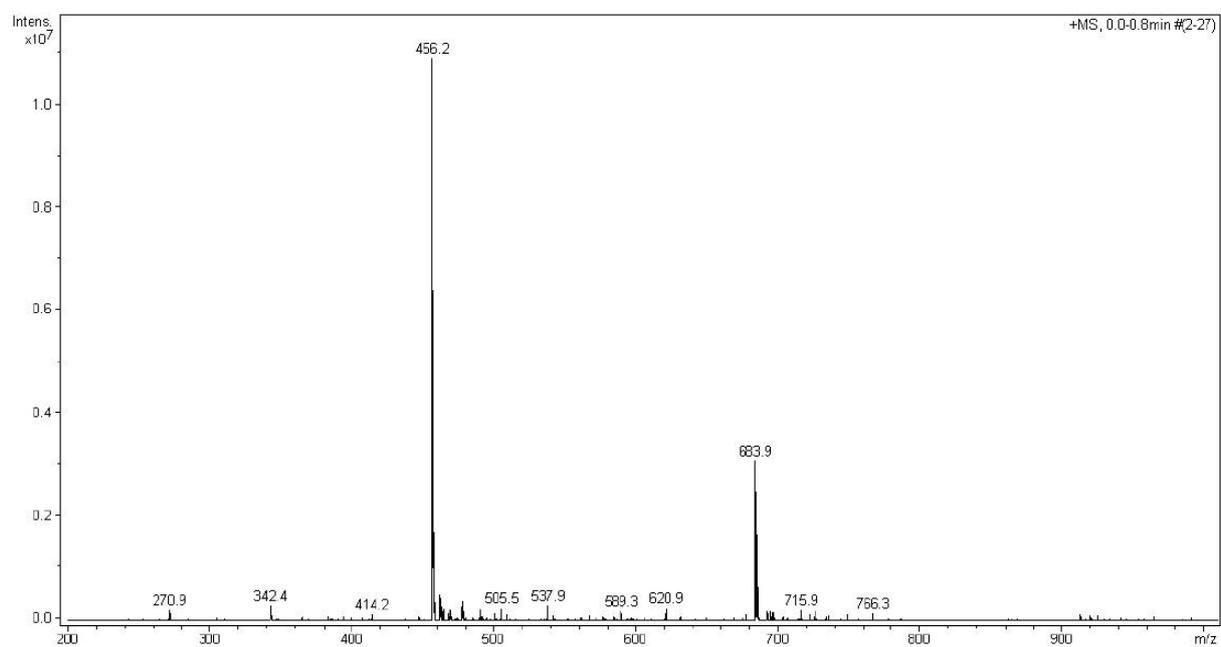
**Fig. S11** ESI-MS spectrum of HQAMAAAHRM (M1-B2).  $[M+H]^+_{\text{calc}}$  (m/z) : 1320.6 ;  $[M+2H]^{2+}_{\text{exp}}$  (m/z) : 660.6 ;  $[M+3H]^{3+}_{\text{exp}}$  (m/z) : 440.8 ;  $[M+2H]^{2+}_{\text{exp}}$  (m/z) : 330.5



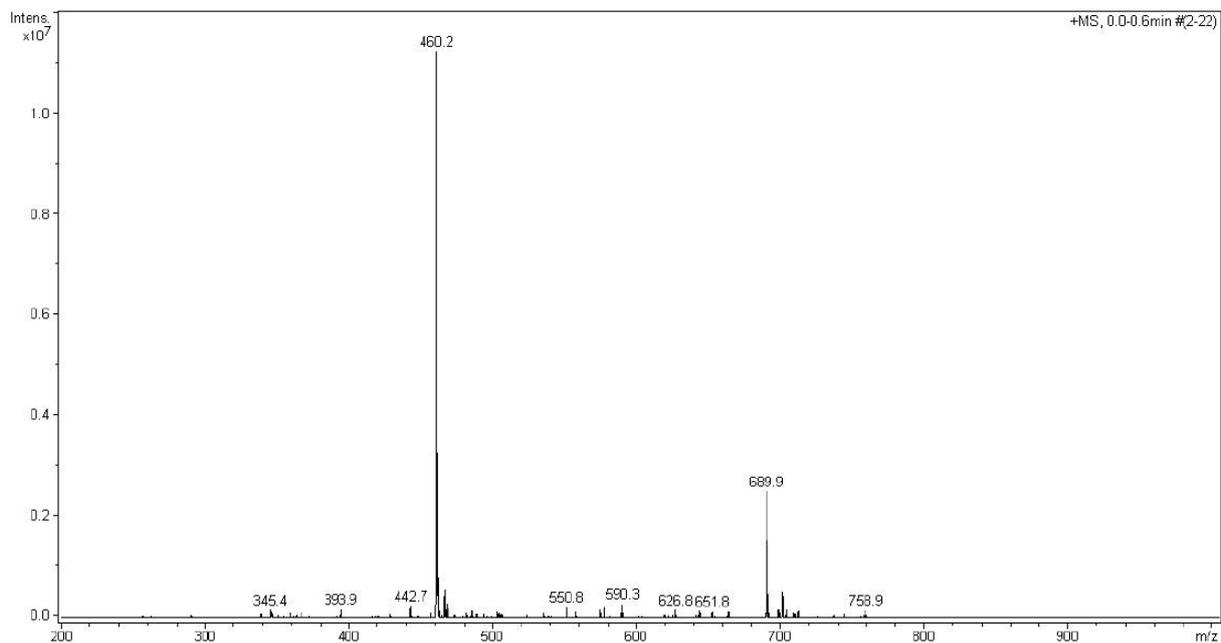
**Fig. S12** ESI-MS spectrum of MQAMAEHRM (M11-B2).  $[M+H]^+_{\text{calc}}$  (m/z) : 1372.6 ;  $[M+2H]^{2+}_{\text{exp}}$  (m/z) : 686.7 ;  $[M+3H]^{3+}_{\text{exp}}$  (m/z) : 458.1



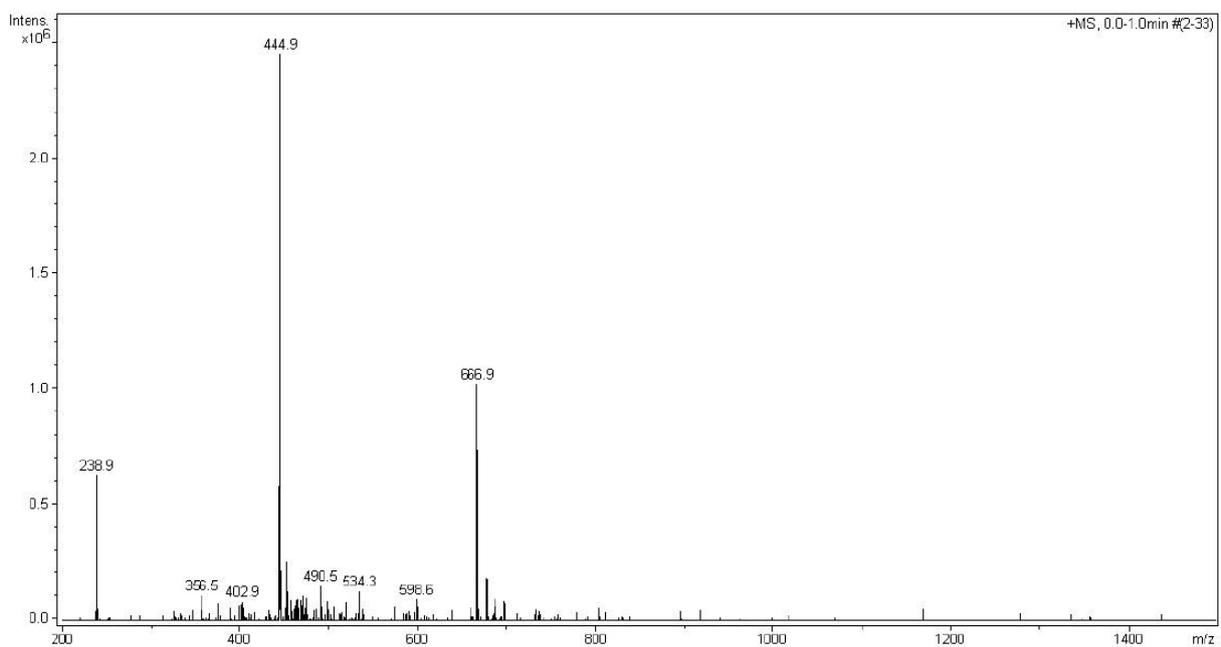
**Fig. S13** ESI-MS spectrum of HQAMAEAMRRM (M13-B2).  $[M+H]^+_{\text{calc}}$  (m/z) : 1372.6 ;  $[M+2H]^{2+}_{\text{exp}}$  (m/z) : 686.6 ;  $[M+3H]^{3+}_{\text{exp}}$  (m/z) : 458.1



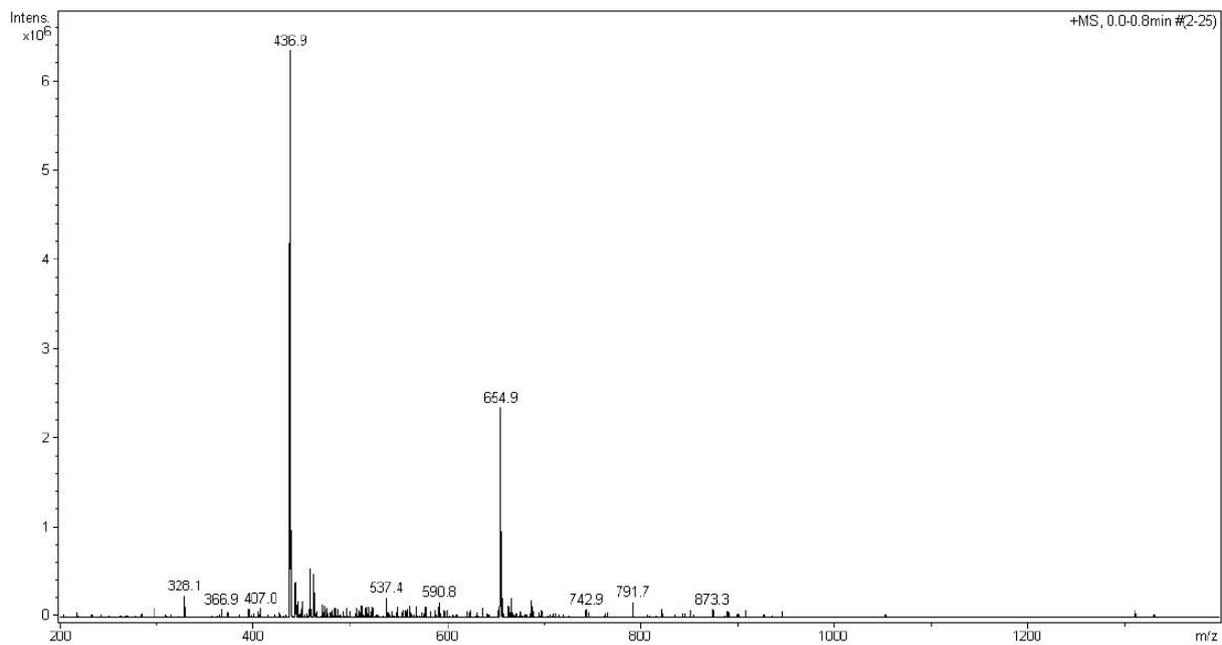
**Fig. S14** ESI-MS spectrum of MKKMAEAMKKM (M17-B2).  $[M+H]^+_{\text{calc}}$  (m/z) : 1367.7 ;  $[M+2H]^{2+}_{\text{exp}}$  (m/z) : 683.9 ;  $[M+3H]^{3+}_{\text{exp}}$  (m/z) : 456.2 ;  $[M+4H]^{4+}_{\text{exp}}$  (m/z) : 342.4



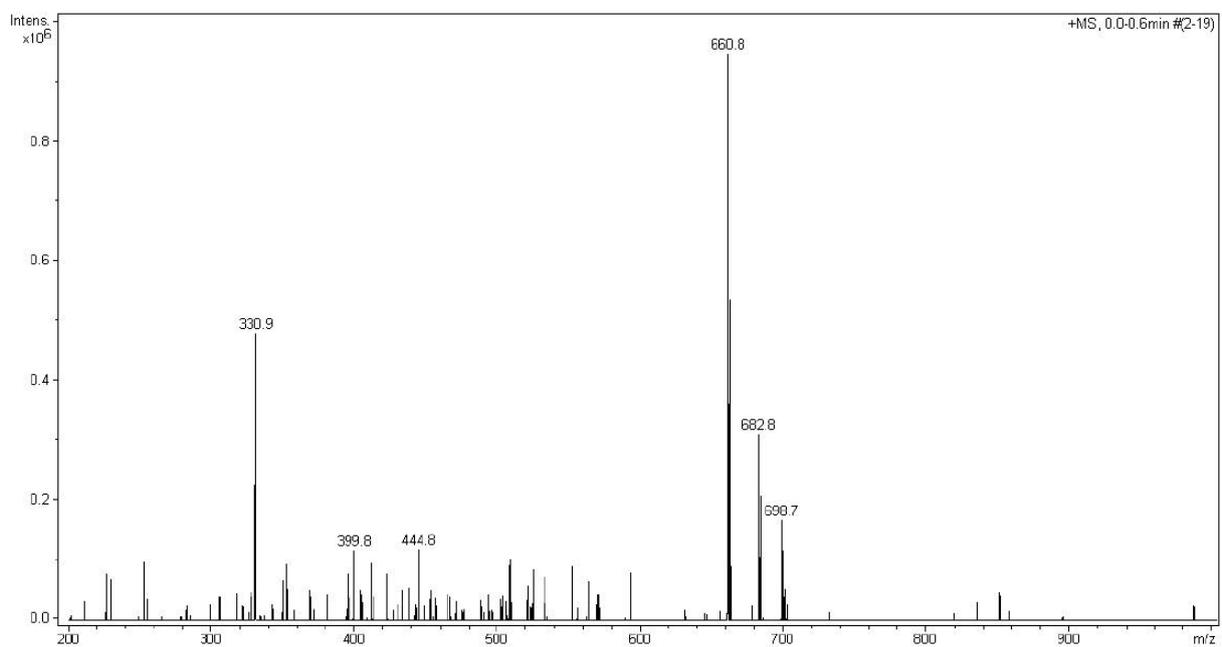
**Fig. S15** ESI-MS spectrum of MKKMAEAHQH (M18-B2).  $[M+H]^+$ <sub>calc</sub> (m/z) : 1379.7 ;  $[M+2H]^{2+}$ <sub>exp</sub> (m/z) : 689.9 ;  $[M+3H]^{3+}$ <sub>exp</sub> (m/z) : 460.2 ;  $[M+4H]^{4+}$ <sub>exp</sub> (m/z) : 345.4



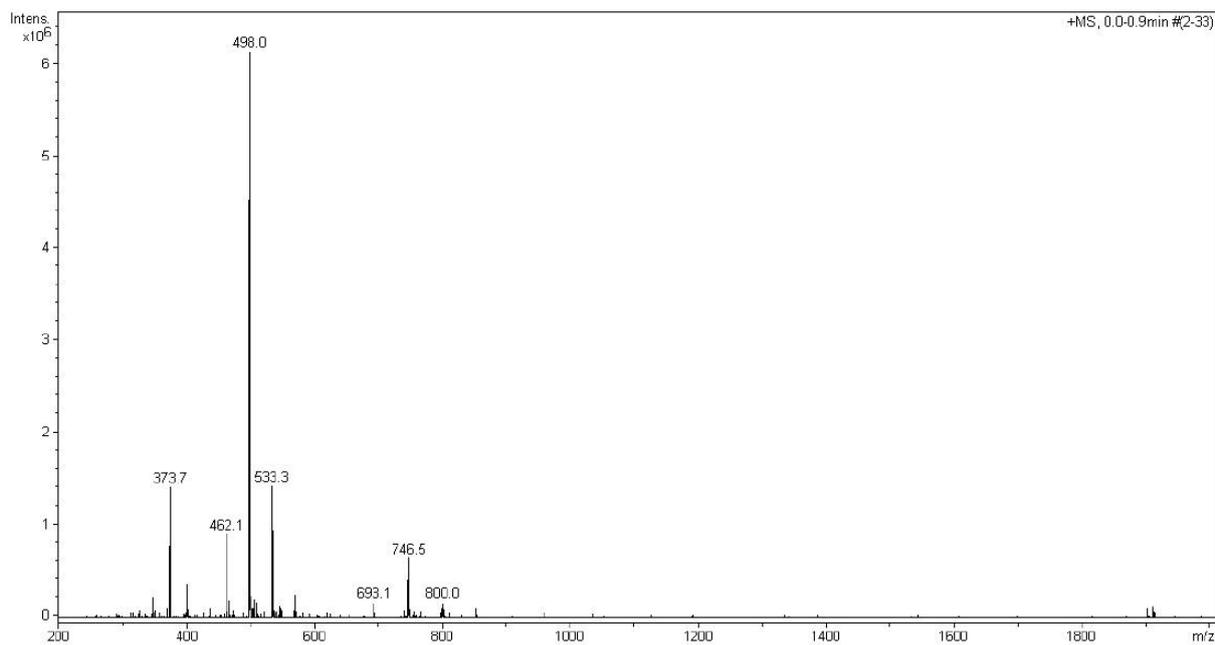
**Fig. S16** ESI-MS spectrum of HQQHAAHQH (M19-B2).  $[M+H]^+$ <sub>calc</sub> (m/z) : 1332.6 ;  $[M+2H]^{2+}$ <sub>exp</sub> (m/z) : 666.9 ;  $[M+3H]^{3+}$ <sub>exp</sub> (m/z) : 444.9 ;  $[M+4Na]^{4+}$ <sub>exp</sub> (m/z) : 356.5



**Fig. S17** ESI-MS spectrum of MKKMAAAMKKM (M20-B2).  $[M+H]^+$  <sub>calc</sub> (m/z) : 1308.7 ;  $[M+2H]^{2+}$  <sub>exp</sub> (m/z) : 654.9 ;  $[M+3H]^{3+}$  <sub>exp</sub> (m/z) : 436.9 ;  $[M+4H]^{4+}$  <sub>exp</sub> (m/z) : 328.1

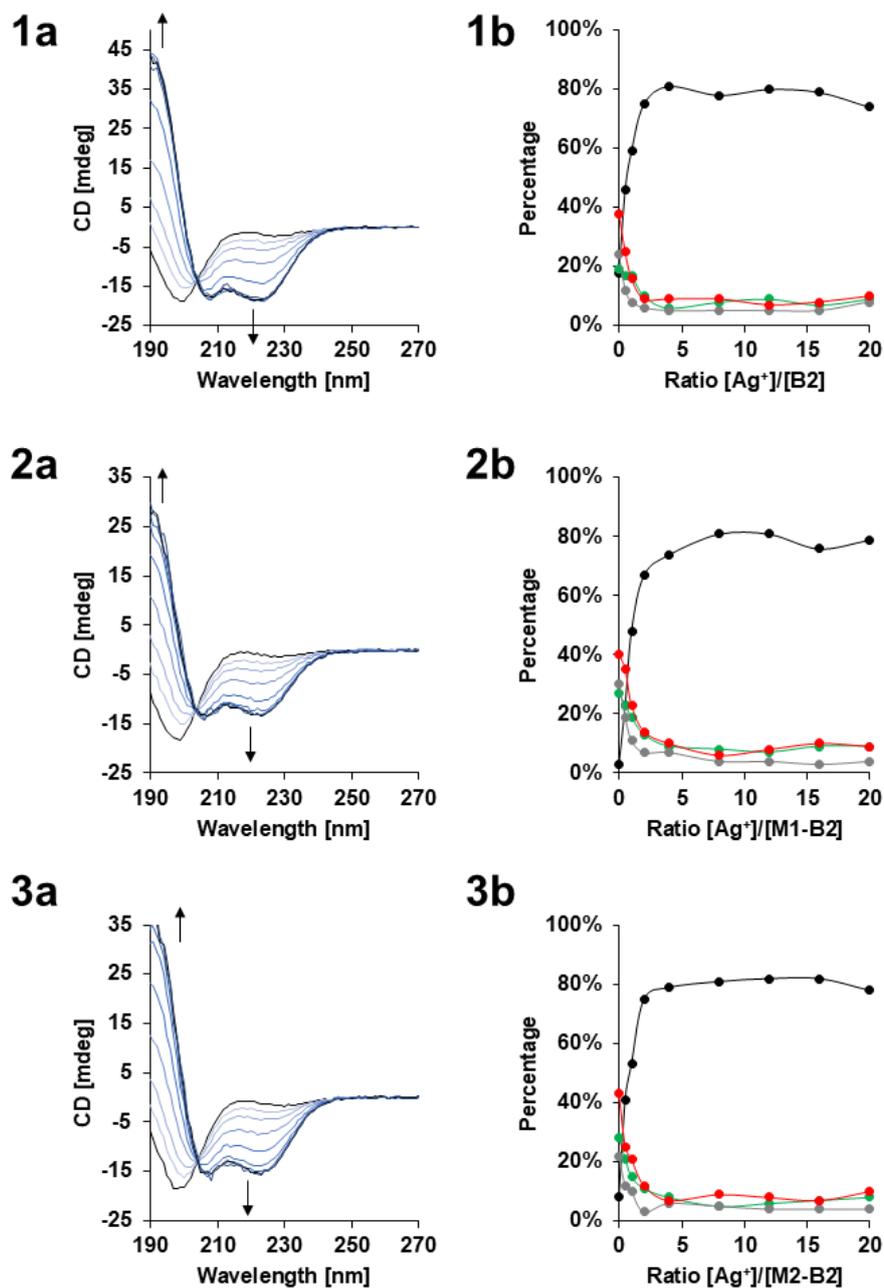


**Fig. S18** ESI-MS spectrum of MKKMAAAHQH (M21-B2).  $[M+H]^+$  <sub>calc</sub> (m/z) : 1320.7 ;  $[M+2H]^{2+}$  <sub>exp</sub> (m/z) : 660.8 ;  $[M+H+Na]^{2+}$  <sub>exp</sub> (m/z) : 682.8 ;  $[M+4H]^{4+}$  <sub>exp</sub> (m/z) : 330.9

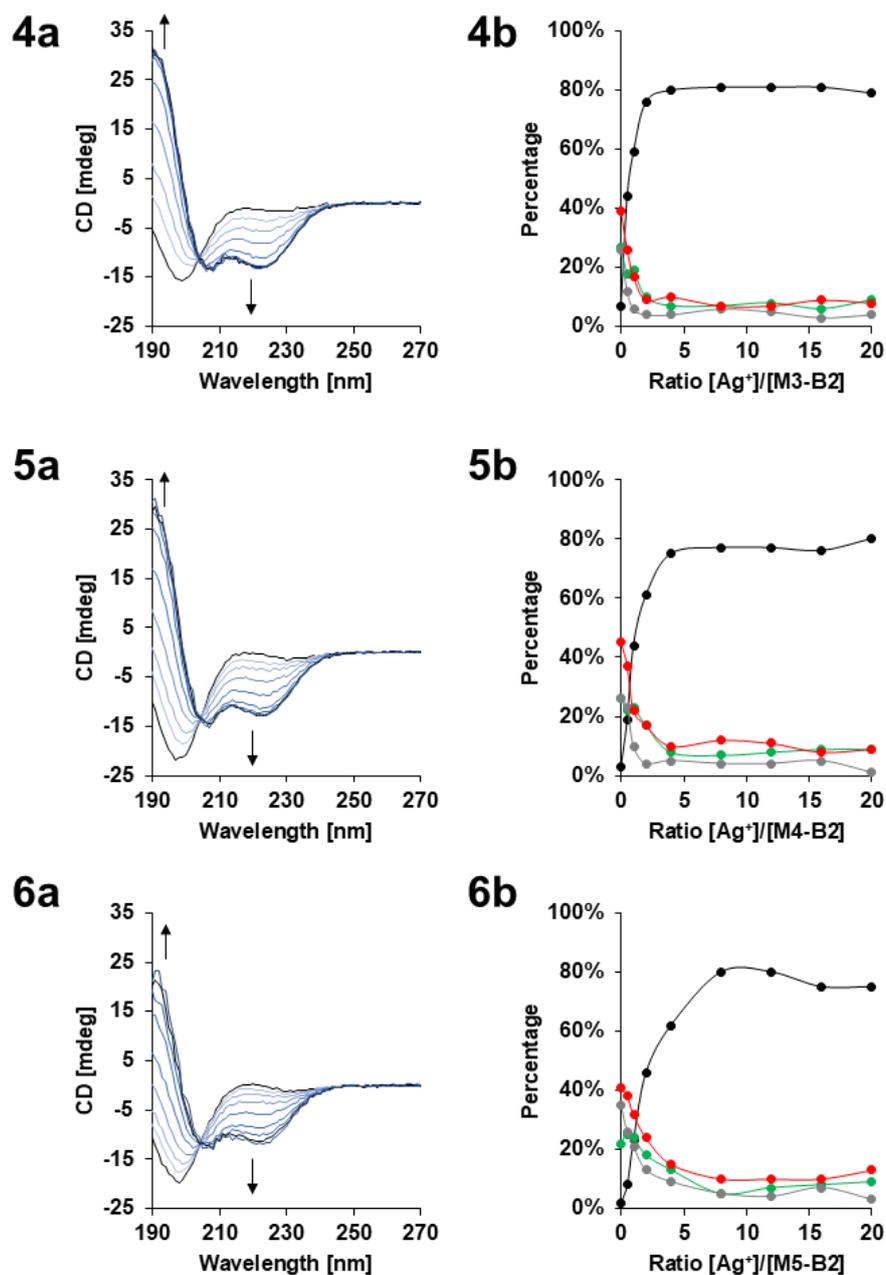


**Fig. S19** ESI-MS spectrum of HQAHAEHRRM (M10-B2) in the presence of excess Ag<sup>+</sup>. [M+H]<sup>+</sup><sub>calc</sub> (m/z) : 1390.7 ; [M+2Ag]<sup>2+</sup><sub>exp</sub> (m/z) : 800.0 ; [M+Ag+H]<sup>2+</sup><sub>exp</sub> (m/z) : 746.5 ; [M+2Ag+H]<sup>3+</sup><sub>exp</sub> (m/z) : 533.3 ; [M+Ag+2H]<sup>3+</sup><sub>exp</sub> (m/z) : 498.0 ; [M+Ag+3H]<sup>4+</sup><sub>exp</sub> (m/z) : 373.7.

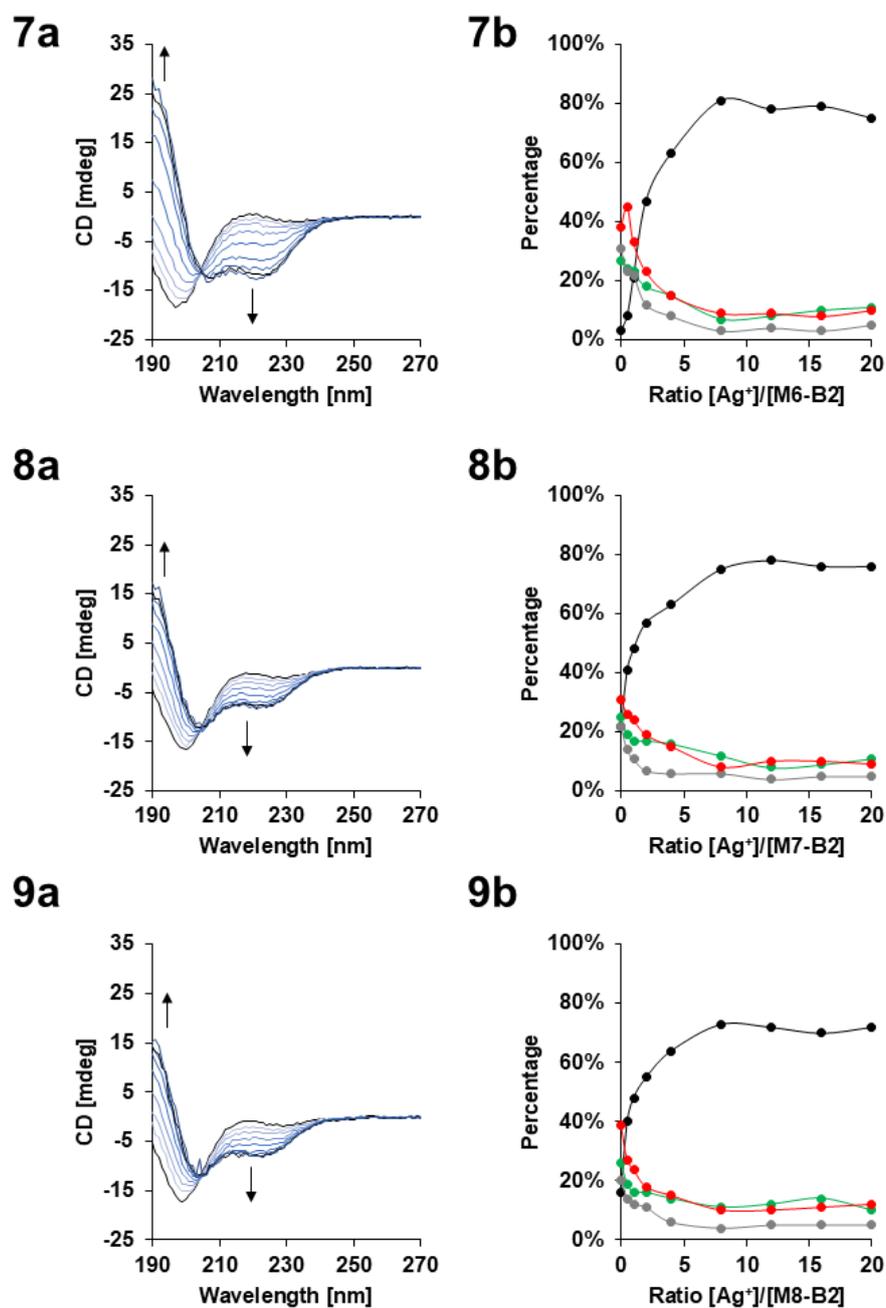
## CD titrations



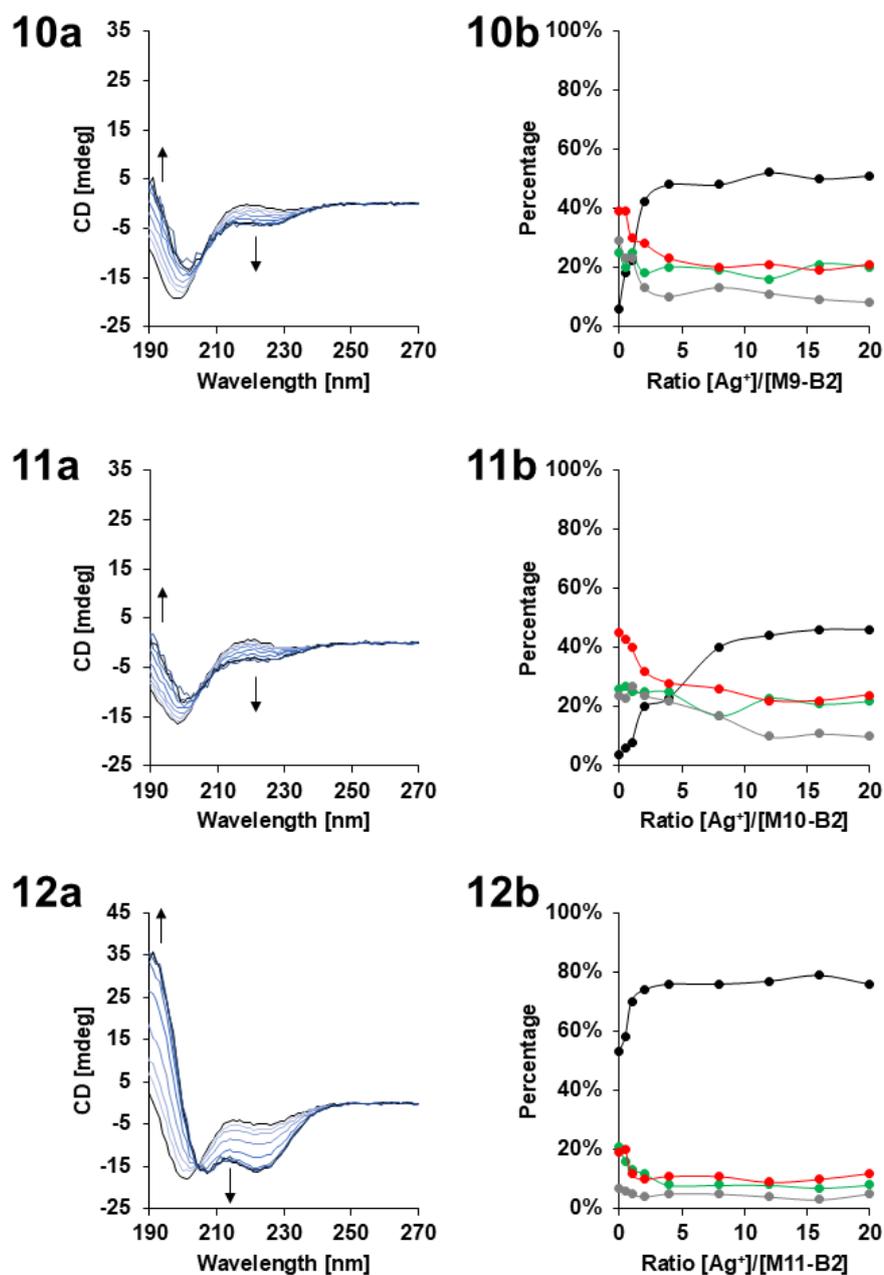
**Fig. S20** (a) CD spectra of peptide at  $1 \cdot 10^{-5}$  M (1: B2, 2: M1-B2, and 3: M2-B2) upon titration with  $\text{Ag}^+$  (0 to 20 equivalents) at  $25^\circ\text{C}$ , showing the evolution of secondary structure upon  $\text{Ag}^+$  binding. (b) Corresponding secondary structure compositions have been calculated using the DichroWeb server with the CDSSTR algorithm.<sup>5-7</sup> Structural elements are designated by specific colors:  $\alpha$ -helix (black),  $\beta$ -strand (green), turn (gray, and unordered (red).



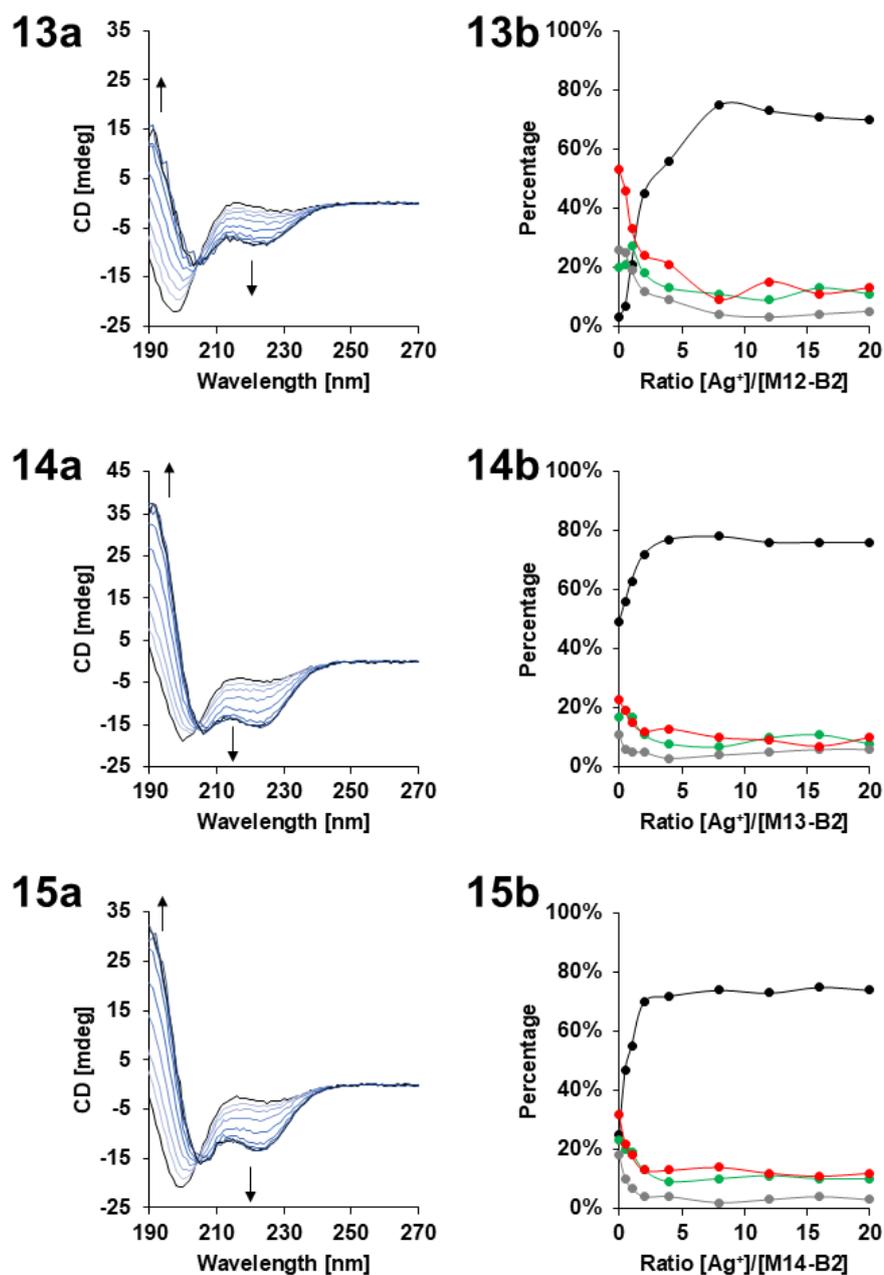
**Fig. S21** (a) CD spectra of peptide at  $1 \cdot 10^{-5}$  M (4: M3-B2, 5: M4-B2, and 6: M5-B2) upon titration with Ag<sup>+</sup> (0 to 20 equivalents) at 25°C, showing the evolution of secondary structure upon Ag<sup>+</sup> binding. (b) Corresponding secondary structure compositions have been calculated using the DichroWeb server with the CDSSTR algorithm.<sup>5-7</sup> Structural elements are designated by specific colors: α-helix (black), β-strand (green), turn (gray, and unordered (red).



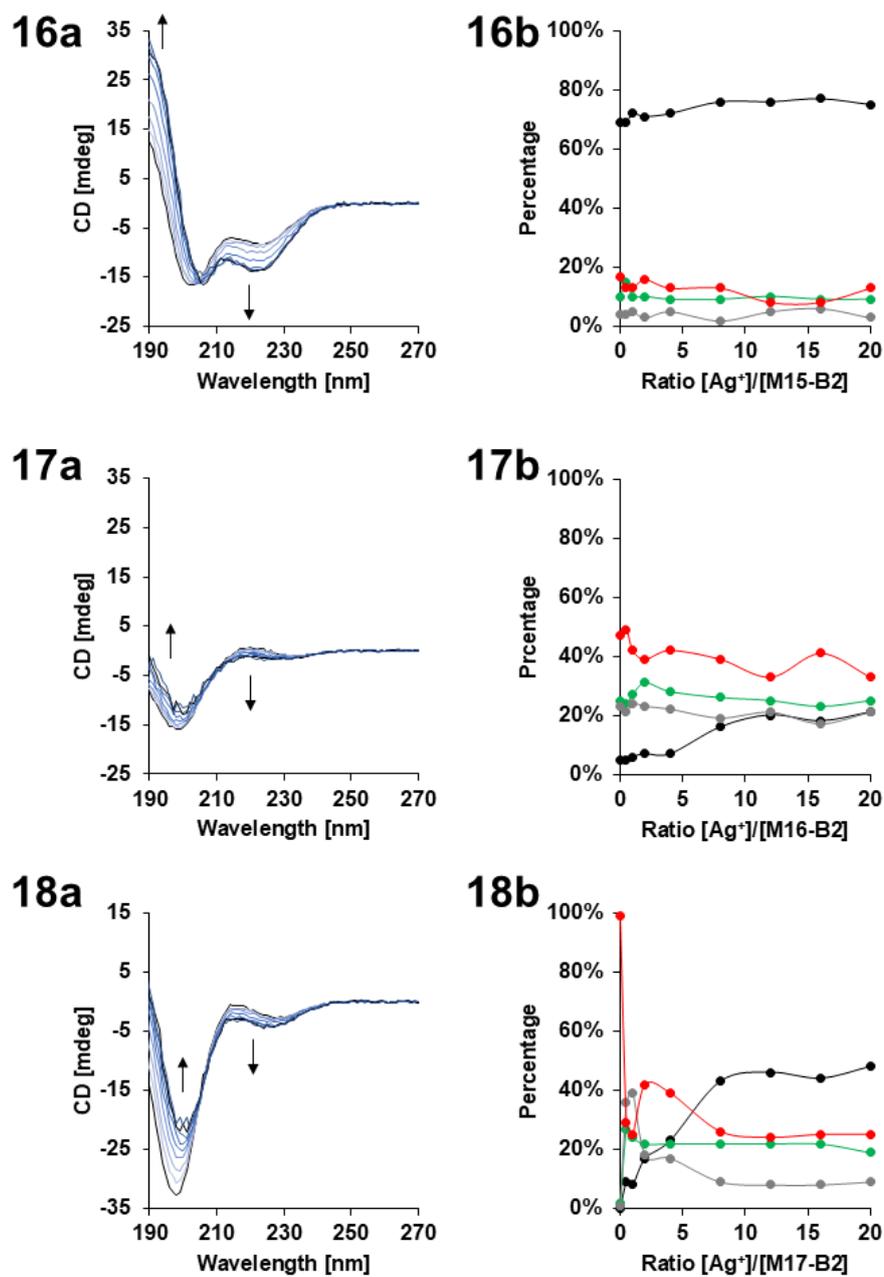
**Fig. S22** (a) CD spectra of peptide at  $1 \cdot 10^{-5}$  M (7: M6-B2, 8: M7-B2, and 9: M8-B2) upon titration with  $\text{Ag}^+$  (0 to 20 equivalents) at  $25^\circ\text{C}$ , showing the evolution of secondary structure upon  $\text{Ag}^+$  binding. (b) Corresponding secondary structure compositions have been calculated using the DichroWeb server with the CDSSTR algorithm.<sup>5-7</sup> Structural elements are designated by specific colors:  $\alpha$ -helix (black),  $\beta$ -strand (green), turn (gray, and unordered (red).



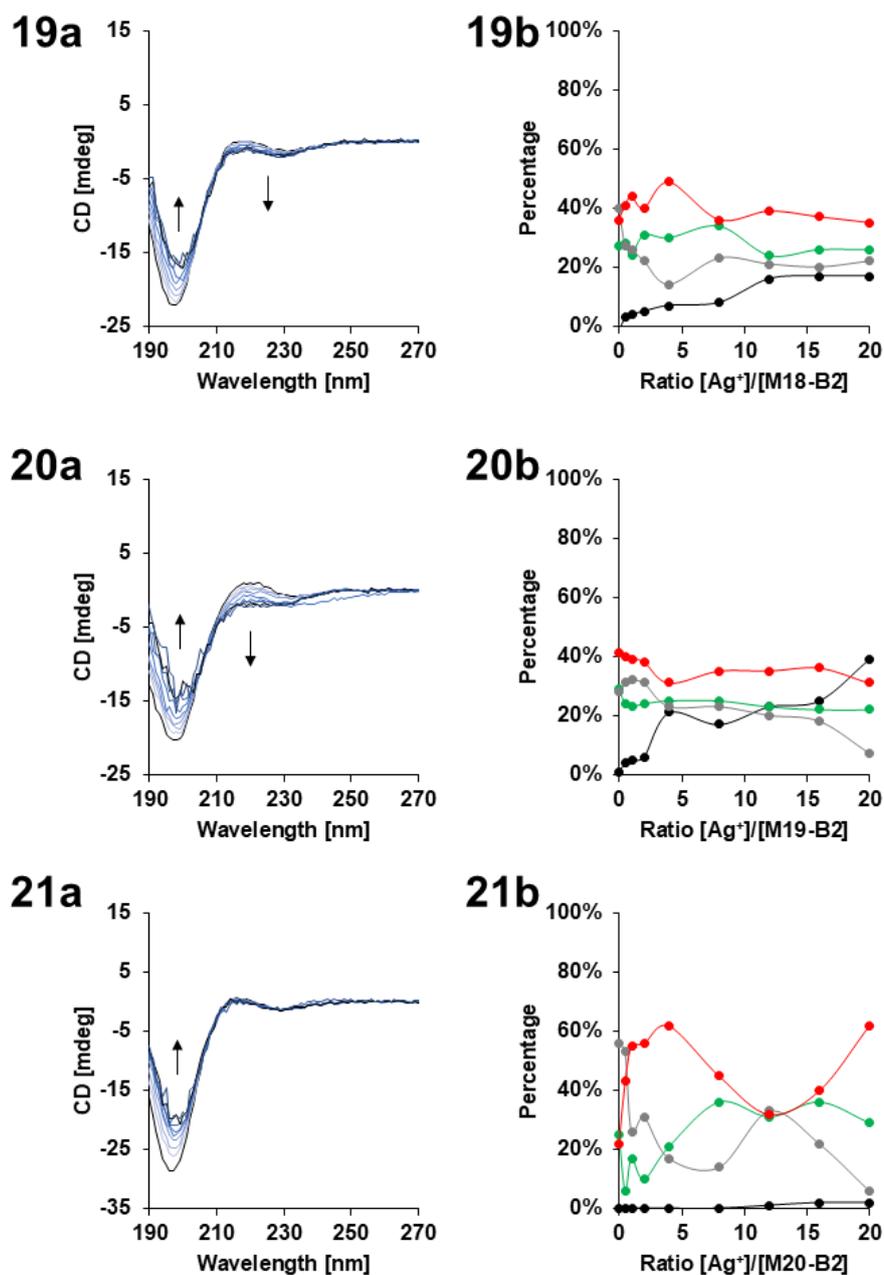
**Fig. S23** (a) CD spectra of peptide at  $1 \cdot 10^{-5}$  M (10: M9-B2, 11: M10-B2, and 12: M11-B2) upon titration with  $\text{Ag}^+$  (0 to 20 equivalents) at  $25^\circ\text{C}$ , showing the evolution of secondary structure upon  $\text{Ag}^+$  binding. (b) Corresponding secondary structure compositions have been calculated using the DichroWeb server with the CDSSTR algorithm.<sup>5-7</sup> Structural elements are designated by specific colors:  $\alpha$ -helix (black),  $\beta$ -strand (green), turn (gray, and unordered (red).



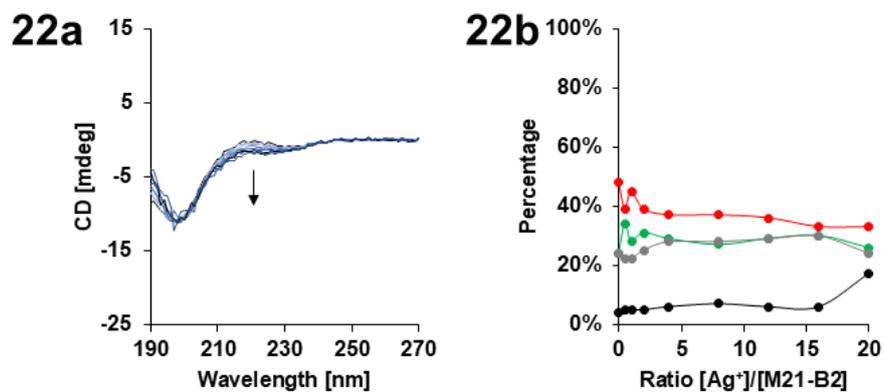
**Fig. S24** (a) CD spectra of peptide at  $1 \cdot 10^{-5}$  M (13: M12-B2, 14: M13-B2, and 15: M14-B2) upon titration with Ag<sup>+</sup> (0 to 20 equivalents) at 25°C, showing the evolution of secondary structure upon Ag<sup>+</sup> binding. (b) Corresponding secondary structure compositions have been calculated using the DichroWeb server with the CDSSTR algorithm.<sup>5-7</sup> Structural elements are designated by specific colors: α-helix (black), β-strand (green), turn (gray, and unordered (red).



**Fig. S25** (a) CD spectra of peptide at  $1 \cdot 10^{-5}$  M (16: M15-B2, 17: M16-B2, and 18: M17-B2) upon titration with  $\text{Ag}^+$  (0 to 20 equivalents) at  $25^\circ\text{C}$ , showing the evolution of secondary structure upon  $\text{Ag}^+$  binding. (b) Corresponding secondary structure compositions have been calculated using the DichroWeb server with the CDSSTR algorithm.<sup>5–7</sup> Structural elements are designated by specific colors:  $\alpha$ -helix (black),  $\beta$ -strand (green), turn (gray, and unordered (red).



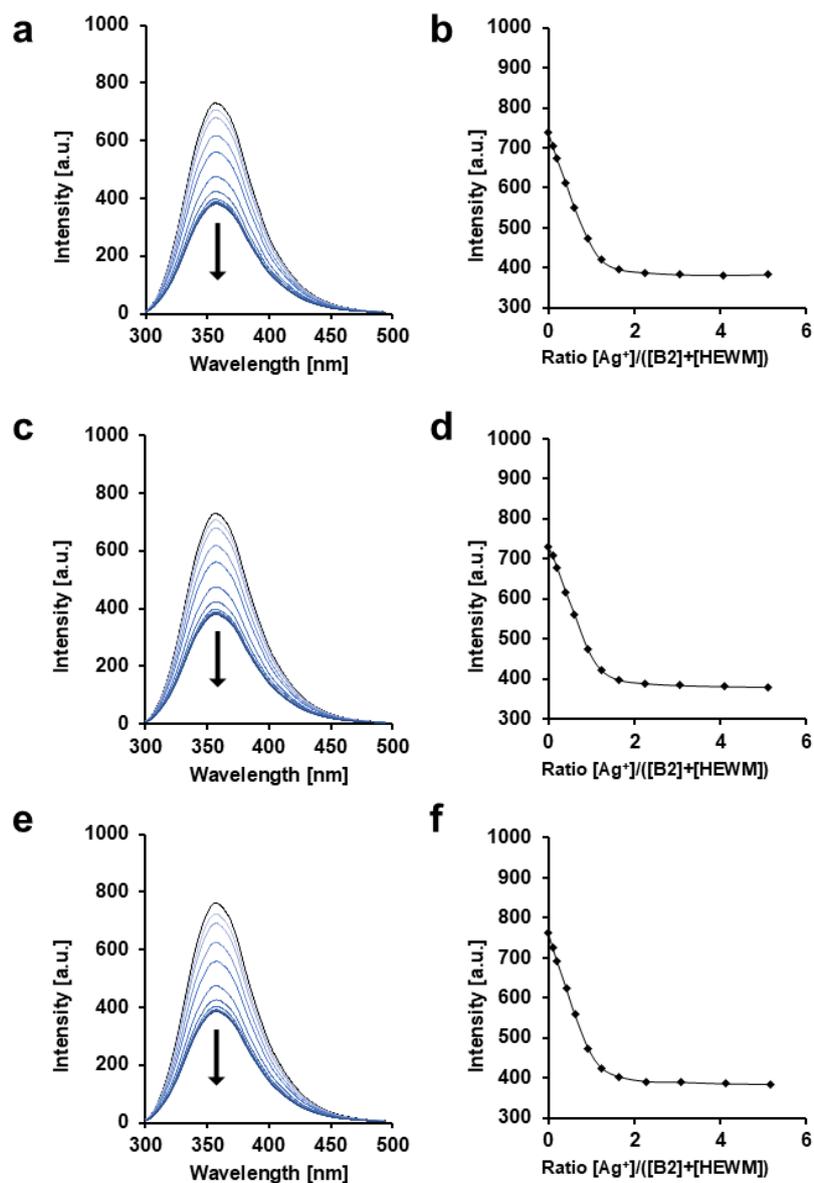
**Fig. S26** (a) CD spectra of peptide at  $1 \cdot 10^{-5}$  M (19: M18-B2, 20: M19-B2, and 21: M20-B2) upon titration with Ag<sup>+</sup> (0 to 20 equivalents) at 25°C, showing the evolution of secondary structure upon Ag<sup>+</sup> binding. (b) Corresponding secondary structure compositions have been calculated using the DichroWeb server with the CDSSTR algorithm.<sup>5-7</sup> Structural elements are designated by specific colors: α-helix (black), β-strand (green), turn (gray, and unordered (red).



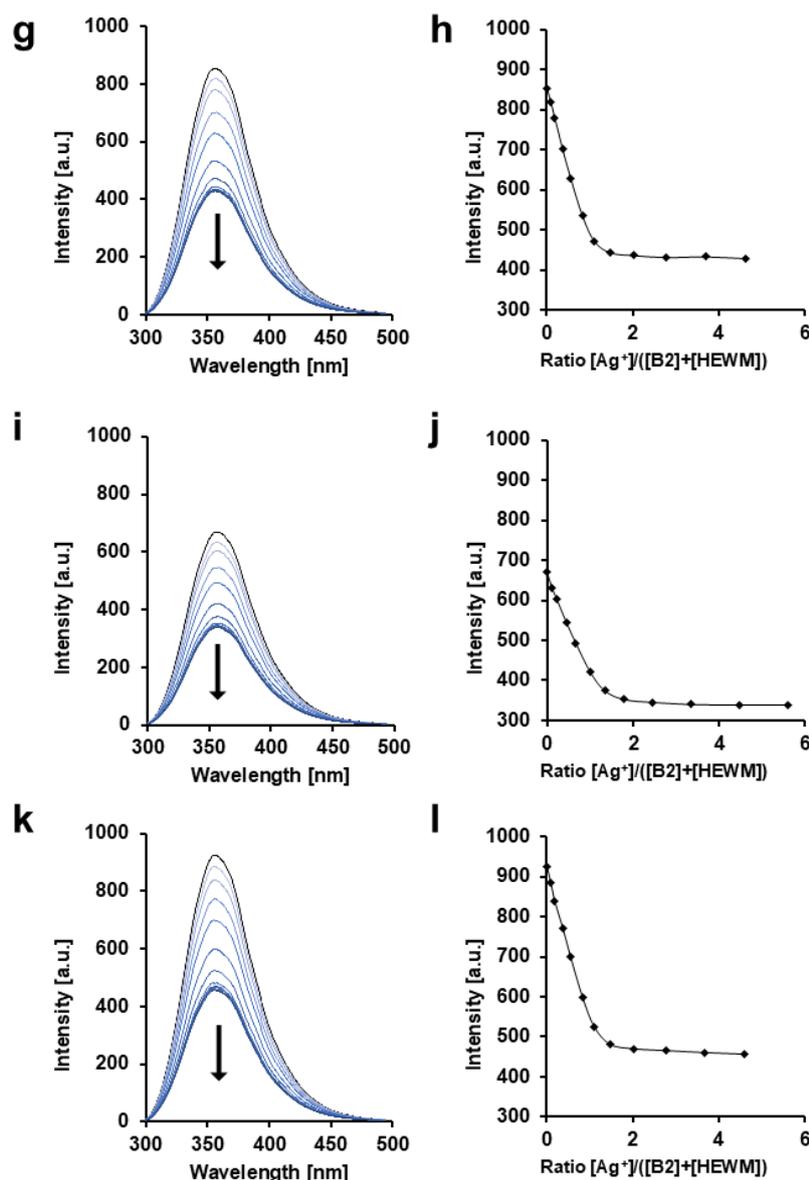
**Fig. S27** (a) CD spectra of peptide at  $1 \cdot 10^{-5}$  M (22: M21-B2) upon titration with  $\text{Ag}^+$  (0 to 20 equivalents) at  $25^\circ\text{C}$ , showing the evolution of secondary structure upon  $\text{Ag}^+$  binding. (b) Corresponding secondary structure compositions have been calculated using the DichroWeb server with the CDSSTR algorithm.<sup>5-7</sup> Structural elements are designated by specific colors:  $\alpha$ -helix (black),  $\beta$ -strand (green), turn (gray, and unordered (red).

## Fluorescence titrations

### HQAMAEAHRRM (B2)



**Fig. S28** HQAMAEAHRRM (B2) / HEWM competition titrations, both at  $1 \cdot 10^{-5}$  M. (a, c & e) Tryptophan fluorescence ( $\lambda_{\text{ex}}$ :280 nm) quench by addition of  $\text{AgNO}_3$  (0 to 5.5 equivalents) to a solution of B2 ( $1 \cdot 10^{-5}$  M) in competition with HEWM probe ( $1 \cdot 10^{-5}$  M), in MOPS buffer (20 equivalents, pH 7.4-7.5) at 25°C. (b, d & f) Plot of the maxima of fluorescence intensities. The solid line corresponds to the fit obtained using Dynafit software.<sup>9,10</sup>



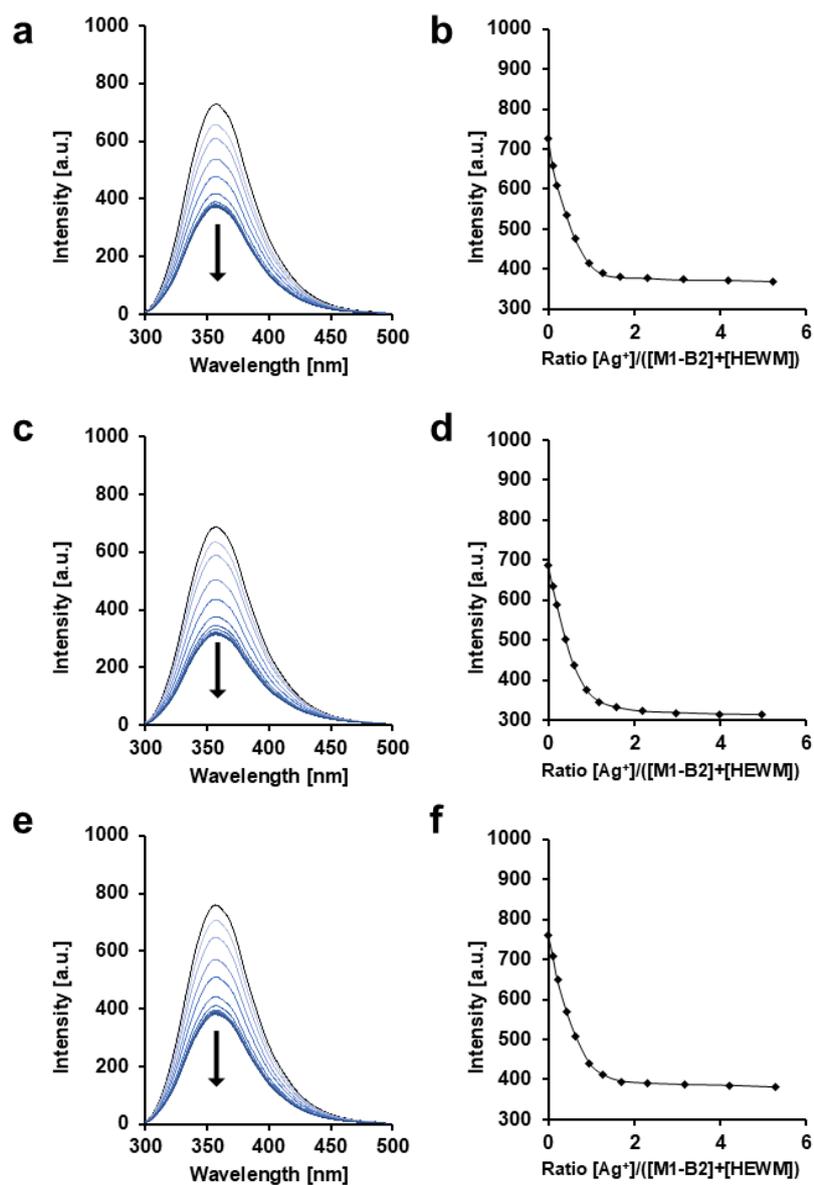
**Fig. S29** HQAMAEHRRM (B2) / HEWM competition titrations, both at  $2 \cdot 10^{-5}$  M. (g, i & k) Tryptophan fluorescence ( $\lambda_{ex}$ :280 nm) quench by addition of  $AgNO_3$  (0 to 5.5 equivalents) to a solution of B2 ( $2 \cdot 10^{-5}$  M) in competition with HEWM probe ( $2 \cdot 10^{-5}$  M), in MOPS buffer (20 equivalents, pH 7.4-7.5) at 25°C. (h, j & l) Plot of the maxima of fluorescence intensities. The solid line corresponds to the fit obtained using Dynafit software.<sup>9,10</sup>

**Table S2** Determination of the binding constants ( $\log(K_{b-1/b-2})$ ) of HQAMAEHRRM peptide

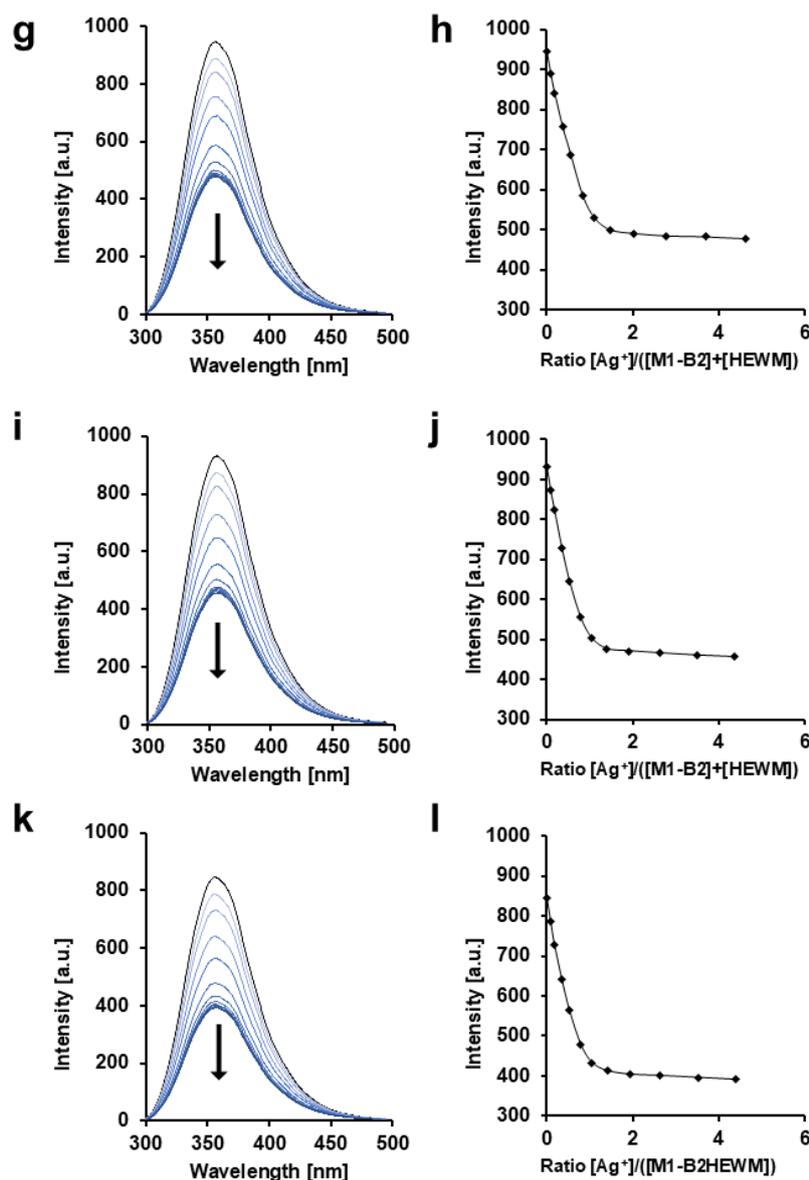
Model	$1 \cdot 10^{-5}$ M <sup>[a]</sup>		$2 \cdot 10^{-5}$ M <sup>[a]</sup>	
HQAMAEHRRM (B2)	$\log(K_{b-1}) = 6.51 \pm 0.02$	$\log(K_{b-2}) = 5.52 \pm 0.05$	$\log(K_{b-1}) = 6.40 \pm 0.02$	$\log(K_{b-2}) = 5.09 \pm 0.06$
	$\log(K_{b-1}) = 6.68 \pm 0.02$	$\log(K_{b-2}) = 5.48 \pm 0.06$	$\log(K_{b-1}) = 6.49 \pm 0.04$	$\log(K_{b-2}) = 5.75 \pm 0.06$
	$\log(K_{b-1}) = 6.52 \pm 0.02$	$\log(K_{b-2}) = 5.41 \pm 0.05$	$\log(K_{b-1}) = 6.47 \pm 0.04$	$\log(K_{b-2}) = 5.53 \pm 0.10$
Average	$\log(K_{b-1}) = 6.51 \pm 0.09$		$\log(K_{b-2}) = 5.46 \pm 0.22$	

<sup>[a]</sup> The values correspond to the peptide and probe concentrations.

HQAMAAAHRM (M1-B2)



**Fig. S30** HQAMAAAHRM (M1-B2) / HEWM competition titrations, both at  $1 \cdot 10^{-5}$  M. (a, c & e) Tryptophan fluorescence ( $\lambda_{\text{ex}}$ :280 nm) quench by addition of  $\text{AgNO}_3$  (0 to 5.5 equivalents) to a solution of M1-B2 ( $1 \cdot 10^{-5}$  M) in competition with HEWM probe ( $1 \cdot 10^{-5}$  M), in MOPS buffer (20 equivalents, pH 7.4-7.5) at 25°C. (b, d & f) Plot of the maxima of fluorescence intensities. The solid line corresponds to the fit obtained using Dynafit software.<sup>9,10</sup>



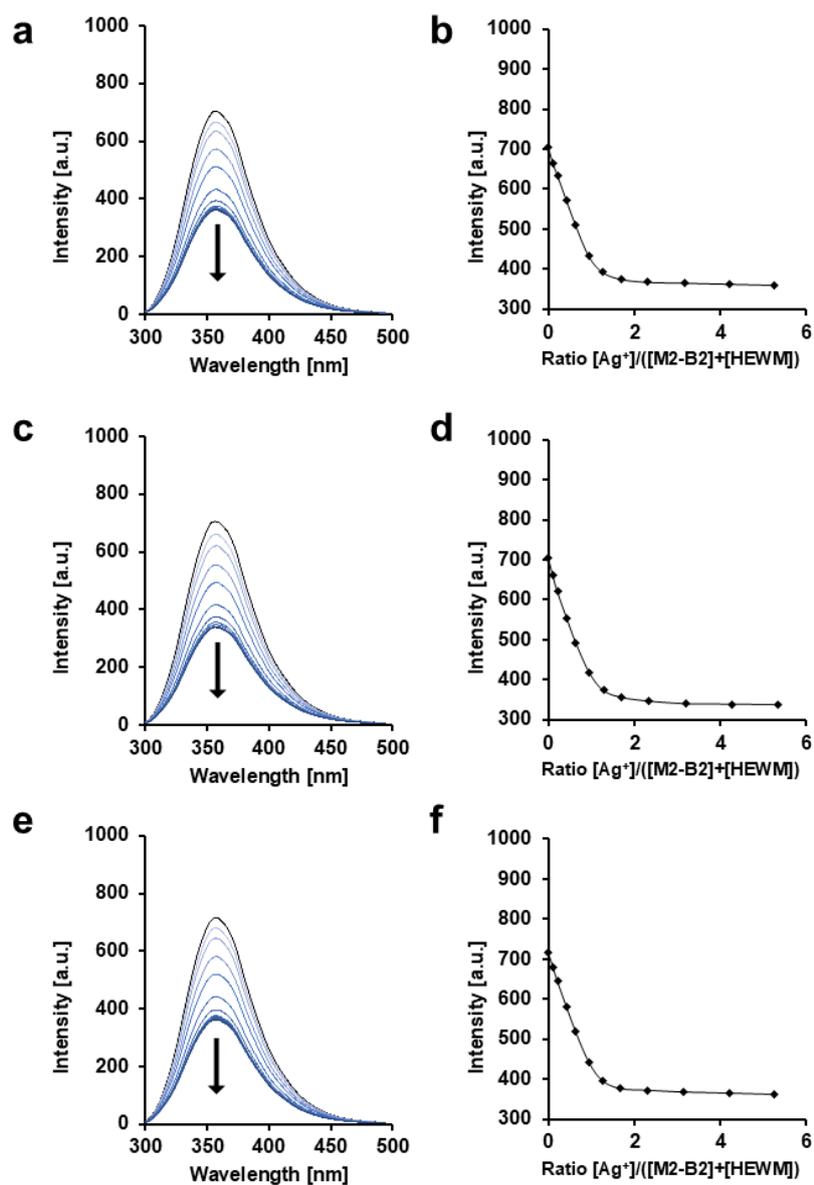
**Fig. S31** HQAMAAHRRM (M1-B2) / HEWM competition titrations, both at  $2 \cdot 10^{-5}$  M. (g, i & k) Tryptophan fluorescence ( $\lambda_{\text{ex}}$ :280 nm) quench by addition of  $\text{AgNO}_3$  (0 to 5.5 equivalents) to a solution of M1-B2 ( $2 \cdot 10^{-5}$  M) in competition with HEWM probe ( $2 \cdot 10^{-5}$  M), in MOPS buffer (20 equivalents, pH 7.4-7.5) at  $25^\circ\text{C}$ . (h, j & l) Plot of the maxima of fluorescence intensities. The solid line corresponds to the fit obtained using Dynafit software.<sup>9,10</sup>

**Table S3** Determination of the binding constants ( $\log(K_{b-1/b-2})$ ) of HQAMAAHRRM peptide

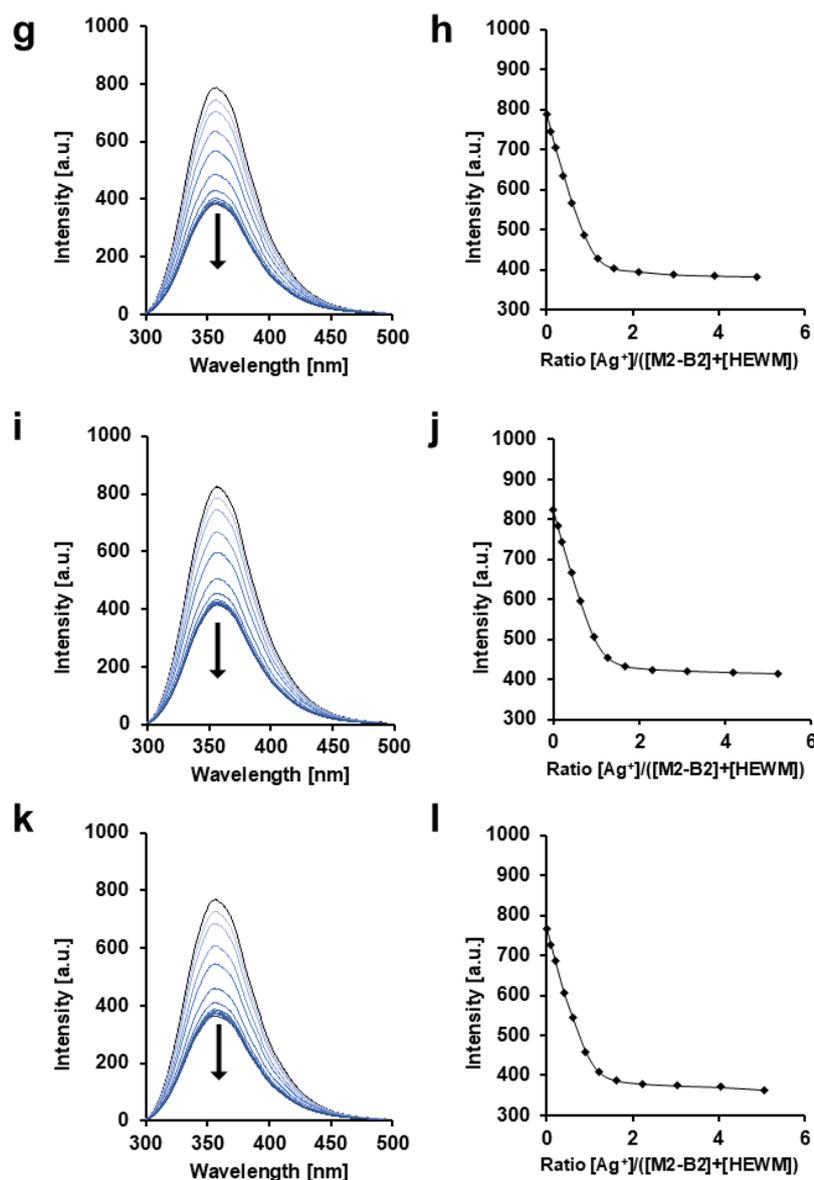
Model	$1 \cdot 10^{-5}$ M <sup>[a]</sup>		$2 \cdot 10^{-5}$ M <sup>[a]</sup>	
HQAMAAHRRM (M1-B2)	$\log(K_{b-1}) = 5.87 \pm 0.10$	$\log(K_{b-2}) = 5.28 \pm 0.29$	$\log(K_{b-1}) = 6.21 \pm 0.05$	$\log(K_{b-2}) = 5.32 \pm 0.16$
	$\log(K_{b-1}) = 6.00 \pm 0.02$	$\log(K_{b-2}) = 5.04 \pm 0.09$	$\log(K_{b-1}) = 6.03 \pm 0.02$	$\log(K_{b-2}) = 4.95 \pm 0.08$
	$\log(K_{b-1}) = 5.98 \pm 0.06$	$\log(K_{b-2}) = 5.43 \pm 0.16$	$\log(K_{b-1}) = 5.89 \pm 0.04$	$\log(K_{b-2}) = 5.06 \pm 0.18$
Average	$\log(K_{b-1}) = 6.00 \pm 0.12$		$\log(K_{b-2}) = 5.18 \pm 0.19$	

<sup>[a]</sup> The values correspond to the peptide and probe concentrations.

HQQMAEAHRRM (M2-B2)



**Fig. S32** HQQMAEAHRRM (M2-B2) / HEWM competition titrations, both at  $1 \cdot 10^{-5}$  M. (a, c & e) Tryptophan fluorescence ( $\lambda_{\text{ex}}$ :280 nm) quench by addition of  $\text{AgNO}_3$  (0 to 5.5 equivalents) to a solution of M2-B2 ( $1 \cdot 10^{-5}$  M) in competition with HEWM probe ( $1 \cdot 10^{-5}$  M), in MOPS buffer (20 equivalents, pH 7.4-7.5) at 25°C. (b, d & f) Plot of the maxima of fluorescence intensities. The solid line corresponds to the fit obtained using Dynafit software.<sup>9,10</sup>



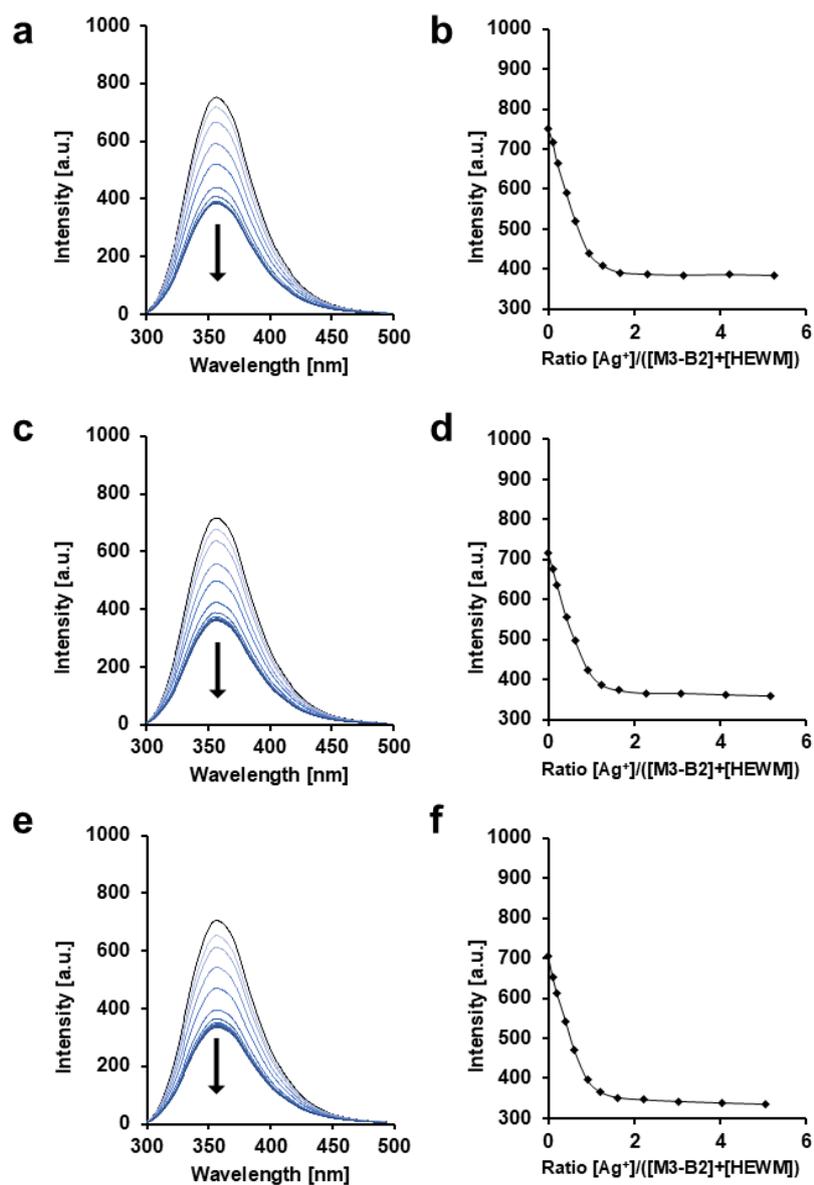
**Fig. S33** HQQMAEAHRRM (M2-B2) / HEWM competition titrations, both at  $2 \cdot 10^{-5}$  M. (g, i & k) Tryptophan fluorescence ( $\lambda_{ex}$ :280 nm) quench by addition of  $\text{AgNO}_3$  (0 to 5.5 equivalents) to a solution of M2-B2 ( $2 \cdot 10^{-5}$  M) in competition with HEWM probe ( $2 \cdot 10^{-5}$  M), in MOPS buffer (20 equivalents, pH 7.4-7.5) at  $25^\circ\text{C}$ . (h, j & l) Plot of the maxima of fluorescence intensities. The solid line corresponds to the fit obtained using Dynafit software.<sup>9,10</sup>

**Table S4** Determination of the binding constants ( $\log(K_{b-1/b-2})$ ) of HQQMAEAHRRM peptide

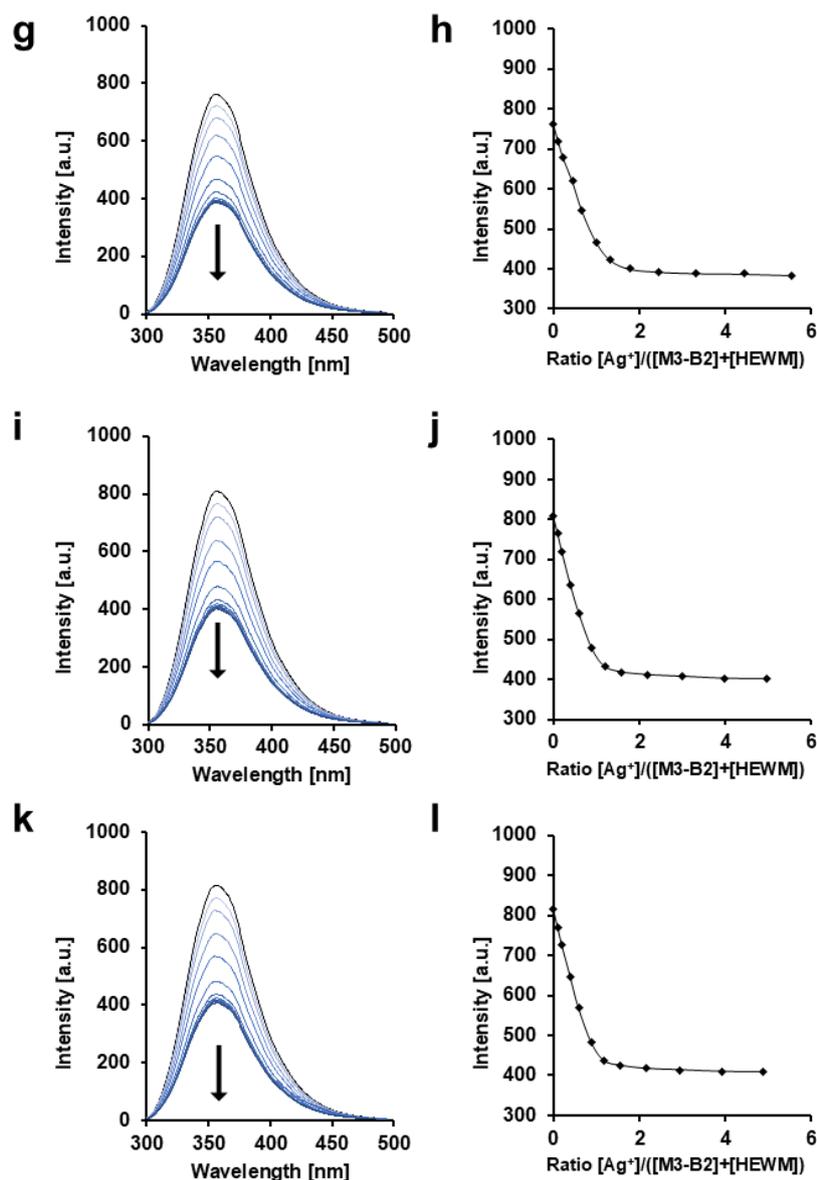
Model	$1 \cdot 10^{-5}$ M <sup>[a]</sup>		$2 \cdot 10^{-5}$ M <sup>[a]</sup>	
HQQMAEAHRRM (M2-B2)	$\log(K_{b-1}) = 6.48 \pm 0.03$	$\log(K_{b-2}) = 5.31 \pm 0.09$	$\log(K_{b-1}) = 6.37 \pm 0.02$	$\log(K_{b-2}) = 5.45 \pm 0.05$
	$\log(K_{b-1}) = 6.33 \pm 0.04$	$\log(K_{b-2}) = 5.58 \pm 0.09$	$\log(K_{b-1}) = 6.44 \pm 0.01$	$\log(K_{b-2}) = 5.38 \pm 0.02$
	$\log(K_{b-1}) = 6.46 \pm 0.03$	$\log(K_{b-2}) = 5.48 \pm 0.08$	$\log(K_{b-1}) = 6.34 \pm 0.03$	$\log(K_{b-2}) = 5.42 \pm 0.08$
Average	$\log(K_{b-1}) = 6.40 \pm 0.06$		$\log(K_{b-2}) = 5.44 \pm 0.09$	

<sup>[a]</sup> The values correspond to the peptide and probe concentrations.

HQAMAEAHKRM (M3-B2)



**Fig. S34** HQAMAEAHKRM (M3-B2) / HEWM competition titrations, both at  $1 \cdot 10^{-5}$  M. (a, c & e) Tryptophan fluorescence ( $\lambda_{\text{ex}}$ :280 nm) quench by addition of  $\text{AgNO}_3$  (0 to 5.5 equivalents) to a solution of M3-B2 ( $1 \cdot 10^{-5}$  M) in competition with HEWM probe ( $1 \cdot 10^{-5}$  M), in MOPS buffer (20 equivalents, pH 7.4-7.5) at 25°C. (b, d & f) Plot of the maxima of fluorescence intensities. The solid line corresponds to the fit obtained using Dynafit software.<sup>9,10</sup>



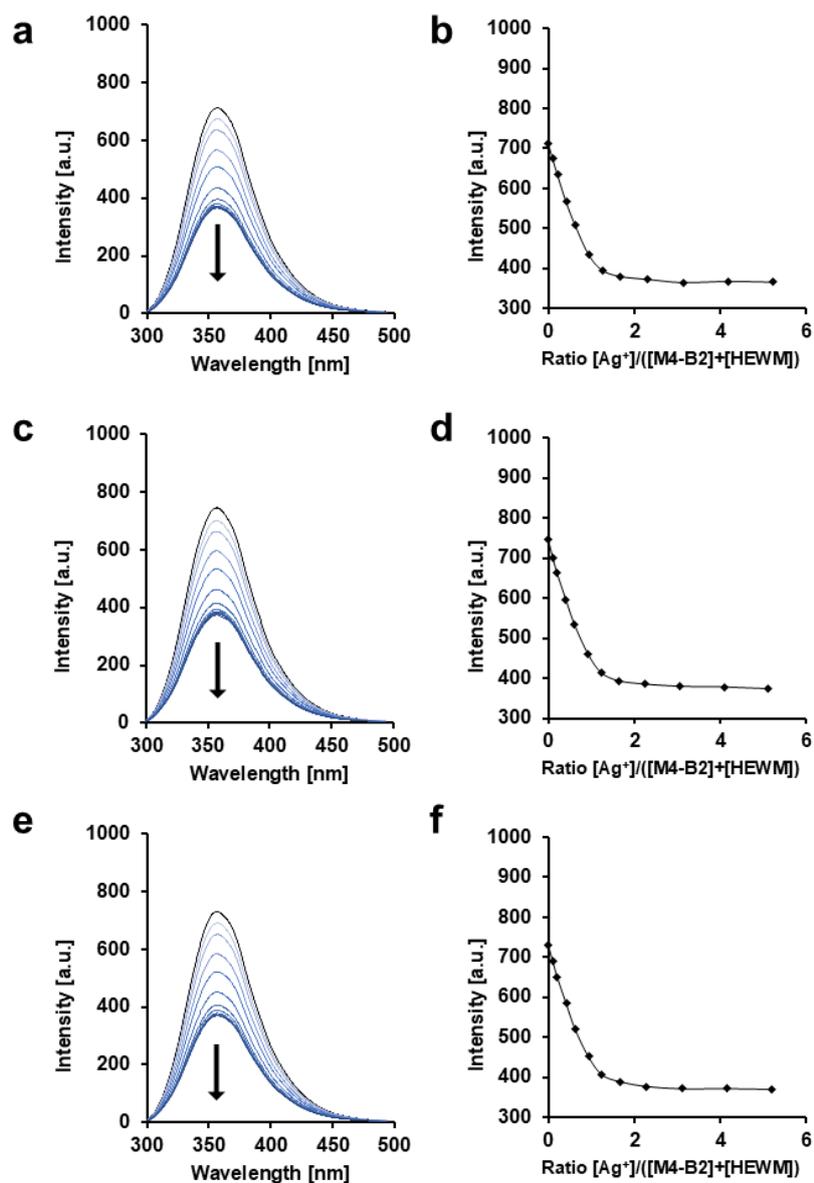
**Fig. S35** HQAMAEAHKRM (M3-B2) / HEWM competition titrations, both at  $2 \cdot 10^{-5}$  M. (g, i & k) Tryptophan fluorescence ( $\lambda_{ex}$ :280 nm) quench by addition of  $\text{AgNO}_3$  (0 to 5.5 equivalents) to a solution of M3-B2 ( $2 \cdot 10^{-5}$  M) in competition with HEWM probe ( $2 \cdot 10^{-5}$  M), in MOPS buffer (20 equivalents, pH 7.4-7.5) at  $25^\circ\text{C}$ . (h, j & l) Plot of the maxima of fluorescence intensities. The solid line corresponds to the fit obtained using Dynafit software.<sup>9,10</sup>

**Table S5** Determination of the binding constants ( $\log(K_{b-1/b-2})$ ) of HQAMAEAHKRM peptide

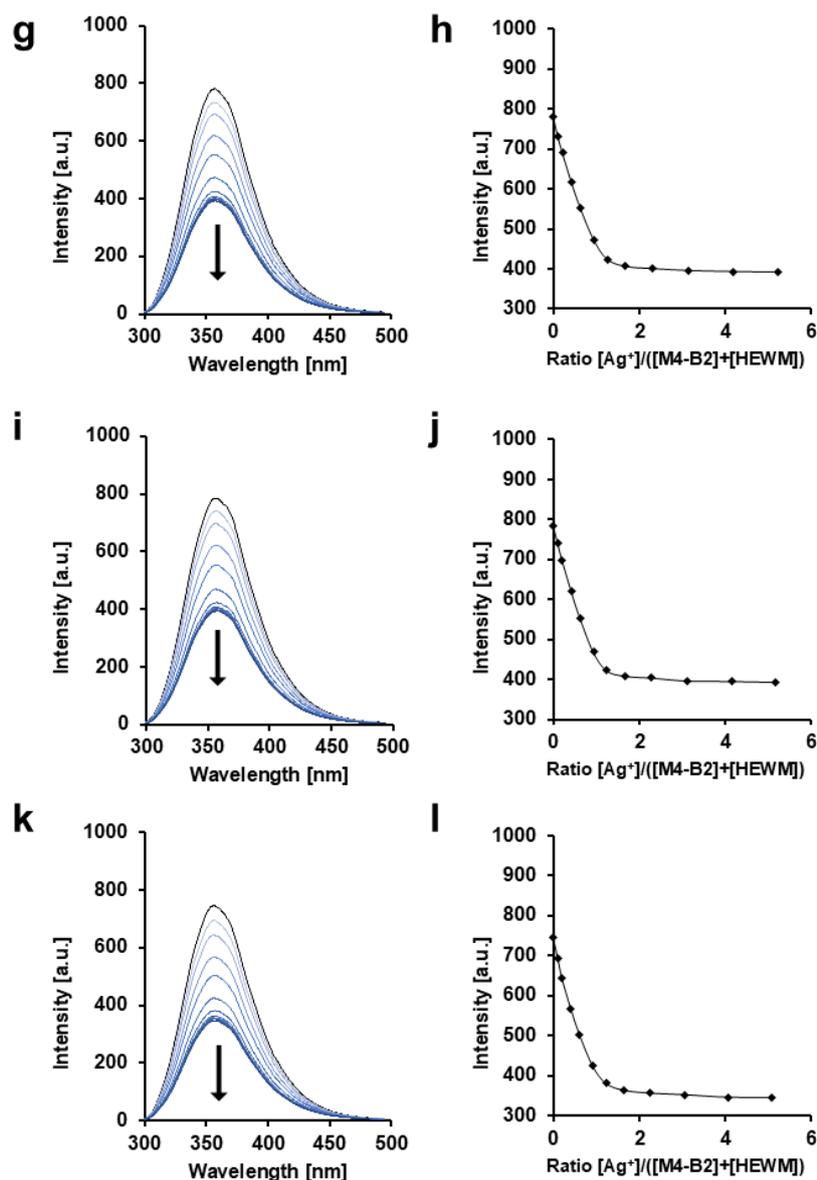
Model	$1 \cdot 10^{-5}$ M <sup>[a]</sup>		$2 \cdot 10^{-5}$ M <sup>[a]</sup>	
HQAMAEAHKRM (M3-B2)	$\log(K_{b-1}) = 6.29 \pm 0.04$	$\log(K_{b-2}) = 4.96 \pm 0.21$	$\log(K_{b-1}) = 6.48 \pm 0.05$	$\log(K_{b-2}) = 5.51 \pm 0.11$
	$\log(K_{b-1}) = 6.25 \pm 0.03$	$\log(K_{b-2}) = 5.15 \pm 0.10$	$\log(K_{b-1}) = 6.27 \pm 0.01$	$\log(K_{b-2}) = 5.04 \pm 0.04$
	$\log(K_{b-1}) = 6.21 \pm 0.04$	$\log(K_{b-2}) = 5.03 \pm 0.24$	$\log(K_{b-1}) = 6.26 \pm 0.02$	$\log(K_{b-2}) = 4.84 \pm 0.10$
Average	$\log(K_{b-1}) = 6.29 \pm 0.09$		$\log(K_{b-2}) = 5.09 \pm 0.23$	

<sup>[a]</sup> The values correspond to the peptide and probe concentrations.

HQQMAEAHKKM (M4-B2)



**Fig. S36** HQQMAEAHKKM (M4-B2) / HEWM competition titrations, both at  $1 \cdot 10^{-5}$  M. (a, c & e) Tryptophan fluorescence ( $\lambda_{ex}$ :280 nm) quench by addition of  $AgNO_3$  (0 to 5.5 equivalents) to a solution of M4-B2 ( $1 \cdot 10^{-5}$  M) in competition with HEWM probe ( $1 \cdot 10^{-5}$  M), in MOPS buffer (20 equivalents, pH 7.4-7.5) at 25°C. (b, d & f) Plot of the maxima of fluorescence intensities. The solid line corresponds to the fit obtained using Dynafit software.<sup>9,10</sup>



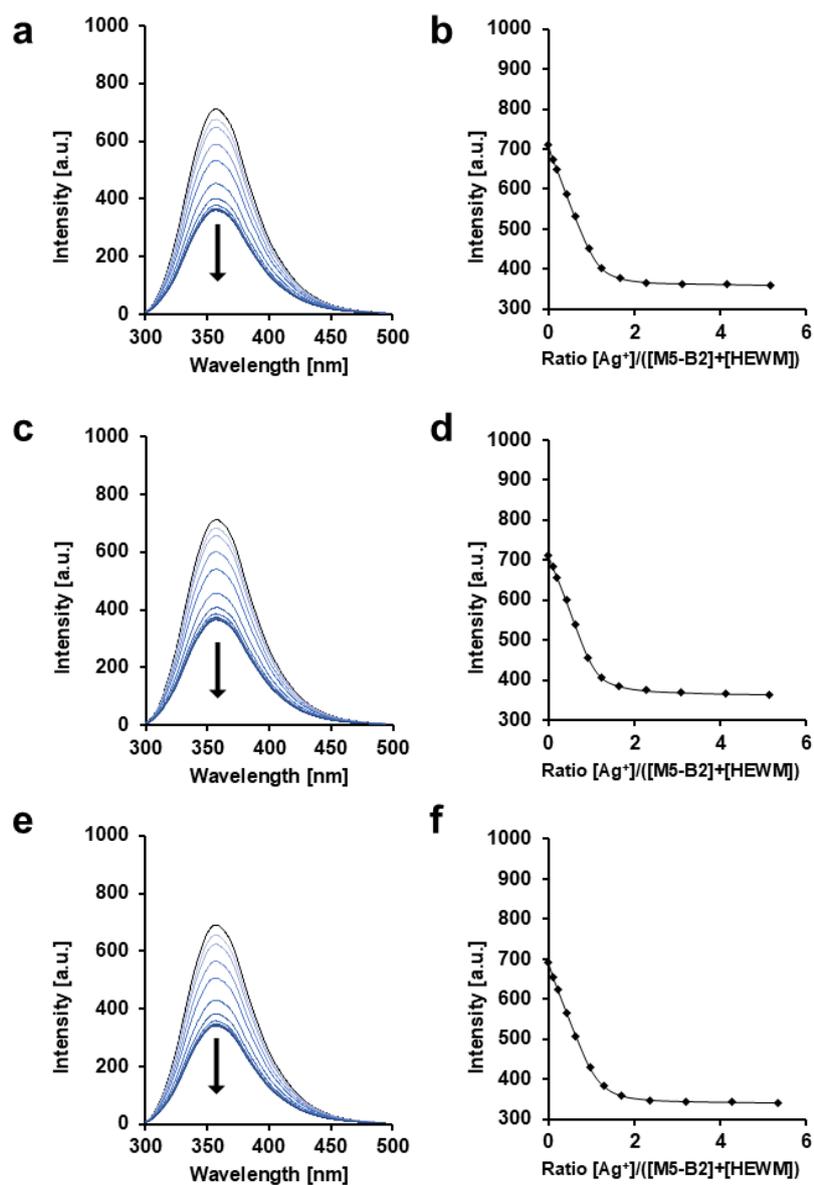
**Fig. S37** HQQMAEAHKKM (M4-B2) / HEWM competition titrations, both at  $2 \cdot 10^{-5}$  M. (g, i & k) Tryptophan fluorescence ( $\lambda_{\text{ex}}$ :280 nm) quench by addition of  $\text{AgNO}_3$  (0 to 5.5 equivalents) to a solution of M4-B2 ( $2 \cdot 10^{-5}$  M) in competition with HEWM probe ( $2 \cdot 10^{-5}$  M), in MOPS buffer (20 equivalents, pH 7.4-7.5) at  $25^\circ\text{C}$ . (h, j & l) Plot of the maxima of fluorescence intensities. The solid line corresponds to the fit obtained using Dynafit software.<sup>9,10</sup>

**Table S6** Determination of the binding constants ( $\log(K_{b-1/b-2})$ ) of HQQMAEAHKKM peptide

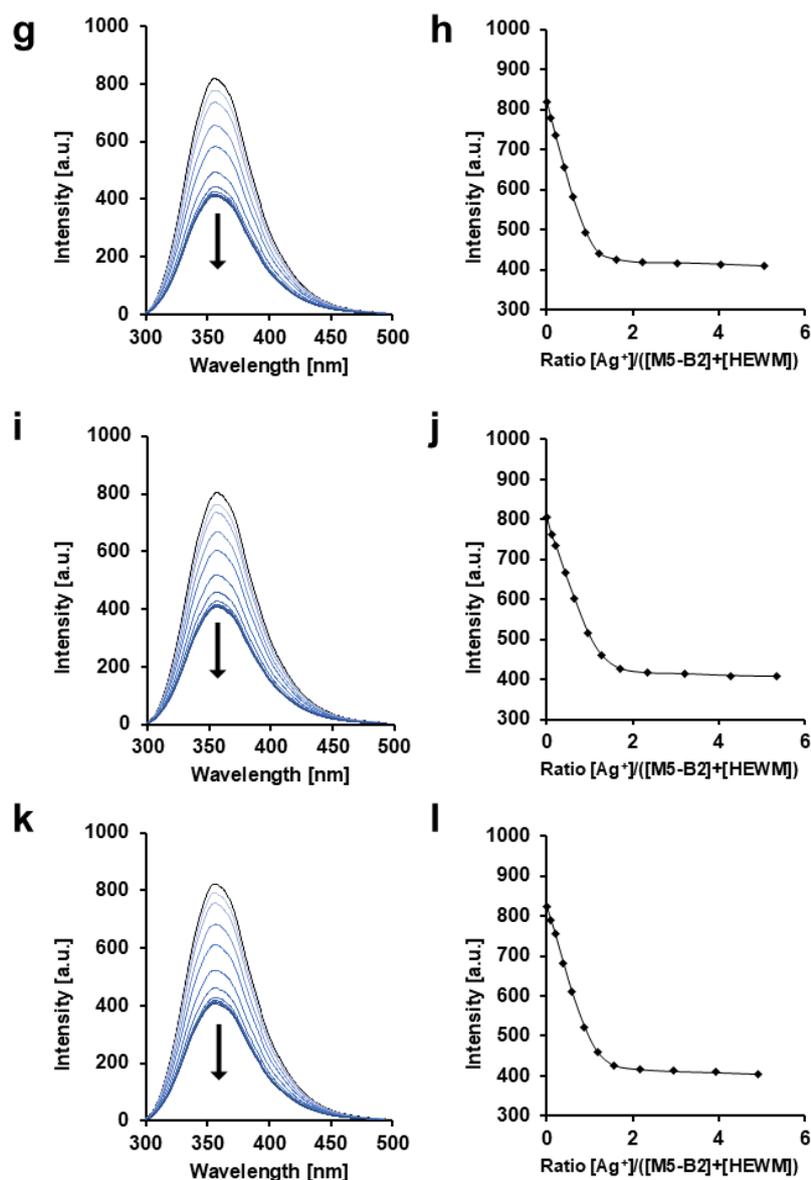
Model	$1 \cdot 10^{-5}$ M <sup>[a]</sup>		$2 \cdot 10^{-5}$ M <sup>[a]</sup>	
HQQMAEAHKKM (M4-B2)	$\log(K_{b-1}) = 6.32 \pm 0.03$	$\log(K_{b-2}) = 5.38 \pm 0.07$	$\log(K_{b-1}) = 6.28 \pm 0.03$	$\log(K_{b-2}) = 5.43 \pm 0.08$
	$\log(K_{b-1}) = 6.30 \pm 0.04$	$\log(K_{b-2}) = 5.58 \pm 0.11$	$\log(K_{b-1}) = 6.33 \pm 0.02$	$\log(K_{b-2}) = 5.23 \pm 0.06$
	$\log(K_{b-1}) = 6.34 \pm 0.06$	$\log(K_{b-2}) = 5.51 \pm 0.06$	$\log(K_{b-1}) = 6.16 \pm 0.04$	$\log(K_{b-2}) = 5.41 \pm 0.11$
Average	$\log(K_{b-1}) = 6.29 \pm 0.07$		$\log(K_{b-2}) = 5.42 \pm 0.12$	

<sup>[a]</sup> The values correspond to the peptide and probe concentrations.

HQAHAEAHRRM (M5-B2)



**Fig. S38** HQAHAEAHRRM (M5-B2) / HEWM competition titrations, both at  $1 \cdot 10^{-5}$  M. (a, c & e) Tryptophan fluorescence ( $\lambda_{\text{ex}}$ :280 nm) quench by addition of  $\text{AgNO}_3$  (0 to 5.5 equivalents) to a solution of M5-B2 ( $1 \cdot 10^{-5}$  M) in competition with HEWM probe ( $1 \cdot 10^{-5}$  M), in MOPS buffer (20 equivalents, pH 7.4-7.5) at 25°C. (b, d & f) Plot of the maxima of fluorescence intensities. The solid line corresponds to the fit obtained using Dynafit software.<sup>9,10</sup>



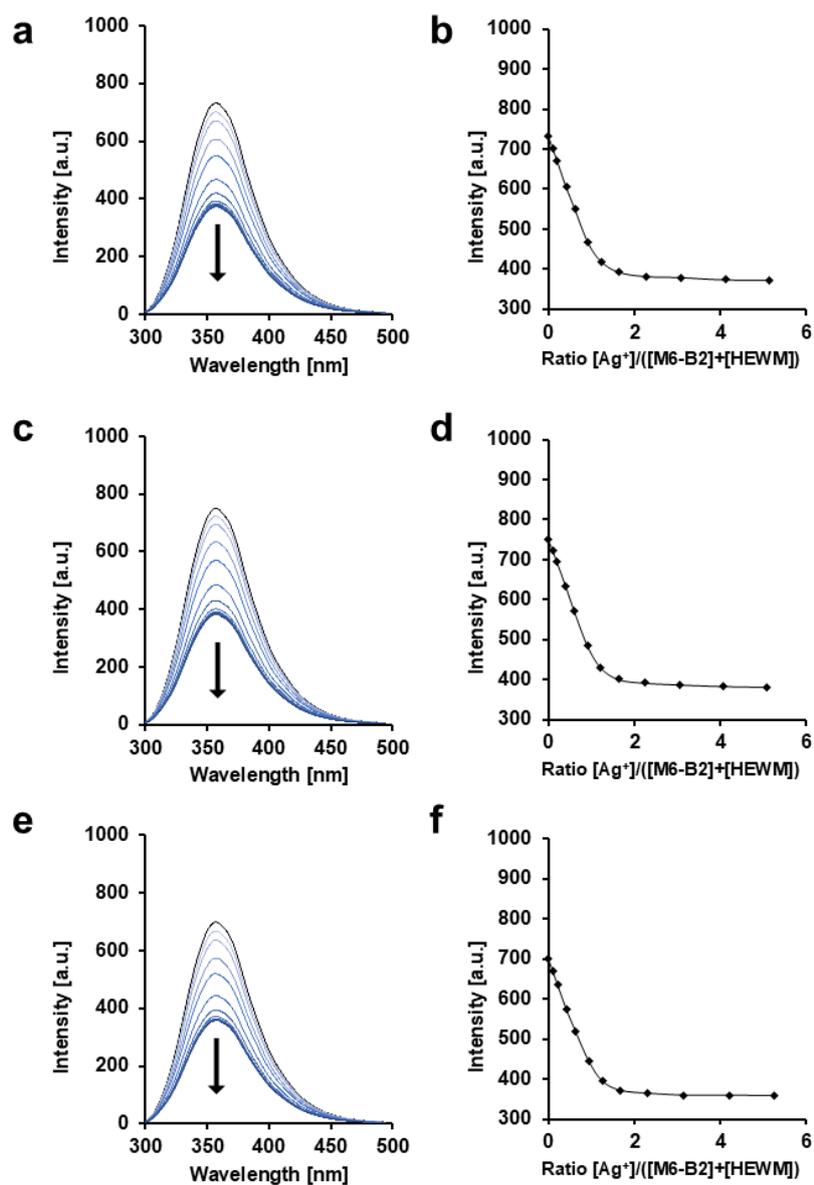
**Fig. S39** HQAHAEHRRM (M5-B2) / HEWM competition titrations, both at  $2 \cdot 10^{-5}$  M. (g, i & k) Tryptophan fluorescence ( $\lambda_{ex}$ :280 nm) quench by addition of  $AgNO_3$  (0 to 5.5 equivalents) to a solution of M5-B2 ( $2 \cdot 10^{-5}$  M) in competition with HEWM probe ( $2 \cdot 10^{-5}$  M), in MOPS buffer (20 equivalents, pH 7.4-7.5) at 25°C. (h, j & l) Plot of the maxima of fluorescence intensities. The solid line corresponds to the fit obtained using Dynafit software.<sup>9,10</sup>

**Table S7** Determination of the binding constants ( $\log(K_{b-1/b-2})$ ) of HQAHAEHRRM peptide

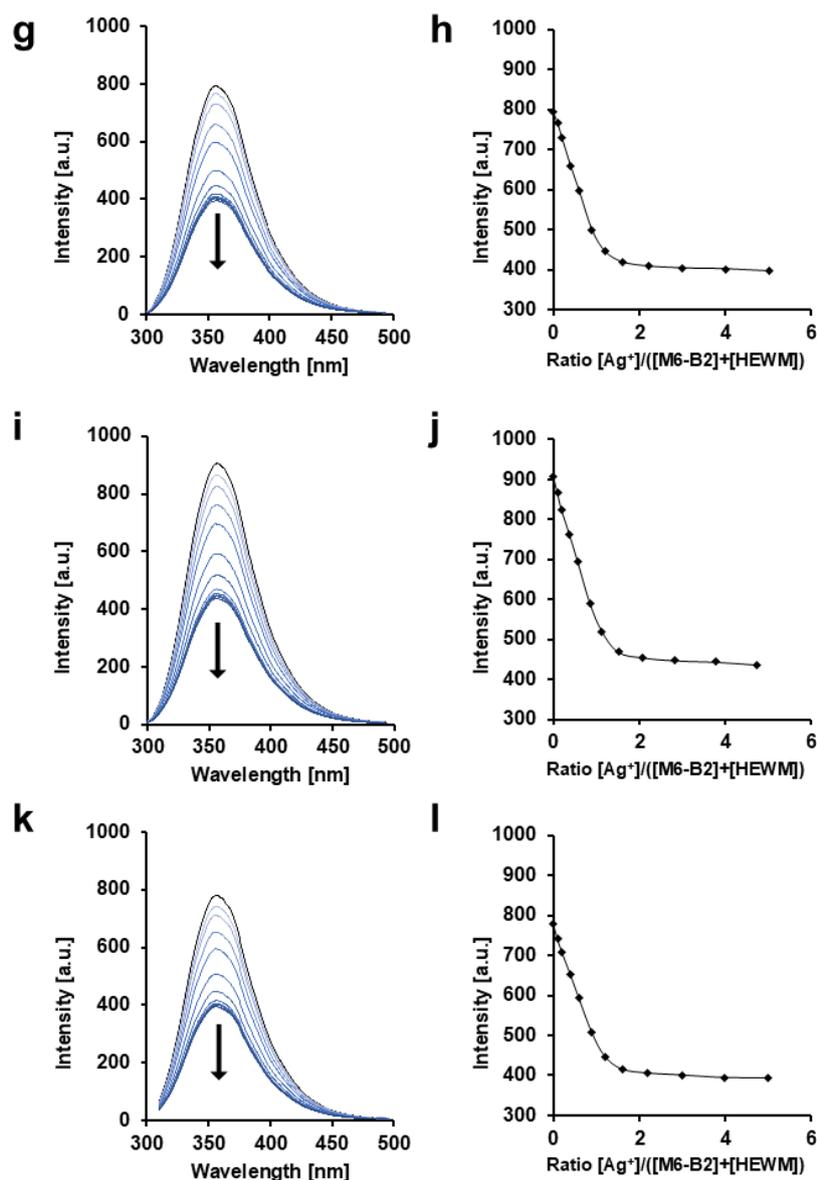
Model	$1 \cdot 10^{-5}$ M <sup>[a]</sup>		$2 \cdot 10^{-5}$ M <sup>[a]</sup>	
HQAHAEHRRM (M5-B2)	$\log(K_{b-1}) = 6.52 \pm 0.10$	$\log(K_{b-2}) = 5.64 \pm 0.07$	$\log(K_{b-1}) = 6.37 \pm 0.02$	$\log(K_{b-2}) = 5.12 \pm 0.05$
	$\log(K_{b-1}) = 6.66 \pm 0.02$	$\log(K_{b-2}) = 5.46 \pm 0.04$	$\log(K_{b-1}) = 6.57 \pm 0.04$	$\log(K_{b-2}) = 5.69 \pm 0.07$
	$\log(K_{b-1}) = 6.54 \pm 0.02$	$\log(K_{b-2}) = 5.60 \pm 0.05$	$\log(K_{b-1}) = 6.52 \pm 0.02$	$\log(K_{b-2}) = 5.42 \pm 0.04$
Average	$\log(K_{b-1}) = 6.53 \pm 0.10$		$\log(K_{b-2}) = 5.49 \pm 0.21$	

<sup>[a]</sup> The values correspond to the peptide and probe concentrations.

HQQHAEAHRRM (M6-B2)



**Fig. S40** HQQHAEAHRRM (M6-B2) / HEWM competition titrations, both at  $1 \cdot 10^{-5}$  M. (a, c & e) Tryptophan fluorescence ( $\lambda_{\text{ex}}$ :280 nm) quench by addition of  $\text{AgNO}_3$  (0 to 5.5 equivalents) to a solution of M6-B2 ( $1 \cdot 10^{-5}$  M) in competition with HEWM probe ( $1 \cdot 10^{-5}$  M), in MOPS buffer (20 equivalents, pH 7.4-7.5) at 25°C. (b, d & f) Plot of the maxima of fluorescence intensities. The solid line corresponds to the fit obtained using Dynafit software.<sup>9,10</sup>



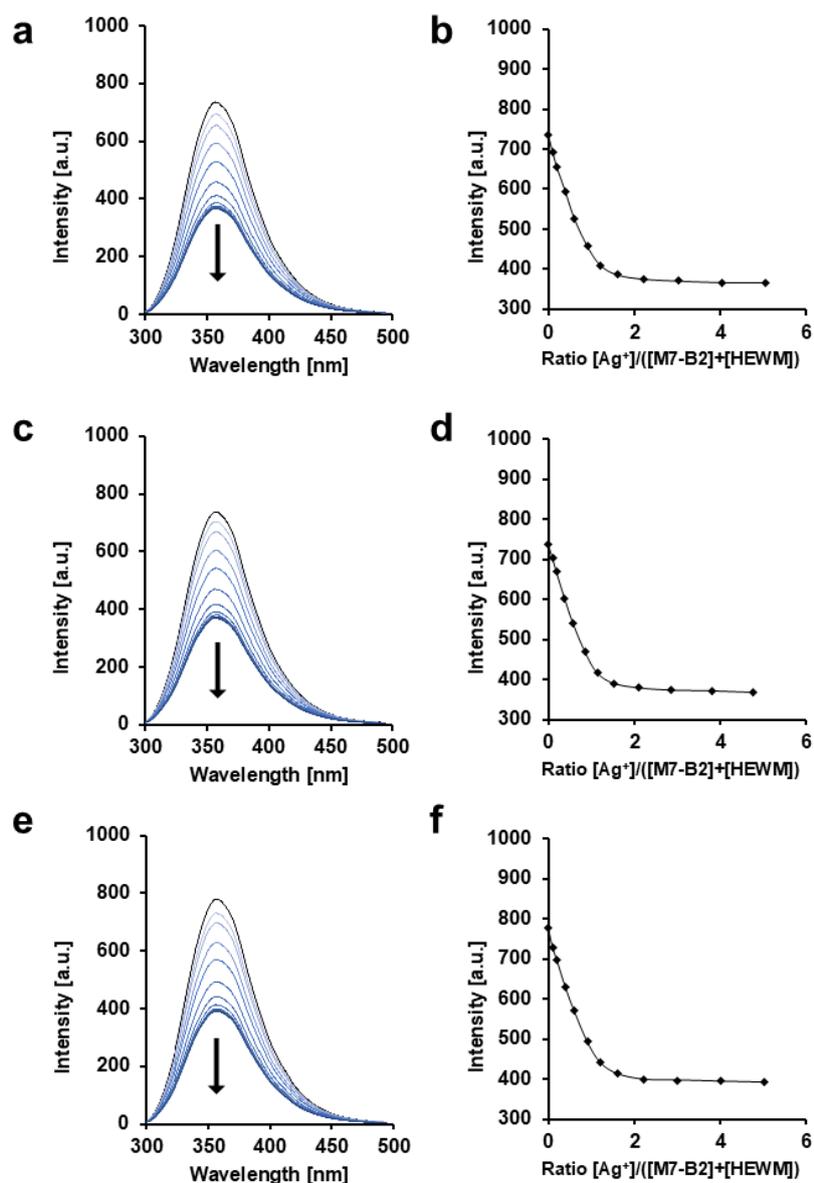
**Fig. S41** HQQHAEHRRM (M6-B2) / HEWM competition titrations, both at  $2 \cdot 10^{-5}$  M. (g, i & k) Tryptophan fluorescence ( $\lambda_{ex}$ :280 nm) quench by addition of  $\text{AgNO}_3$  (0 to 5.5 equivalents) to a solution of M6-B2 ( $2 \cdot 10^{-5}$  M) in competition with HEWM probe ( $2 \cdot 10^{-5}$  M), in MOPS buffer (20 equivalents, pH 7.4-7.5) at 25°C. (h, j & l) Plot of the maxima of fluorescence intensities. The solid line corresponds to the fit obtained using Dynafit software.<sup>9,10</sup>

**Table S8** Determination of the binding constants ( $\log(K_{b-1/b-2})$ ) of HQQHAEHRRM peptide

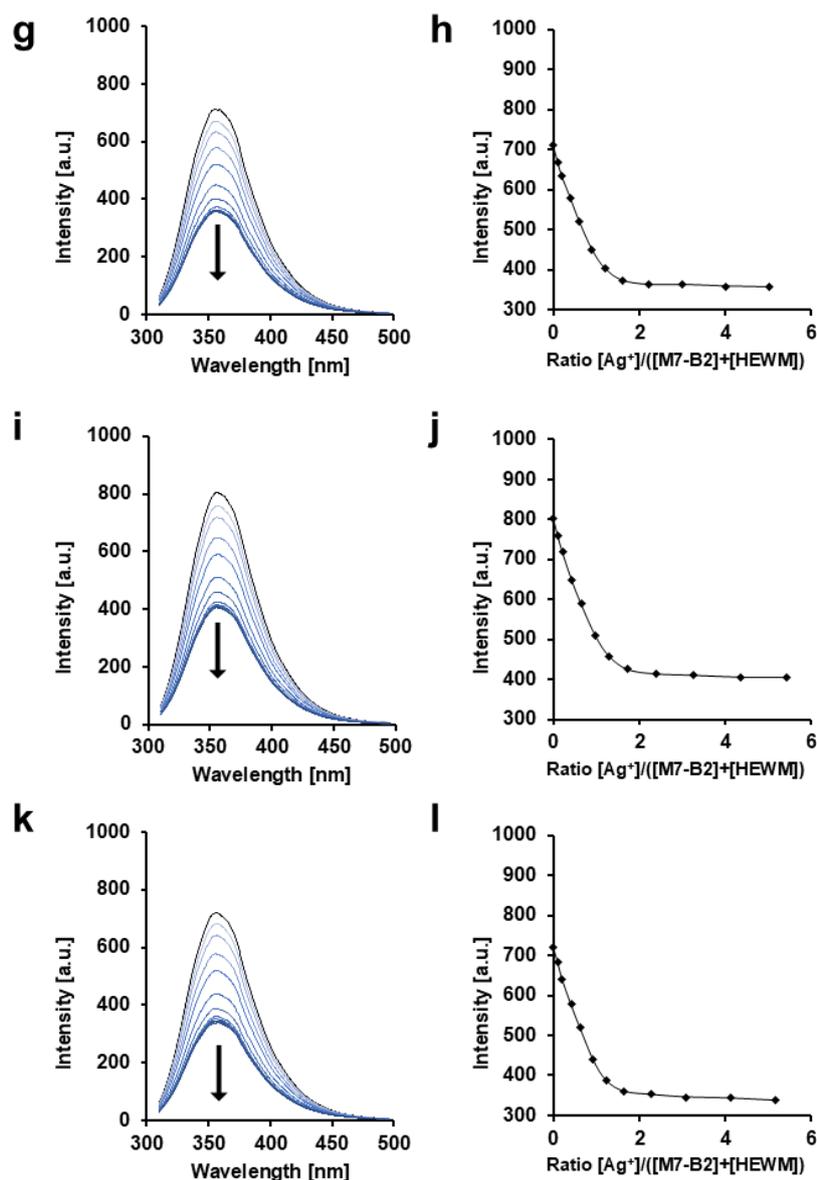
Model	$1 \cdot 10^{-5}$ M <sup>[a]</sup>		$2 \cdot 10^{-5}$ M <sup>[a]</sup>	
HQQHAEHRRM (M6-B2)	$\log(K_{b-1}) = 6.57 \pm 0.03$	$\log(K_{b-2}) = 5.50 \pm 0.07$	$\log(K_{b-1}) = 6.59 \pm 0.04$	$\log(K_{b-2}) = 5.32 \pm 0.10$
	$\log(K_{b-1}) = 6.66 \pm 0.02$	$\log(K_{b-2}) = 5.48 \pm 0.04$	$\log(K_{b-1}) = 6.54 \pm 0.06$	$\log(K_{b-2}) = 5.74 \pm 0.12$
	$\log(K_{b-1}) = 6.50 \pm 0.02$	$\log(K_{b-2}) = 5.59 \pm 0.03$	$\log(K_{b-1}) = 6.52 \pm 0.05$	$\log(K_{b-2}) = 5.59 \pm 0.10$
Average	$\log(K_{b-1}) = 6.56 \pm 0.06$		$\log(K_{b-2}) = 5.55 \pm 0.15$	

<sup>[a]</sup> The values correspond to the peptide and probe concentrations.

HQAMAEARRH (M7-B2)



**Fig. S42** HQAMAEARRH (M7-B2) / HEWM competition titrations, both at  $1 \cdot 10^{-5}$  M. (a, c & e) Tryptophan fluorescence ( $\lambda_{\text{ex}}$ :280 nm) quench by addition of  $\text{AgNO}_3$  (0 to 5.5 equivalents) to a solution of M7-B2 ( $1 \cdot 10^{-5}$  M) in competition with HEWM probe ( $1 \cdot 10^{-5}$  M), in MOPS buffer (20 equivalents, pH 7.4-7.5) at 25°C. (b, d & f) Plot of the maxima of fluorescence intensities. The solid line corresponds to the fit obtained using Dynafit software.<sup>9,10</sup>



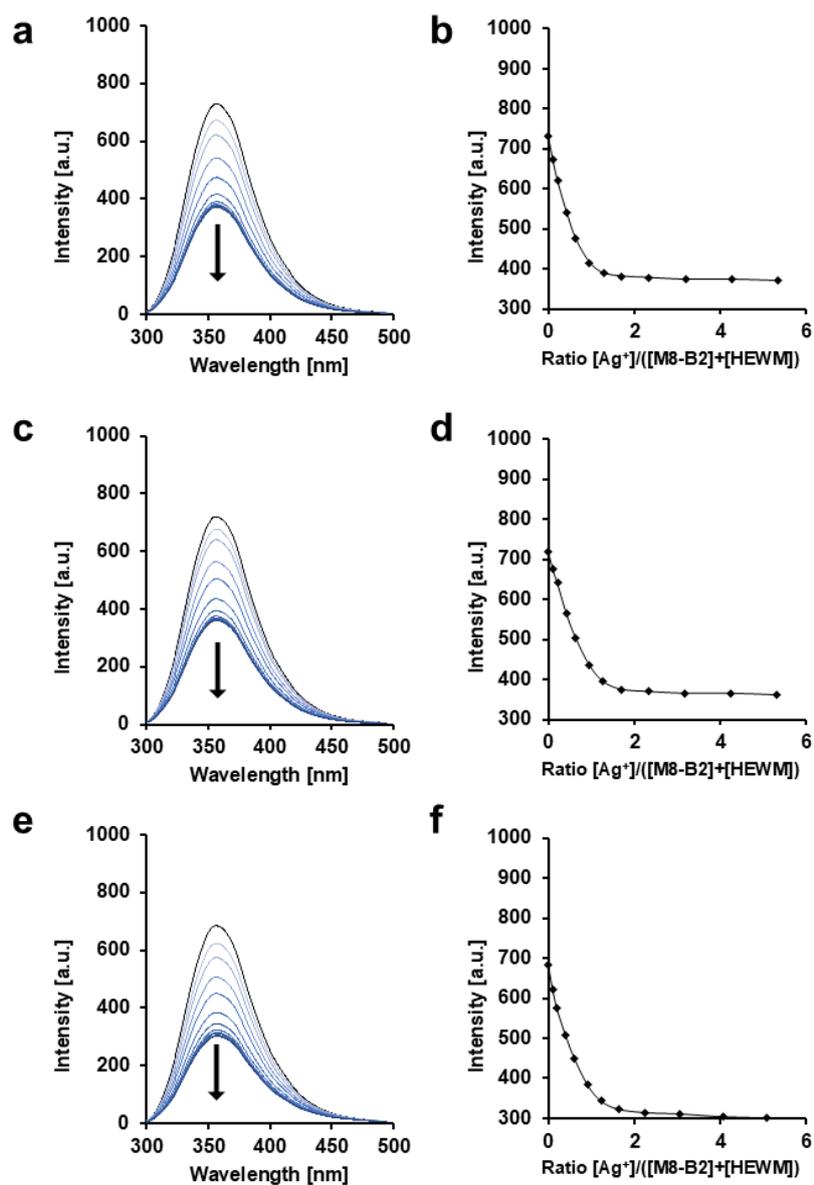
**Fig. S43** HQAMAEARRH (M7-B2) / HEWM competition titrations, both at  $2 \cdot 10^{-5}$  M. (g, i & k) Tryptophan fluorescence ( $\lambda_{ex}$ :280 nm) quench by addition of  $\text{AgNO}_3$  (0 to 5.5 equivalents) to a solution of M7-B2 ( $2 \cdot 10^{-5}$  M) in competition with HEWM probe ( $2 \cdot 10^{-5}$  M), in MOPS buffer (20 equivalents, pH 7.4-7.5) at  $25^\circ\text{C}$ . (h, j & l) Plot of the maxima of fluorescence intensities. The solid line corresponds to the fit obtained using Dynafit software.<sup>9,10</sup>

**Table S9** Determination of the binding constants ( $\log(K_{b-1/b-2})$ ) of HQAMAEARRH peptide

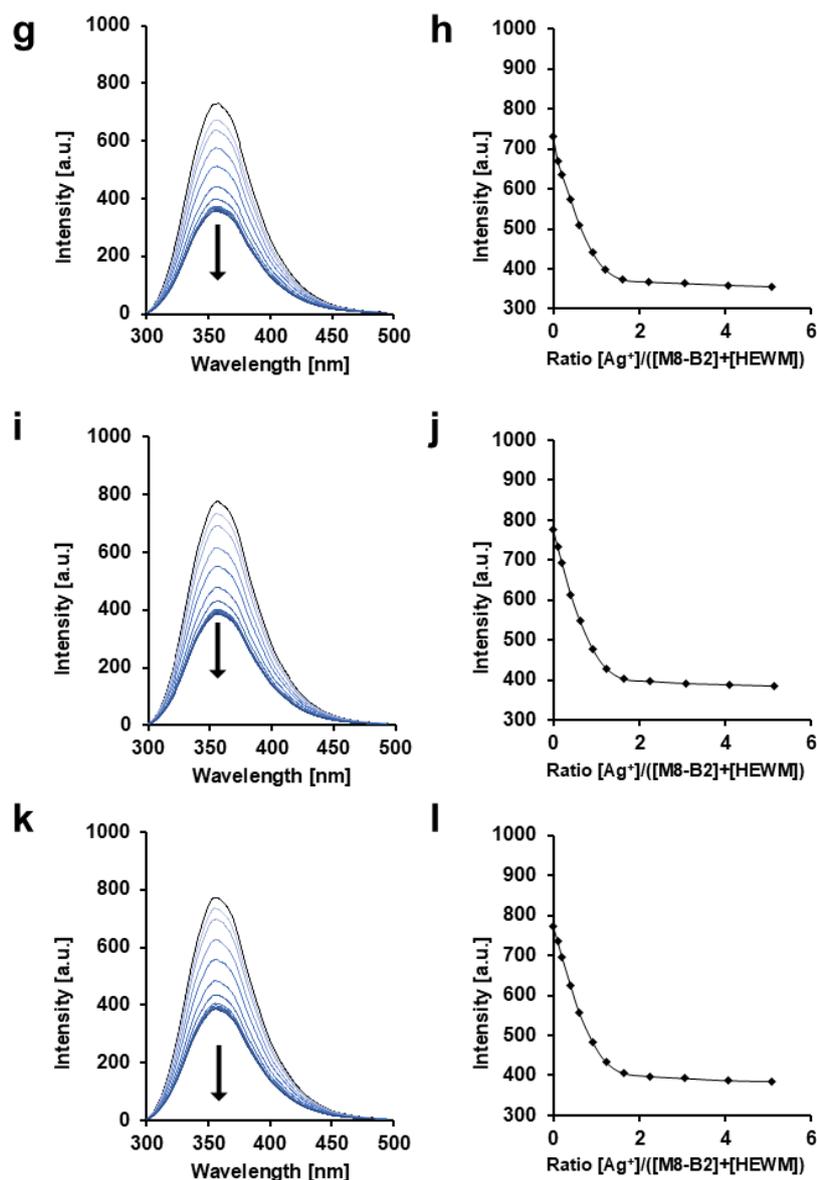
Model	$1 \cdot 10^{-5}$ M <sup>[a]</sup>		$2 \cdot 10^{-5}$ M <sup>[a]</sup>	
HQAMAEARRH (M7-B2)	$\log(K_{b-1}) = 6.33 \pm 0.03$	$\log(K_{b-2}) = 5.57 \pm 0.08$	$\log(K_{b-1}) = 6.31 \pm 0.06$	$\log(K_{b-2}) = 5.67 \pm 0.13$
	$\log(K_{b-1}) = 6.38 \pm 0.02$	$\log(K_{b-2}) = 5.48 \pm 0.05$	$\log(K_{b-1}) = 6.37 \pm 0.03$	$\log(K_{b-2}) = 5.84 \pm 0.05$
	$\log(K_{b-1}) = 6.31 \pm 0.05$	$\log(K_{b-2}) = 5.71 \pm 0.11$	$\log(K_{b-1}) = 6.41 \pm 0.04$	$\log(K_{b-2}) = 5.68 \pm 0.08$
Average	$\log(K_{b-1}) = 6.35 \pm 0.04$		$\log(K_{b-2}) = 5.66 \pm 0.13$	

<sup>[a]</sup> The values correspond to the peptide and probe concentrations.

HQAMAEAHKRH (M8-B2)



**Fig. S44** HQAMAEAHKRH (M8-B2) / HEWM competition titrations, both at  $1 \cdot 10^{-5}$  M. (a, c & e) Tryptophan fluorescence ( $\lambda_{\text{ex}}$ :280 nm) quench by addition of  $\text{AgNO}_3$  (0 to 5.5 equivalents) to a solution of M8-B2 ( $1 \cdot 10^{-5}$  M) in competition with HEWM probe ( $1 \cdot 10^{-5}$  M), in MOPS buffer (20 equivalents, pH 7.4-7.5) at 25°C. (b, d & f) Plot of the maxima of fluorescence intensities. The solid line corresponds to the fit obtained using Dynafit software.<sup>9,10</sup>



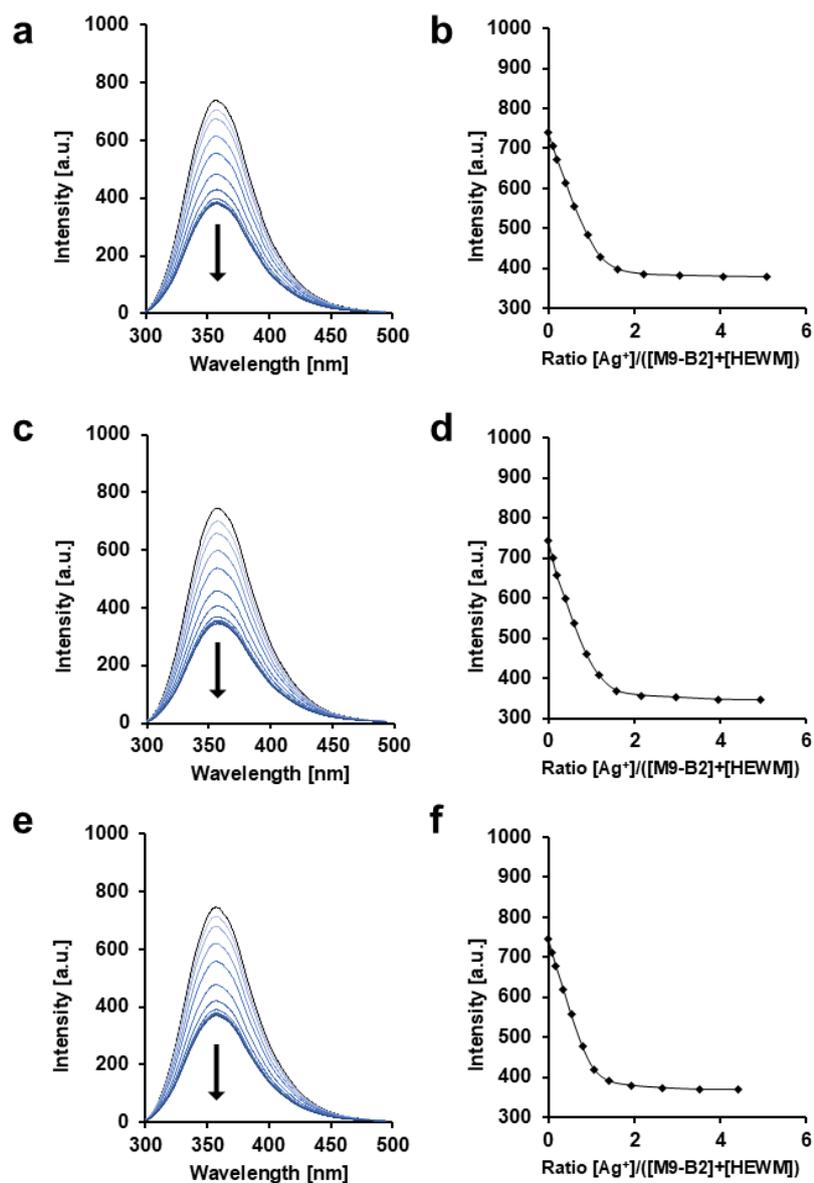
**Fig. S45** HQAMAEAKRH (M8-B2) / HEWM competition titrations, both at  $2 \cdot 10^{-5}$  M. (g, i & k) Tryptophan fluorescence ( $\lambda_{ex}$ :280 nm) quench by addition of  $\text{AgNO}_3$  (0 to 5.5 equivalents) to a solution of M8-B2 ( $2 \cdot 10^{-5}$  M) in competition with HEWM probe ( $2 \cdot 10^{-5}$  M), in MOPS buffer (20 equivalents, pH 7.4-7.5) at  $25^\circ\text{C}$ . (h, j & l) Plot of the maxima of fluorescence intensities. The solid line corresponds to the fit obtained using Dynafit software.<sup>9,10</sup>

**Table S10** Determination of the binding constants ( $\log(K_{b-1/b-2})$ ) of HQAMAEAKRH peptide

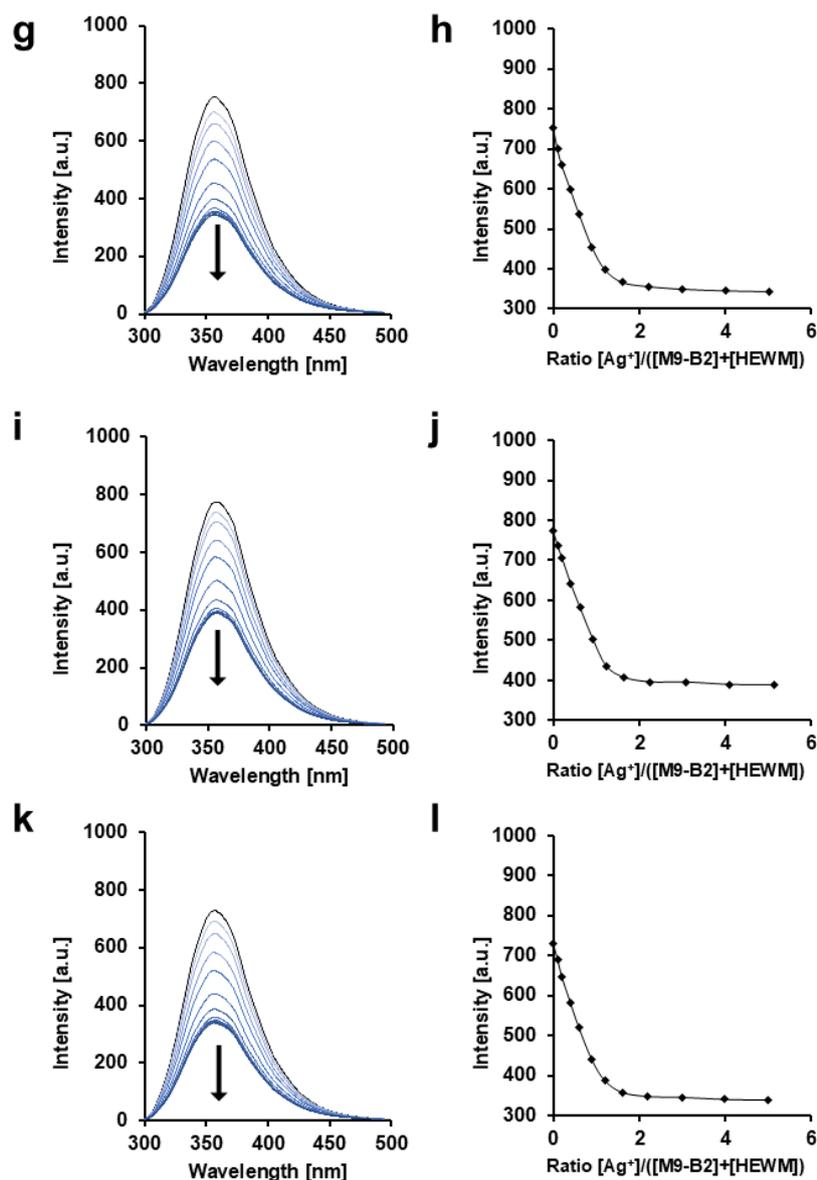
Model	$1 \cdot 10^{-5}$ M <sup>[a]</sup>		$2 \cdot 10^{-5}$ M <sup>[a]</sup>	
HQAMAEAKRH (M8-B2)	$\log(K_{b-1}) = 5.95 \pm 0.03$	$\log(K_{b-2}) = 5.16 \pm 0.13$	$\log(K_{b-1}) = 6.21 \pm 0.08$	$\log(K_{b-2}) = 5.57 \pm 0.19$
	$\log(K_{b-1}) = 6.28 \pm 0.03$	$\log(K_{b-2}) = 5.47 \pm 0.07$	$\log(K_{b-1}) = 6.27 \pm 0.02$	$\log(K_{b-2}) = 5.48 \pm 0.04$
	$\log(K_{b-1}) = 6.00 \pm 0.10$	$\log(K_{b-2}) = 5.74 \pm 0.21$	$\log(K_{b-1}) = 6.37 \pm 0.03$	$\log(K_{b-2}) = 5.47 \pm 0.08$
Average	$\log(K_{b-1}) = 6.18 \pm 0.17$		$\log(K_{b-2}) = 5.48 \pm 0.19$	

<sup>[a]</sup> The values correspond to the peptide and probe concentrations.

HQAMAEAHQQH (M9-B2)



**Fig. S46** HQAMAEAHQQH (M9-B2) / HEWM competition titrations, both at  $1 \cdot 10^{-5}$  M. (a, c & e) Tryptophan fluorescence ( $\lambda_{\text{ex}}$ :280 nm) quench by addition of  $\text{AgNO}_3$  (0 to 5.5 equivalents) to a solution of M9-B2 ( $1 \cdot 10^{-5}$  M) in competition with HEWM probe ( $1 \cdot 10^{-5}$  M), in MOPS buffer (20 equivalents, pH 7.4-7.5) at 25°C. (b, d & f) Plot of the maxima of fluorescence intensities. The solid line corresponds to the fit obtained using Dynafit software.<sup>9,10</sup>



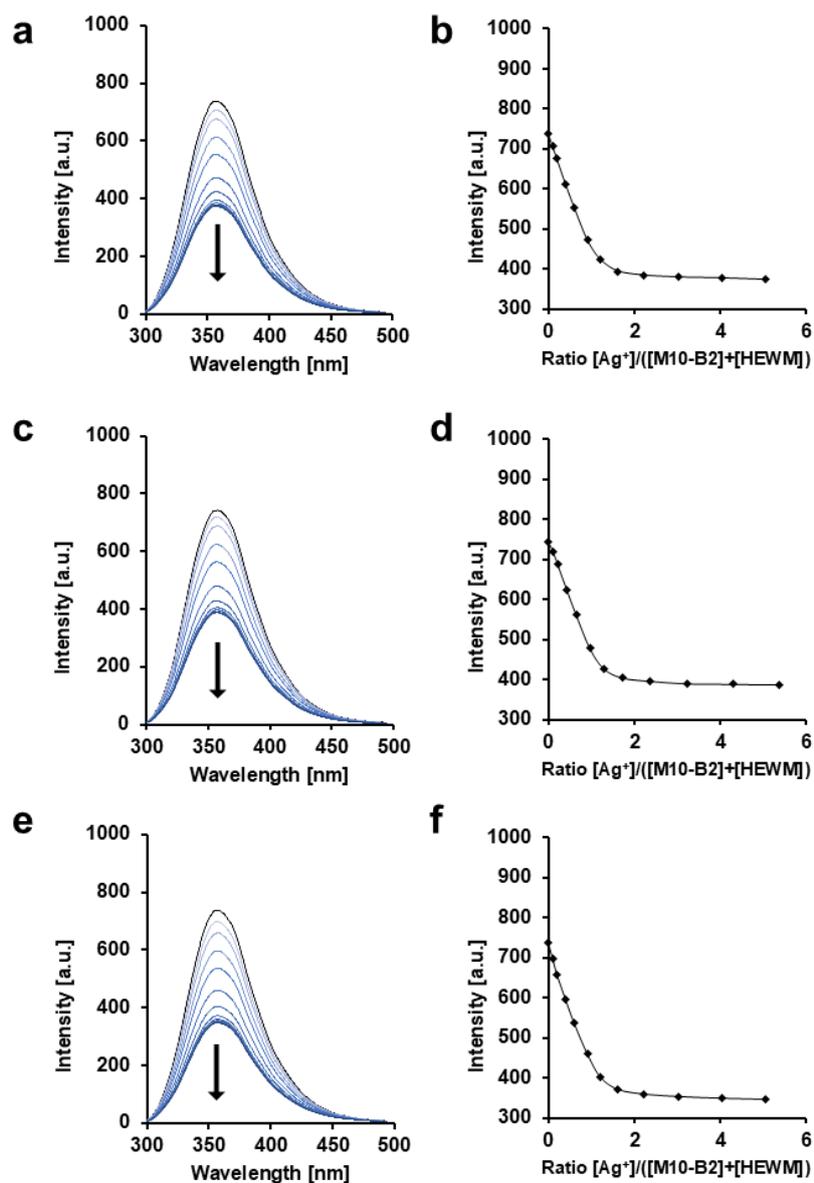
**Fig. S47** HQAMAEAHQQH (M9-B2) / HEWM competition titrations, both at  $2 \cdot 10^{-5}$  M. (g, i & k) Tryptophan fluorescence ( $\lambda_{ex}$ :280 nm) quench by addition of  $\text{AgNO}_3$  (0 to 5.5 equivalents) to a solution of M9-B2 ( $2 \cdot 10^{-5}$  M) in competition with HEWM probe ( $2 \cdot 10^{-5}$  M), in MOPS buffer (20 equivalents, pH 7.4-7.5) at 25°C. (h, j & l) Plot of the maxima of fluorescence intensities. The solid line corresponds to the fit obtained using Dynafit software.<sup>9,10</sup>

**Table S11** Determination of the binding constants ( $\log(K_{b-1/b-2})$ ) of HQAMAEAHQQH peptide

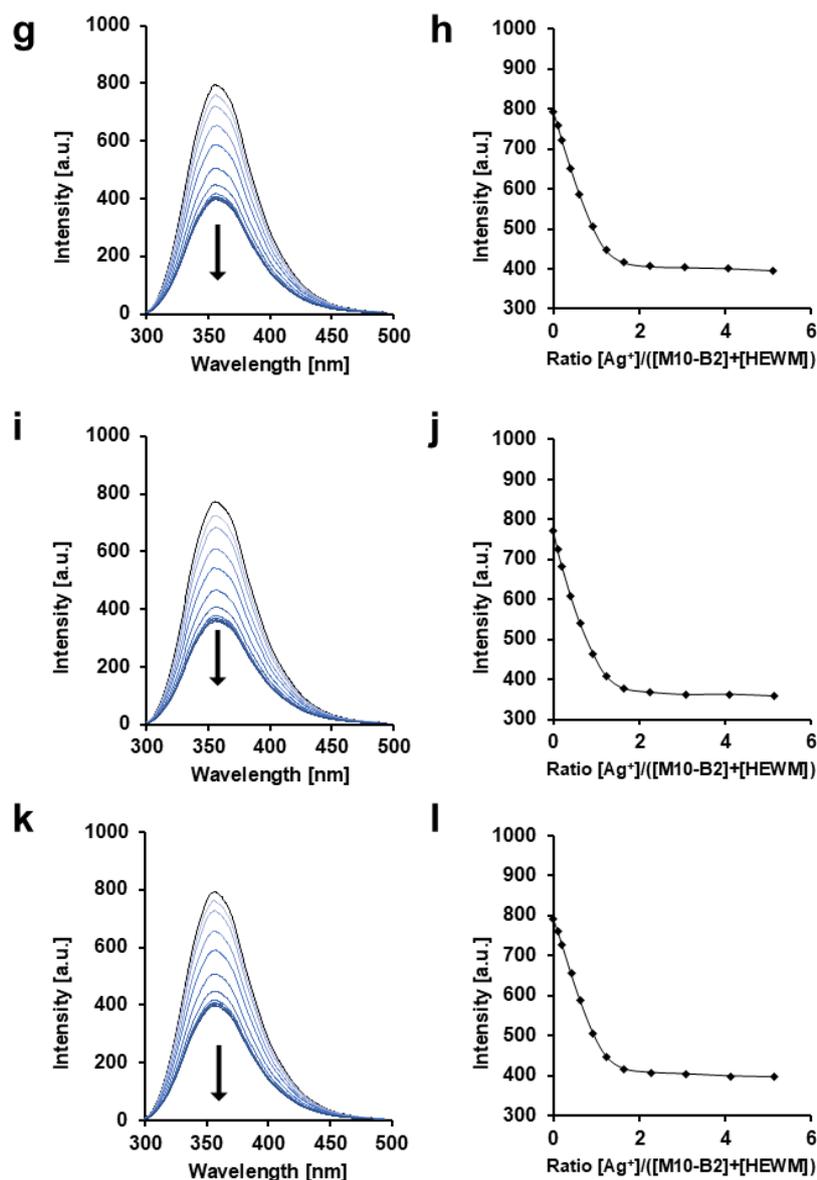
Model	$1 \cdot 10^{-5}$ M <sup>[a]</sup>		$2 \cdot 10^{-5}$ M <sup>[a]</sup>	
HQAMAEAHQQH (M9-B2)	$\log(K_{b-1}) = 6.49 \pm 0.02$	$\log(K_{b-2}) = 5.67 \pm 0.03$	$\log(K_{b-1}) = 6.34 \pm 0.08$	$\log(K_{b-2}) = 5.72 \pm 0.16$
	$\log(K_{b-1}) = 6.33 \pm 0.06$	$\log(K_{b-2}) = 5.80 \pm 0.12$	$\log(K_{b-1}) = 6.55 \pm 0.04$	$\log(K_{b-2}) = 5.69 \pm 0.07$
	$\log(K_{b-1}) = 6.43 \pm 0.01$	$\log(K_{b-2}) = 5.15 \pm 0.05$	$\log(K_{b-1}) = 6.37 \pm 0.03$	$\log(K_{b-2}) = 5.55 \pm 0.06$
Average	$\log(K_{b-1}) = 6.42 \pm 0.09$		$\log(K_{b-2}) = 5.60 \pm 0.23$	

<sup>[a]</sup> The values correspond to the peptide and probe concentrations.

HQAHAEAHRRH (M10-B2)



**Fig. S48** HQAHAEAHRRH (M10-B2) / HEWM competition titrations, both at  $1 \cdot 10^{-5}$  M. (a, c & e) Tryptophan fluorescence ( $\lambda_{\text{ex}}$ :280 nm) quench by addition of  $\text{AgNO}_3$  (0 to 5.5 equivalents) to a solution of M10-B2 ( $1 \cdot 10^{-5}$  M) in competition with HEWM probe ( $1 \cdot 10^{-5}$  M), in MOPS buffer (20 equivalents, pH 7.4-7.5) at 25°C. (b, d & f) Plot of the maxima of fluorescence intensities. The solid line corresponds to the fit obtained using Dynafit software.<sup>9,10</sup>



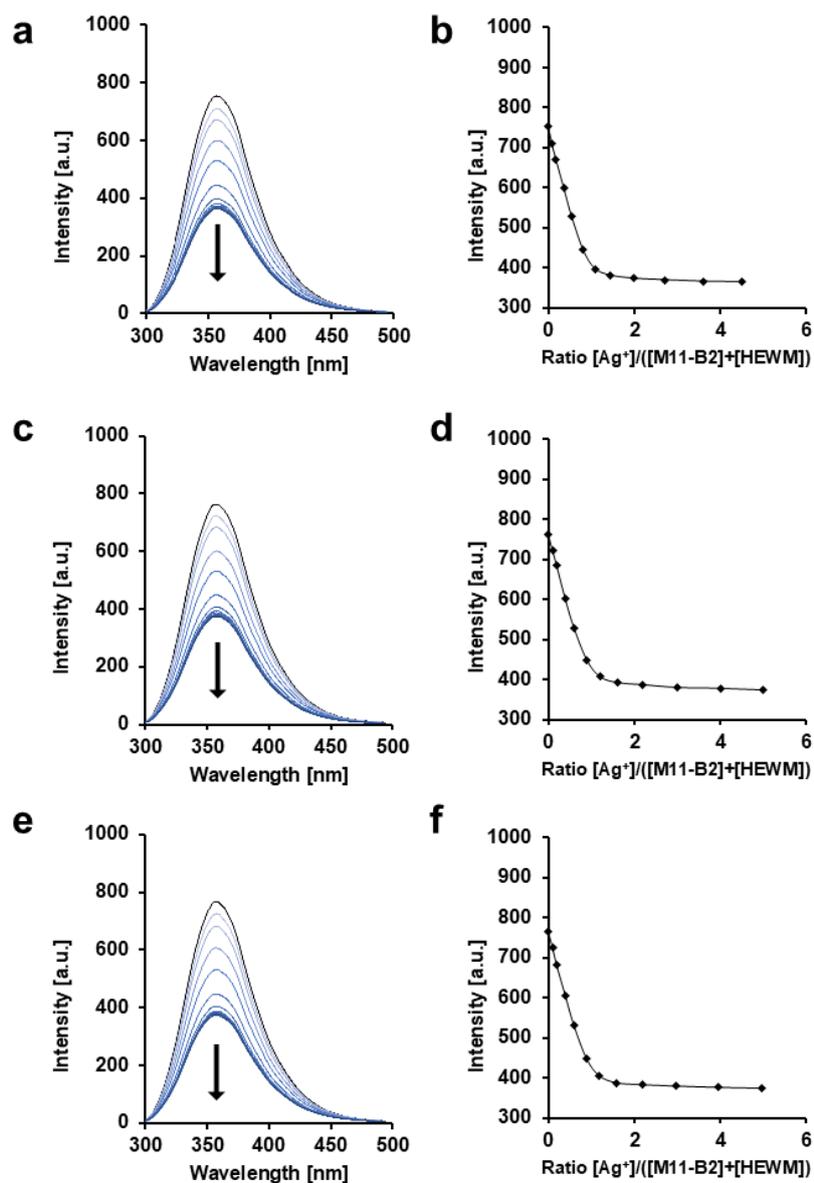
**Fig. S49** HQAHAEARRH (M10-B2) / HEWM competition titrations, both at  $2 \cdot 10^{-5}$  M. (g, i & k) Tryptophan fluorescence ( $\lambda_{\text{ex}}$ :280 nm) quench by addition of  $\text{AgNO}_3$  (0 to 5.5 equivalents) to a solution of M10-B2 ( $2 \cdot 10^{-5}$  M) in competition with HEWM probe ( $2 \cdot 10^{-5}$  M), in MOPS buffer (20 equivalents, pH 7.4-7.5) at  $25^\circ\text{C}$ . (h, j & l) Plot of the maxima of fluorescence intensities. The solid line corresponds to the fit obtained using Dynafit software.<sup>9,10</sup>

**Table S12** Determination of the binding constants ( $\log(K_{b-1/b-2})$ ) of HQAHAEARRH peptide

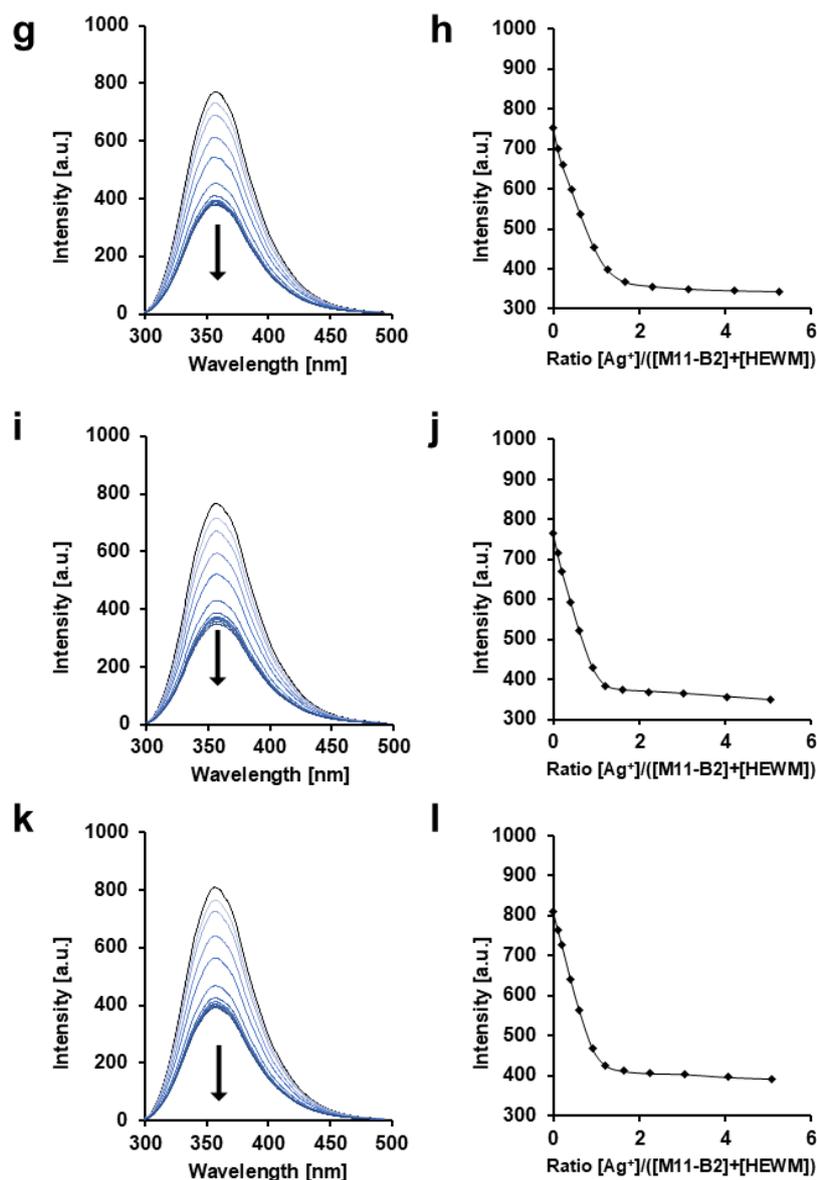
Model	$1 \cdot 10^{-5}$ M <sup>[a]</sup>		$2 \cdot 10^{-5}$ M <sup>[a]</sup>	
HQAHAEARRH (M10-B2)	$\log(K_{b-1}) = 6.53 \pm 0.05$	$\log(K_{b-2}) = 5.50 \pm 0.03$	$\log(K_{b-1}) = 6.47 \pm 0.02$	$\log(K_{b-2}) = 5.55 \pm 0.04$
	$\log(K_{b-1}) = 6.67 \pm 0.03$	$\log(K_{b-2}) = 5.58 \pm 0.06$	$\log(K_{b-1}) = 6.28 \pm 0.02$	$\log(K_{b-2}) = 5.76 \pm 0.04$
	$\log(K_{b-1}) = 6.41 \pm 0.03$	$\log(K_{b-2}) = 5.76 \pm 0.06$	$\log(K_{b-1}) = 6.55 \pm 0.02$	$\log(K_{b-2}) = 5.54 \pm 0.05$
Average	$\log(K_{b-1}) = 6.49 \pm 0.13$		$\log(K_{b-2}) = 5.62 \pm 0.11$	

<sup>[a]</sup> The values correspond to the peptide and probe concentrations.

MQAMAEHRRM (M11-B2)



**Fig. S50** MQAMAEHRRM (M11-B2) / HEWM competition titrations, both at  $1 \cdot 10^{-5}$  M. (a, c & e) Tryptophan fluorescence ( $\lambda_{\text{ex}}$ :280 nm) quench by addition of  $\text{AgNO}_3$  (0 to 5.5 equivalents) to a solution of M11-B2 ( $1 \cdot 10^{-5}$  M) in competition with HEWM probe ( $1 \cdot 10^{-5}$  M), in MOPS buffer (20 equivalents, pH 7.4-7.5) at 25°C. (b, d & f) Plot of the maxima of fluorescence intensities. The solid line corresponds to the fit obtained using Dynafit software.<sup>9,10</sup>



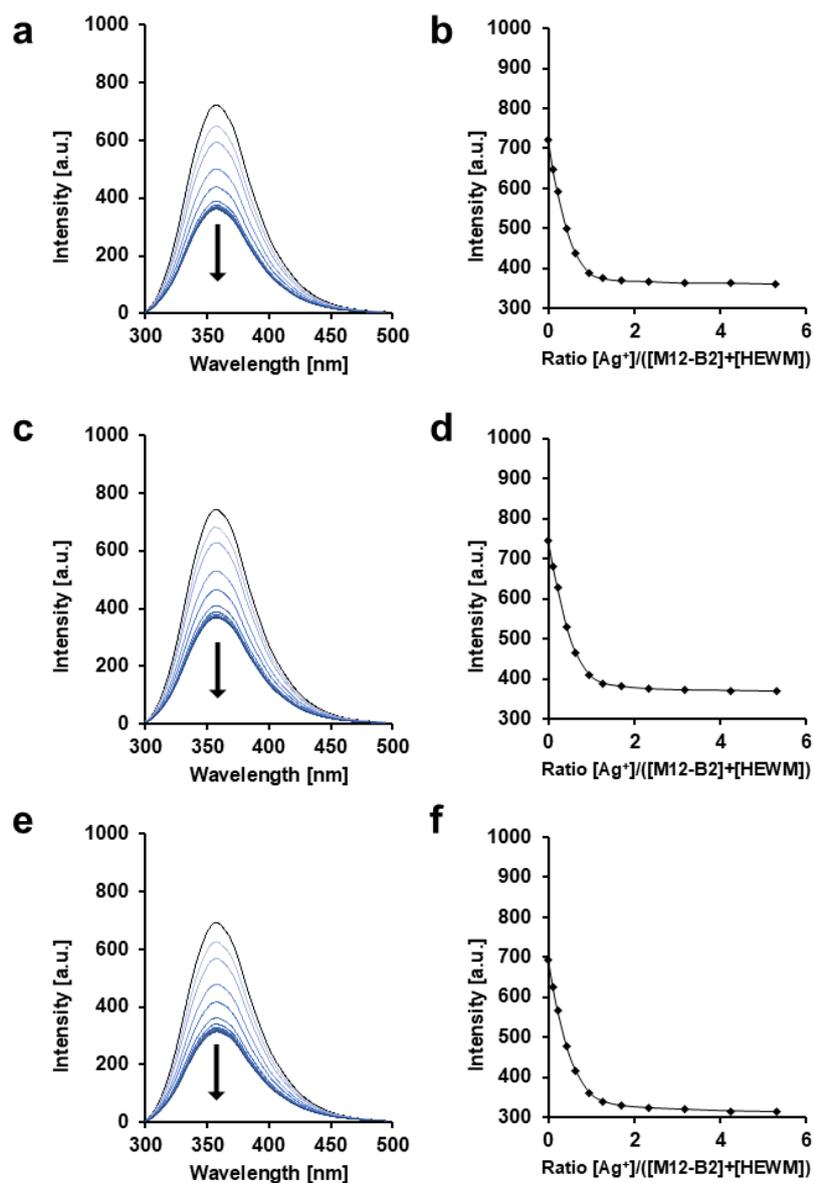
**Fig. S51** MQAMAEHRRM (M11-B2) / HEWM competition titrations, both at  $2 \cdot 10^{-5}$  M. (g, i & k) Tryptophan fluorescence ( $\lambda_{ex}$ :280 nm) quench by addition of  $\text{AgNO}_3$  (0 to 5.5 equivalents) to a solution of M11-B2 ( $2 \cdot 10^{-5}$  M) in competition with HEWM probe ( $2 \cdot 10^{-5}$  M), in MOPS buffer (20 equivalents, pH 7.4-7.5) at  $25^\circ\text{C}$ . (h, j & l) Plot of the maxima of fluorescence intensities. The solid line corresponds to the fit obtained using Dynafit software.<sup>9,10</sup>

**Table S13** Determination of the binding constants ( $\log(K_{b-1/b-2})$ ) of MQAMAEHRRM peptide

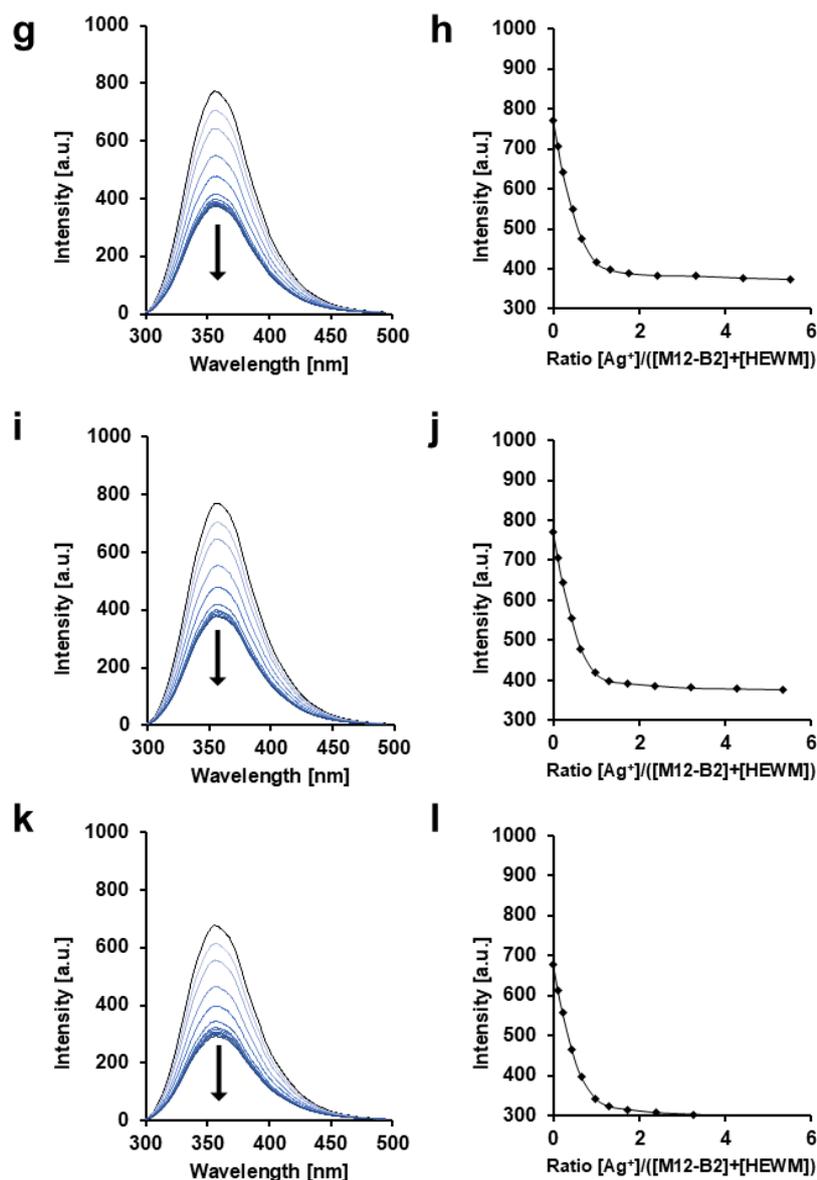
Model	$1 \cdot 10^{-5}$ M <sup>[a]</sup>		$2 \cdot 10^{-5}$ M <sup>[a]</sup>	
MQAMAEHRRM (M11-B2)	$\log(K_{b-1}) = 6.24 \pm 0.02$	$\log(K_{b-2}) = 4.69 \pm 0.16$	$\log(K_{b-1}) = 6.40 \pm 0.02$	$\log(K_{b-2}) = 5.16 \pm 0.06$
	$\log(K_{b-1}) = 6.32 \pm 0.04$	$\log(K_{b-2}) = 5.09 \pm 0.20$	$\log(K_{b-1}) = 6.31 \pm 0.04$	$\log(K_{b-2}) = 5.09 \pm 0.21$
	$\log(K_{b-1}) = 6.31 \pm 0.02$	$\log(K_{b-2}) = 5.02 \pm 0.10$	$\log(K_{b-1}) = 6.37 \pm 0.02$	$\log(K_{b-2}) = 4.88 \pm 0.12$
Average	$\log(K_{b-1}) = 6.32 \pm 0.05$		$\log(K_{b-2}) = 4.99 \pm 0.18$	

<sup>[a]</sup> The values correspond to the peptide and probe concentrations.

MKKMAEAHRRM (M12-B2)



**Fig. S52** MKKMAEAHRRM (M12-B2) / HEWM competition titrations, both at  $1 \cdot 10^{-5}$  M. (a, c & e) Tryptophan fluorescence ( $\lambda_{ex}$ :280 nm) quench by addition of  $AgNO_3$  (0 to 5.5 equivalents) to a solution of M12-B2 ( $1 \cdot 10^{-5}$  M) in competition with HEWM probe ( $1 \cdot 10^{-5}$  M), in MOPS buffer (20 equivalents, pH 7.4-7.5) at 25°C. (b, d & f) Plot of the maxima of fluorescence intensities. The solid line corresponds to the fit obtained using Dynafit software.<sup>9,10</sup>



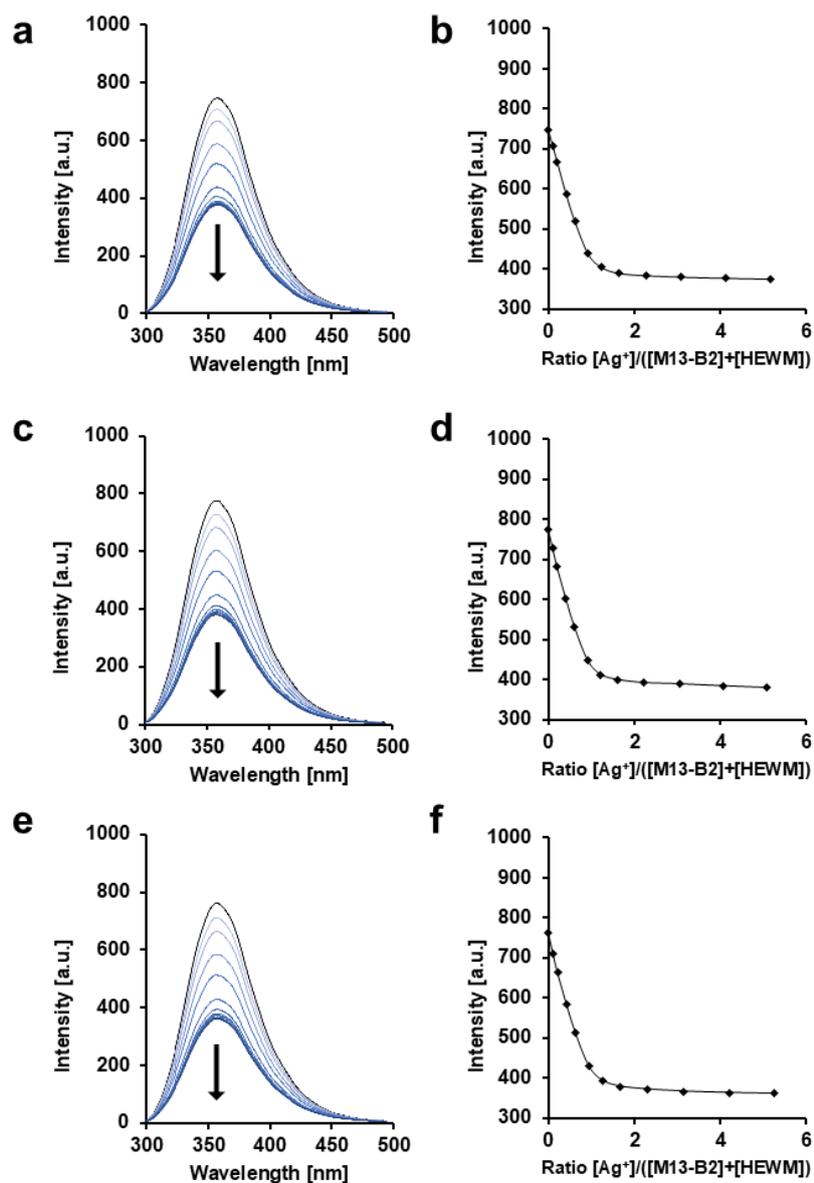
**Fig. S53** MKKMAEAHRRM (M12-B2) / HEWM competition titrations, both at  $2 \cdot 10^{-5}$  M. (g, i & k) Tryptophan fluorescence ( $\lambda_{\text{ex}}$ :280 nm) quench by addition of  $\text{AgNO}_3$  (0 to 5.5 equivalents) to a solution of M12-B2 ( $2 \cdot 10^{-5}$  M) in competition with HEWM probe ( $2 \cdot 10^{-5}$  M), in MOPS buffer (20 equivalents, pH 7.4-7.5) at  $25^\circ\text{C}$ . (h, j & l) Plot of the maxima of fluorescence intensities. The solid line corresponds to the fit obtained using Dynafit software.<sup>9,10</sup>

**Table S14** Determination of the binding constants ( $\log(K_{b-1/b-2})$ ) of MKKMAEAHRRM peptide

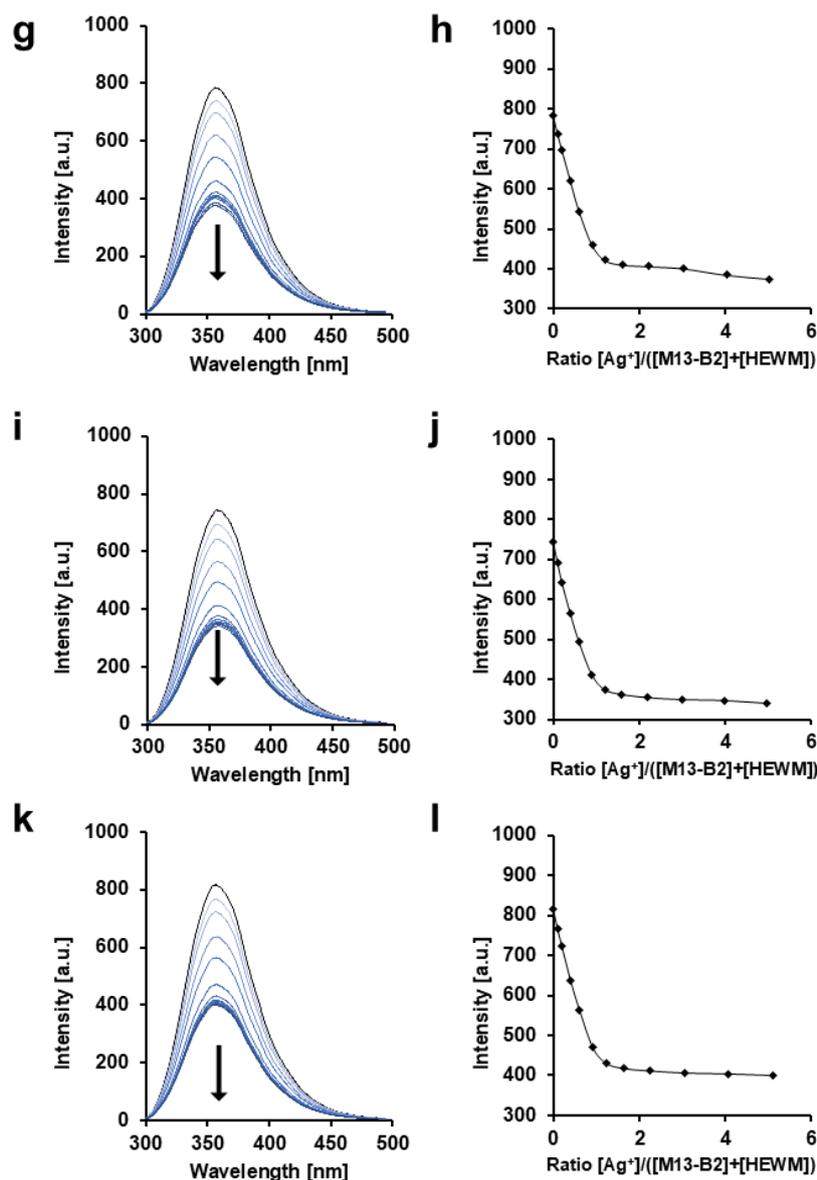
Model	$1 \cdot 10^{-5}$ M <sup>[a]</sup>		$2 \cdot 10^{-5}$ M <sup>[a]</sup>	
MKKMAEAHRRM (M12-B2)	$\log(K_{b-1}) = 5.62 \pm 0.06$	$\log(K_{b-2}) = 4.92 \pm 0.32$	$\log(K_{b-1}) = 5.83 \pm 0.04$	$\log(K_{b-2}) = 5.03 \pm 0.19$
	$\log(K_{b-1}) = 5.82 \pm 0.02$	$\log(K_{b-2}) = 5.01 \pm 0.08$	$\log(K_{b-1}) = 5.84 \pm 0.03$	$\log(K_{b-2}) = 4.89 \pm 0.19$
	$\log(K_{b-1}) = 5.74 \pm 0.05$	$\log(K_{b-2}) = 5.37 \pm 0.15$	$\log(K_{b-1}) = 5.85 \pm 0.04$	$\log(K_{b-2}) = 5.12 \pm 0.19$
Average	$\log(K_{b-1}) = 5.78 \pm 0.09$		$\log(K_{b-2}) = 5.06 \pm 0.17$	

<sup>[a]</sup> The values correspond to the peptide and probe concentrations.

HQAMAEAMRRM (M13-B2)



**Fig. S54** HQAMAEAMRRM (M13-B2) / HEWM competition titrations, both at  $1 \cdot 10^{-5}$  M. (a, c & e) Tryptophan fluorescence ( $\lambda_{\text{ex}}$ :280 nm) quench by addition of  $\text{AgNO}_3$  (0 to 5.5 equivalents) to a solution of M13-B2 ( $1 \cdot 10^{-5}$  M) in competition with HEWM probe ( $1 \cdot 10^{-5}$  M), in MOPS buffer (20 equivalents, pH 7.4-7.5) at 25°C. (b, d & f) Plot of the maxima of fluorescence intensities. The solid line corresponds to the fit obtained using Dynafit software.<sup>9,10</sup>



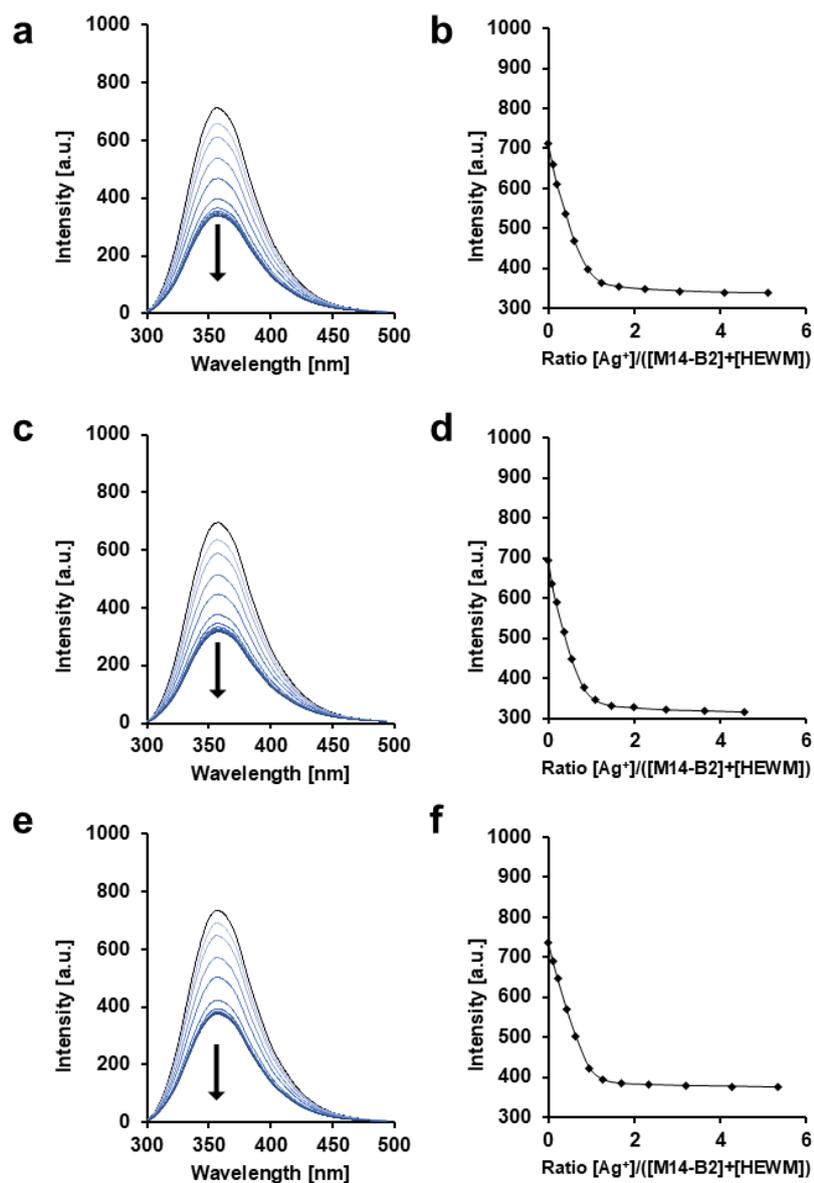
**Fig. S55** HQAMAEAMRRM (M13-B2) / HEWM competition titrations, both at  $2 \cdot 10^{-5}$  M. (g, i & k) Tryptophan fluorescence ( $\lambda_{\text{ex}}$ :280 nm) quench by addition of  $\text{AgNO}_3$  (0 to 5.5 equivalents) to a solution of M13-B2 ( $2 \cdot 10^{-5}$  M) in competition with HEWM probe ( $2 \cdot 10^{-5}$  M), in MOPS buffer (20 equivalents, pH 7.4-7.5) at  $25^\circ\text{C}$ . (h, j & l) Plot of the maxima of fluorescence intensities. The solid line corresponds to the fit obtained using Dynafit software.<sup>9,10</sup>

**Table S15** Determination of the binding constants ( $\log(K_{b-1/b-2})$ ) of HQAMAEAMRRM peptide

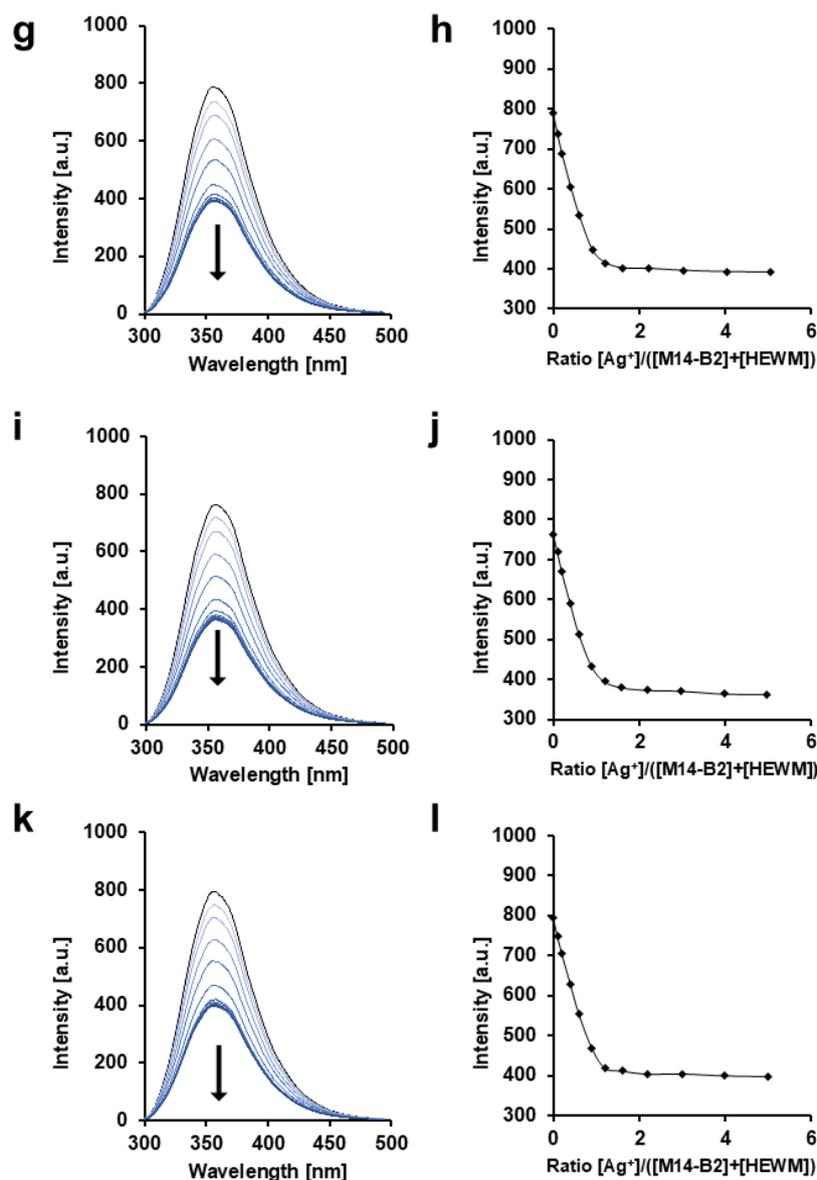
Model	$1 \cdot 10^{-5}$ M <sup>[a]</sup>		$2 \cdot 10^{-5}$ M <sup>[a]</sup>	
HQAMAEAMRRM (M13-B2)	$\log(K_{b-1}) = 6.32 \pm 0.02$	$\log(K_{b-2}) = 4.89 \pm 0.13$	$\log(K_{b-1}) = 6.33 \pm 0.05$	$\log(K_{b-2}) = 5.04 \pm 0.38$
	$\log(K_{b-1}) = 6.24 \pm 0.05$	$\log(K_{b-2}) = 5.10 \pm 0.25$	$\log(K_{b-1}) = 6.16 \pm 0.05$	$\log(K_{b-2}) = 5.12 \pm 0.24$
	$\log(K_{b-1}) = 6.25 \pm 0.03$	$\log(K_{b-2}) = 5.24 \pm 0.13$	$\log(K_{b-1}) = 6.28 \pm 0.01$	$\log(K_{b-2}) = 4.94 \pm 0.07$
Average	$\log(K_{b-1}) = 5.26 \pm 0.06$		$\log(K_{b-2}) = 5.06 \pm 0.13$	

<sup>[a]</sup> The values correspond to the peptide and probe concentrations.

HQAMAEAMKKM (M14-B2)



**Fig. S56** HQAMAEAMKKM (M14-B2) / HEWM competition titrations, both at  $1 \cdot 10^{-5}$  M. (a, c & e) Tryptophan fluorescence ( $\lambda_{\text{ex}}$ :280 nm) quench by addition of  $\text{AgNO}_3$  (0 to 5.5 equivalents) to a solution of M14-B2 ( $1 \cdot 10^{-5}$  M) in competition with HEWM probe ( $1 \cdot 10^{-5}$  M), in MOPS buffer (20 equivalents, pH 7.4-7.5) at 25°C. (b, d & f) Plot of the maxima of fluorescence intensities. The solid line corresponds to the fit obtained using Dynafit software.<sup>9,10</sup>



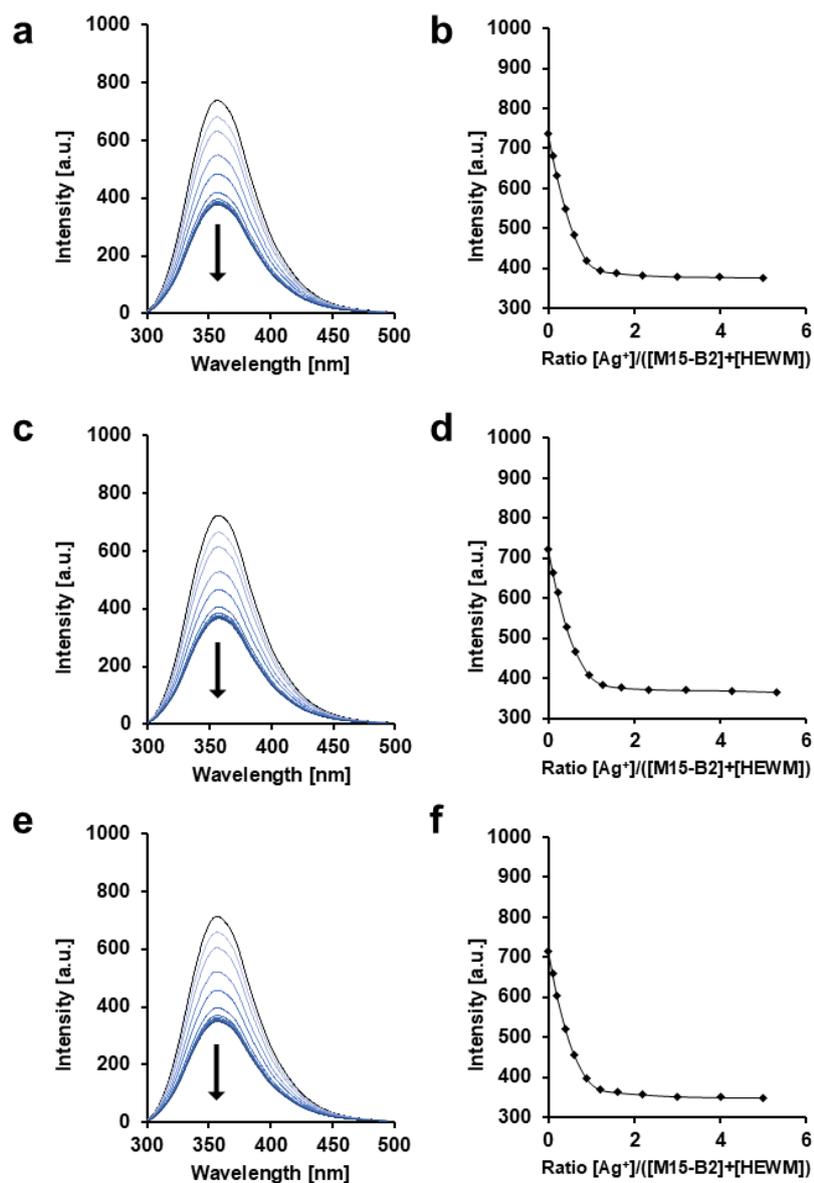
**Fig. S57** HQAMAEAMKKM (M14-B2) / HEWM competition titrations, both at  $2 \cdot 10^{-5}$  M. (g, i & k) Tryptophan fluorescence ( $\lambda_{ex}$ :280 nm) quench by addition of  $\text{AgNO}_3$  (0 to 5.5 equivalents) to a solution of M14-B2 ( $2 \cdot 10^{-5}$  M) in competition with HEWM probe ( $2 \cdot 10^{-5}$  M), in MOPS buffer (20 equivalents, pH 7.4-7.5) at  $25^\circ\text{C}$ . (h, j & l) Plot of the maxima of fluorescence intensities. The solid line corresponds to the fit obtained using Dynafit software.<sup>9,10</sup>

**Table S16** Determination of the binding constants ( $\log(K_{b-1/b-2})$ ) of HQAMAEAMKKM peptide

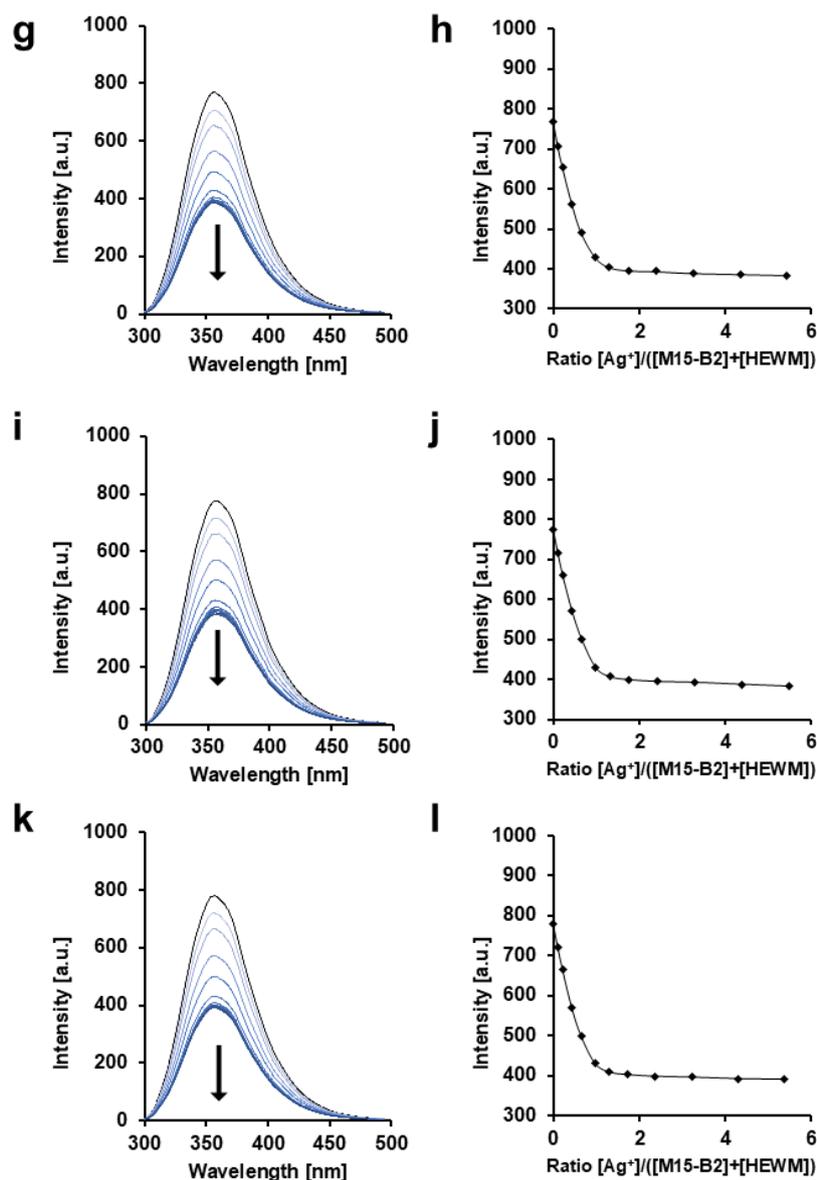
Model	$1 \cdot 10^{-5}$ M <sup>[a]</sup>		$2 \cdot 10^{-5}$ M <sup>[a]</sup>	
HQAMAEAMKKM (M14-B2)	$\log(K_{b-1}) = 6.07 \pm 0.05$	$\log(K_{b-2}) = 5.23 \pm 0.20$	$\log(K_{b-1}) = 6.17 \pm 0.02$	$\log(K_{b-2}) = 4.74 \pm 0.09$
	$\log(K_{b-1}) = 5.93 \pm 0.05$	$\log(K_{b-2}) = 4.94 \pm 0.32$	$\log(K_{b-1}) = 6.21 \pm 0.02$	$\log(K_{b-2}) = 4.88 \pm 0.10$
	$\log(K_{b-1}) = 6.28 \pm 0.01$	$\log(K_{b-2}) = 4.93 \pm 0.06$	$\log(K_{b-1}) = 6.28 \pm 0.02$	$\log(K_{b-2}) = 4.90 \pm 0.10$
Average	$\log(K_{b-1}) = 6.15 \pm 0.13$		$\log(K_{b-2}) = 4.94 \pm 0.16$	

<sup>[a]</sup> The values correspond to the peptide and probe concentrations.

MQAMAEAMRRM (M15-B2)



**Fig. S58** MQAMAEAMRRM (M15-B2) / HEWM competition titrations, both at  $1 \cdot 10^{-5}$  M. (a, c & e) Tryptophan fluorescence ( $\lambda_{\text{ex}}$ :280 nm) quench by addition of  $\text{AgNO}_3$  (0 to 5.5 equivalents) to a solution of M15-B2 ( $1 \cdot 10^{-5}$  M) in competition with HEWM probe ( $1 \cdot 10^{-5}$  M), in MOPS buffer (20 equivalents, pH 7.4-7.5) at 25°C. (b, d & f) Plot of the maxima of fluorescence intensities. The solid line corresponds to the fit obtained using Dynafit software.<sup>9,10</sup>



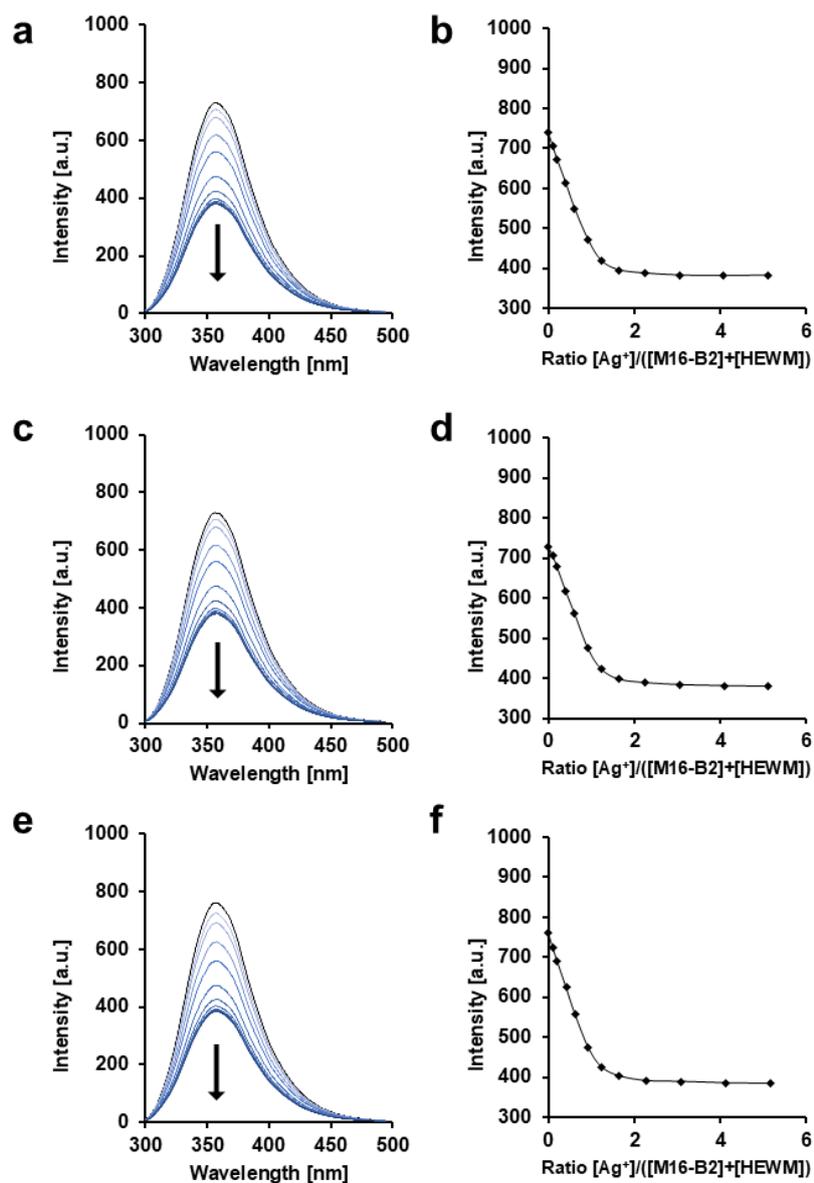
**Fig. S59** MQAMAEAMRRM (M15-B2) / HEWM competition titrations, both at  $2 \cdot 10^{-5}$  M. (g, i & k) Tryptophan fluorescence ( $\lambda_{\text{ex}}$ :280 nm) quench by addition of  $\text{AgNO}_3$  (0 to 5.5 equivalents) to a solution of M15-B2 ( $2 \cdot 10^{-5}$  M) in competition with HEWM probe ( $2 \cdot 10^{-5}$  M), in MOPS buffer (20 equivalents, pH 7.4-7.5) at  $25^\circ\text{C}$ . (h, j & l) Plot of the maxima of fluorescence intensities. The solid line corresponds to the fit obtained using Dynafit software.<sup>9,10</sup>

**Table S17** Determination of the binding constants ( $\log(K_{b-1/b-2})$ ) of MQAMAEAMRRM peptide

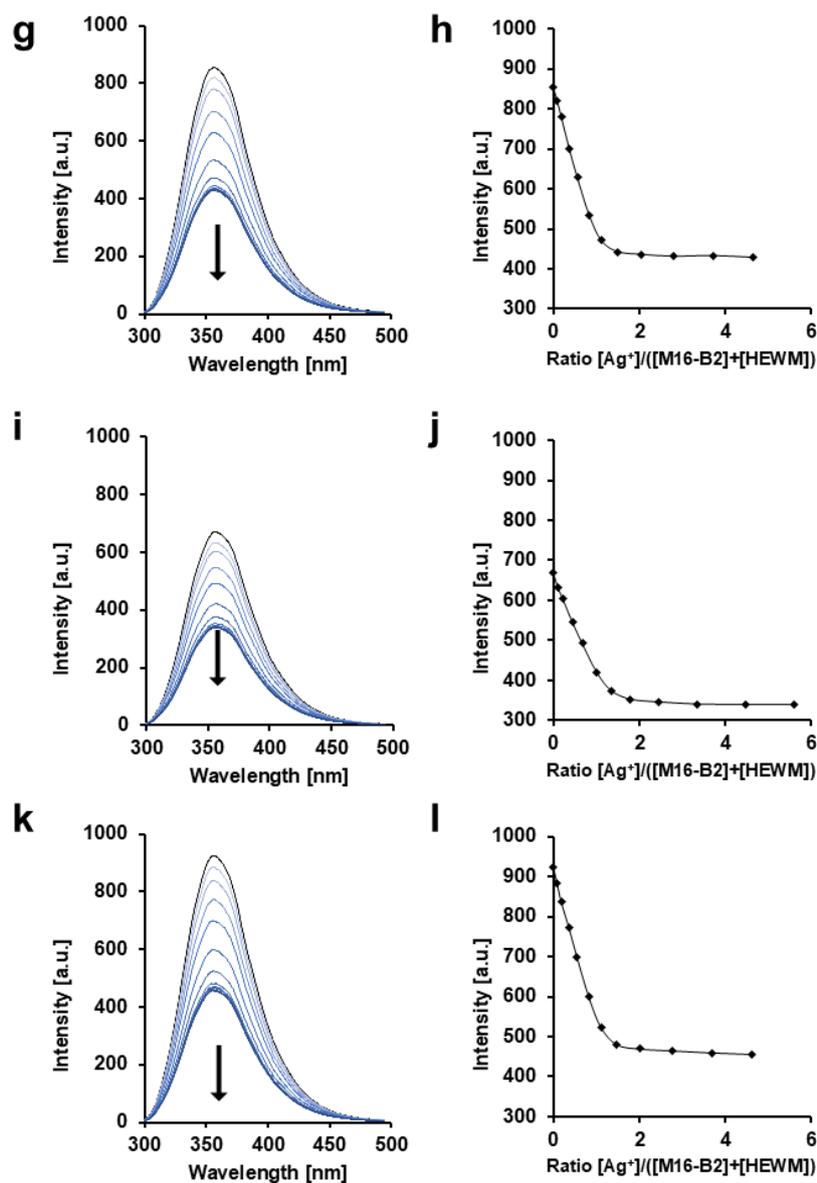
Model	$1 \cdot 10^{-5}$ M <sup>[a]</sup>		$2 \cdot 10^{-5}$ M <sup>[a]</sup>	
MQAMAEAMRRM (M15-B2)	$\log(K_{b-1}) = 5.91 \pm 0.02$	$\log(K_{b-2}) = 4.80 \pm 0.14$	$\log(K_{b-1}) = 5.92 \pm 0.02$	$\log(K_{b-2}) = 5.02 \pm 0.10$
	$\log(K_{b-1}) = 5.90 \pm 0.02$	$\log(K_{b-2}) = 5.09 \pm 0.08$	$\log(K_{b-1}) = 6.02 \pm 0.03$	$\log(K_{b-2}) = 5.00 \pm 0.17$
	$\log(K_{b-1}) = 5.83 \pm 0.03$	$\log(K_{b-2}) = 5.09 \pm 0.14$	$\log(K_{b-1}) = 5.94 \pm 0.01$	$\log(K_{b-2}) = 4.78 \pm 0.06$
Average	$\log(K_{b-1}) = 5.92 \pm 0.06$		$\log(K_{b-2}) = 4.96 \pm 0.14$	

<sup>[a]</sup> The values correspond to the peptide and probe concentrations.

HQQHAEAHQQH (M16-B2)



**Fig. S60** HQQHAEAHQQH (M16-B2) / HEWM competition titrations, both at  $1 \cdot 10^{-5}$  M. (a, c & e) Tryptophan fluorescence ( $\lambda_{\text{ex}}$ :280 nm) quench by addition of  $\text{AgNO}_3$  (0 to 5.5 equivalents) to a solution of M16-B2 ( $1 \cdot 10^{-5}$  M) in competition with HEWM probe ( $1 \cdot 10^{-5}$  M), in MOPS buffer (20 equivalents, pH 7.4-7.5) at 25°C. (b, d & f) Plot of the maxima of fluorescence intensities. The solid line corresponds to the fit obtained using Dynafit software.<sup>9,10</sup>



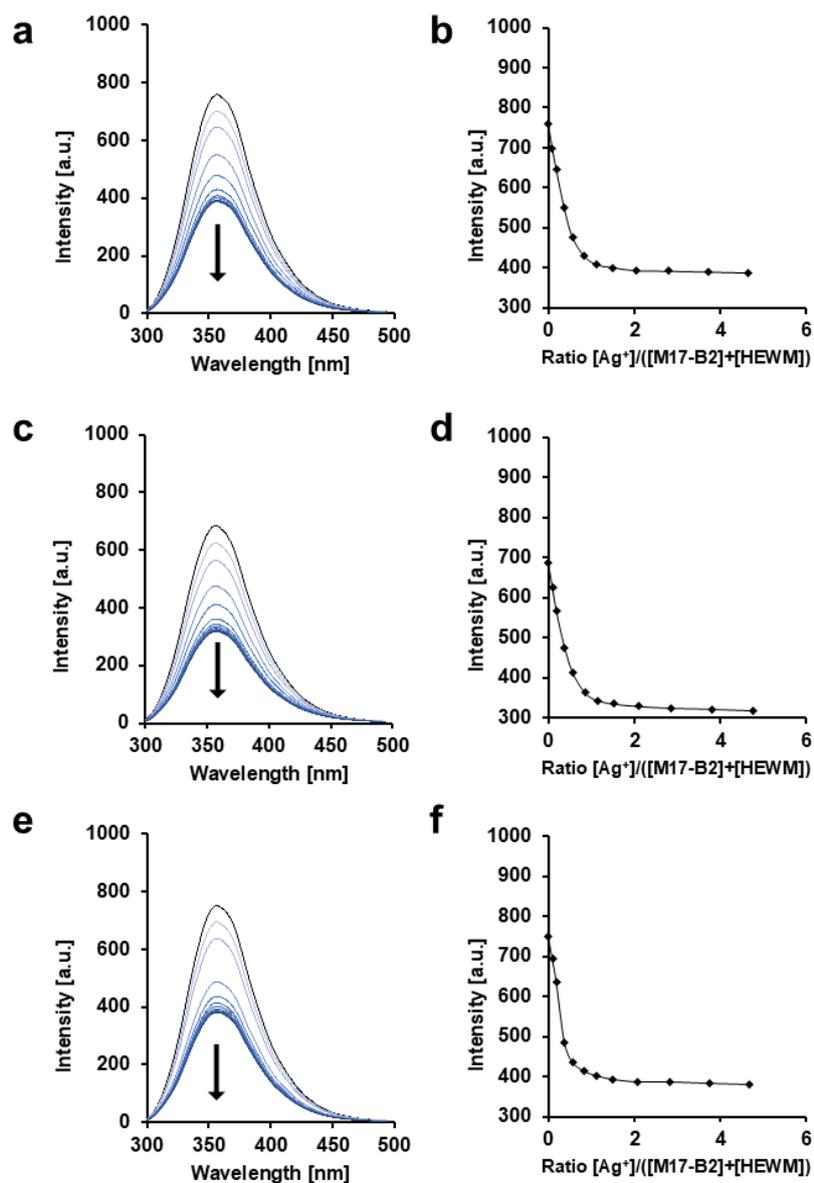
**Fig. S61** HQQHAEAHQQH (M16-B2) / HEWM competition titrations, both at  $2 \cdot 10^{-5}$  M. (g, i & k) Tryptophan fluorescence ( $\lambda_{\text{ex}}$ :280 nm) quench by addition of  $\text{AgNO}_3$  (0 to 5.5 equivalents) to a solution of M16-B2 ( $2 \cdot 10^{-5}$  M) in competition with HEWM probe ( $2 \cdot 10^{-5}$  M), in MOPS buffer (20 equivalents, pH 7.4-7.5) at  $25^\circ\text{C}$ . (h, j & l) Plot of the maxima of fluorescence intensities. The solid line corresponds to the fit obtained using Dynafit software.<sup>9,10</sup>

**Table S18** Determination of the binding constants ( $\log(K_{b-1/b-2})$ ) of HQQHAEAHQQH peptide

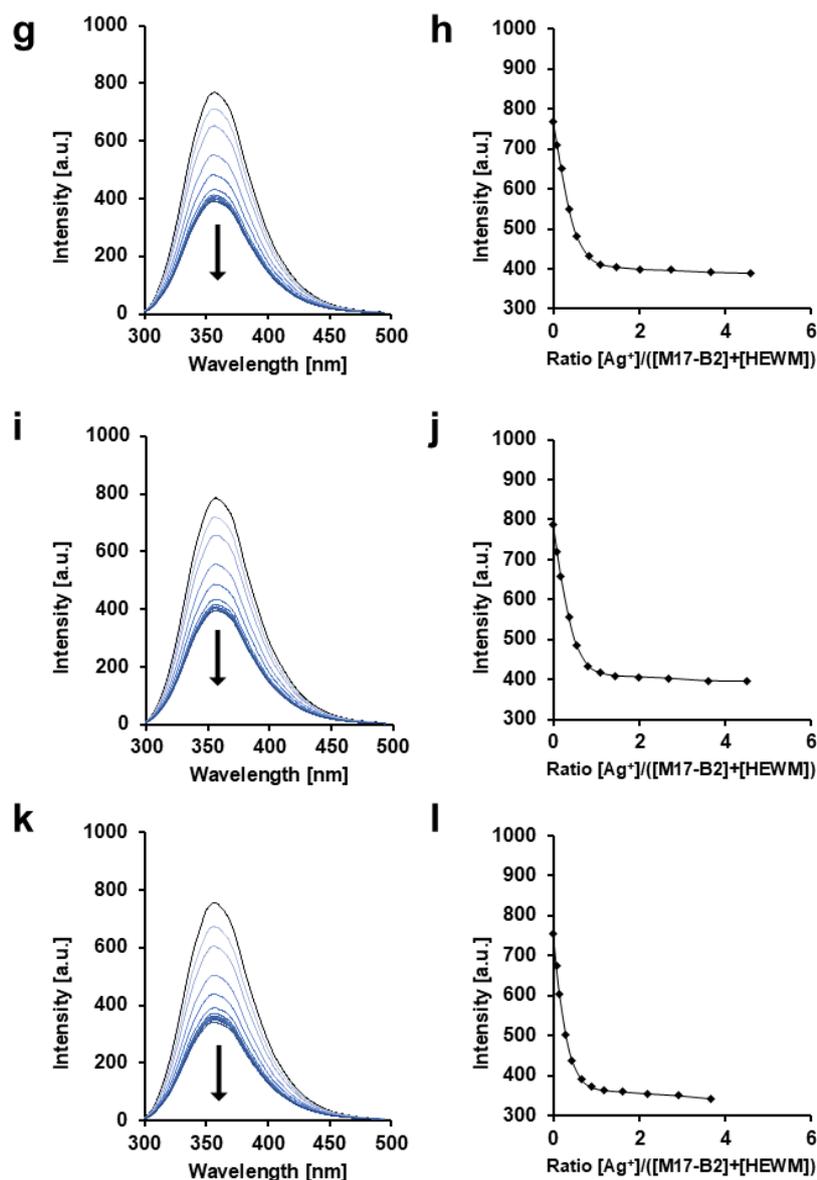
Model	$1 \cdot 10^{-5}$ M <sup>[a]</sup>		$2 \cdot 10^{-5}$ M <sup>[a]</sup>	
HQQHAEAHQQH (M16-B2)	$\log(K_{b-1}) = 6.79 \pm 0.03$	$\log(K_{b-2}) = 5.94 \pm 0.04$	$\log(K_{b-1}) = 6.77 \pm 0.02$	$\log(K_{b-2}) = 6.00 \pm 0.02$
	$\log(K_{b-1}) = 6.53 \pm 0.04$	$\log(K_{b-2}) = 5.92 \pm 0.06$	$\log(K_{b-1}) = 6.74 \pm 0.03$	$\log(K_{b-2}) = 6.05 \pm 0.04$
	$\log(K_{b-1}) = 6.84 \pm 0.03$	$\log(K_{b-2}) = 5.89 \pm 0.03$	$\log(K_{b-1}) = 6.83 \pm 0.02$	$\log(K_{b-2}) = 6.10 \pm 0.03$
Average	$\log(K_{b-1}) = 6.75 \pm 0.11$		$\log(K_{b-2}) = 5.98 \pm 0.08$	

<sup>[a]</sup> The values correspond to the peptide and probe concentrations.

MKKMAEAMKKM (M17-B2)



**Fig. S62** MKKMAEAMKKM (M17-B2) / HEWM competition titrations, both at  $1 \cdot 10^{-5}$  M. (a, c & e) Tryptophan fluorescence ( $\lambda_{\text{ex}}$ :280 nm) quench by addition of  $\text{AgNO}_3$  (0 to 5.5 equivalents) to a solution of M17-B2 ( $1 \cdot 10^{-5}$  M) in competition with HEWM probe ( $1 \cdot 10^{-5}$  M), in MOPS buffer (20 equivalents, pH 7.4-7.5) at 25°C. (b, d & f) Plot of the maxima of fluorescence intensities. The solid line corresponds to the fit obtained using Dynafit software.<sup>9,10</sup>



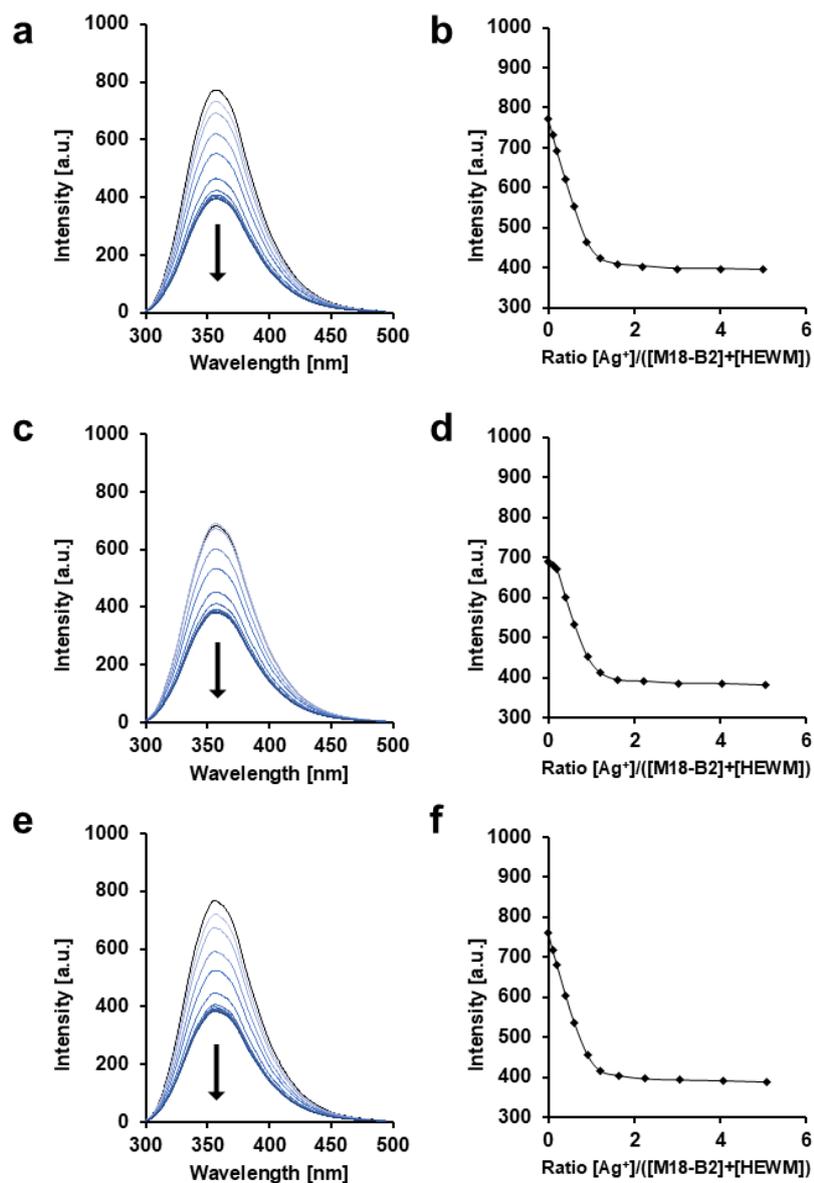
**Fig. S63** MKKMAEAMKKM (M17-B2) / HEWM competition titrations, both at  $2 \cdot 10^{-5}$  M. (g, i & k) Tryptophan fluorescence ( $\lambda_{\text{ex}}$ :280 nm) quench by addition of  $\text{AgNO}_3$  (0 to 5.5 equivalents) to a solution of M17-B2 ( $2 \cdot 10^{-5}$  M) in competition with HEWM probe ( $2 \cdot 10^{-5}$  M), in MOPS buffer (20 equivalents, pH 7.4-7.5) at  $25^\circ\text{C}$ . (h, j & l) Plot of the maxima of fluorescence intensities. The solid line corresponds to the fit obtained using Dynafit software.<sup>9,10</sup>

**Table S19** Determination of the binding constants ( $\log(K_{b-1/b-2})$ ) of MKKMAEAMKKM peptide

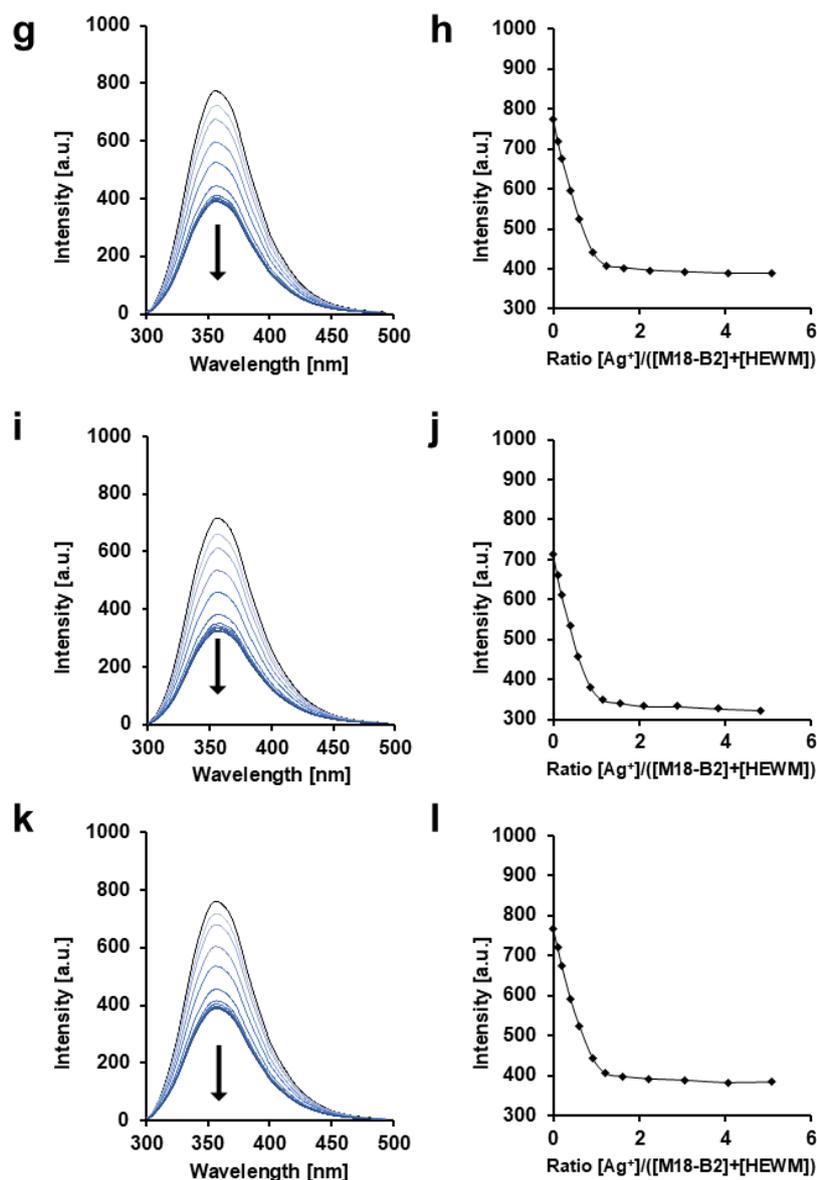
Model	$1 \cdot 10^{-5}$ M <sup>[a]</sup>		$2 \cdot 10^{-5}$ M <sup>[a]</sup>	
MKKMAEAMKKM (M17-B2)	$\log(K_{b-1}) = 5.68 \pm 0.02$	$\log(K_{b-2}) = 4.35 \pm 0.37$	$\log(K_{b-1}) = 5.59 \pm 0.02$	$\log(K_{b-2}) = 4.28 \pm 0.33$
	$\log(K_{b-1}) = 5.70 \pm 0.03$	$\log(K_{b-2}) = 4.94 \pm 0.23$	$\log(K_{b-1}) = 5.49 \pm 0.02$	$\log(K_{b-2}) = 4.46 \pm 0.21$
	$\log(K_{b-1}) = 5.62 \pm 0.06$	$\log(K_{b-2}) = 4.62 \pm 0.38$	$\log(K_{b-1}) = 5.21 \pm 0.09$	$\log(K_{b-2}) = 4.77 \pm 0.40$
Average	$\log(K_{b-1}) = 5.55 \pm 0.18$		$\log(K_{b-2}) = 4.57 \pm 0.24$	

<sup>[a]</sup> The values correspond to the peptide and probe concentrations.

MKKMAEAHQH (M18-B2)



**Fig. S64** MKKMAEAHQH (M18-B2) / HEWM competition titrations, both at  $1 \cdot 10^{-5}$  M. (a, c & e) Tryptophan fluorescence ( $\lambda_{\text{ex}}$ :280 nm) quench by addition of  $\text{AgNO}_3$  (0 to 5.5 equivalents) to a solution of M18-B2 ( $1 \cdot 10^{-5}$  M) in competition with HEWM probe ( $1 \cdot 10^{-5}$  M), in MOPS buffer (20 equivalents, pH 7.4-7.5) at 25°C. (b, d & f) Plot of the maxima of fluorescence intensities. The solid line corresponds to the fit obtained using Dynafit software.<sup>9,10</sup>



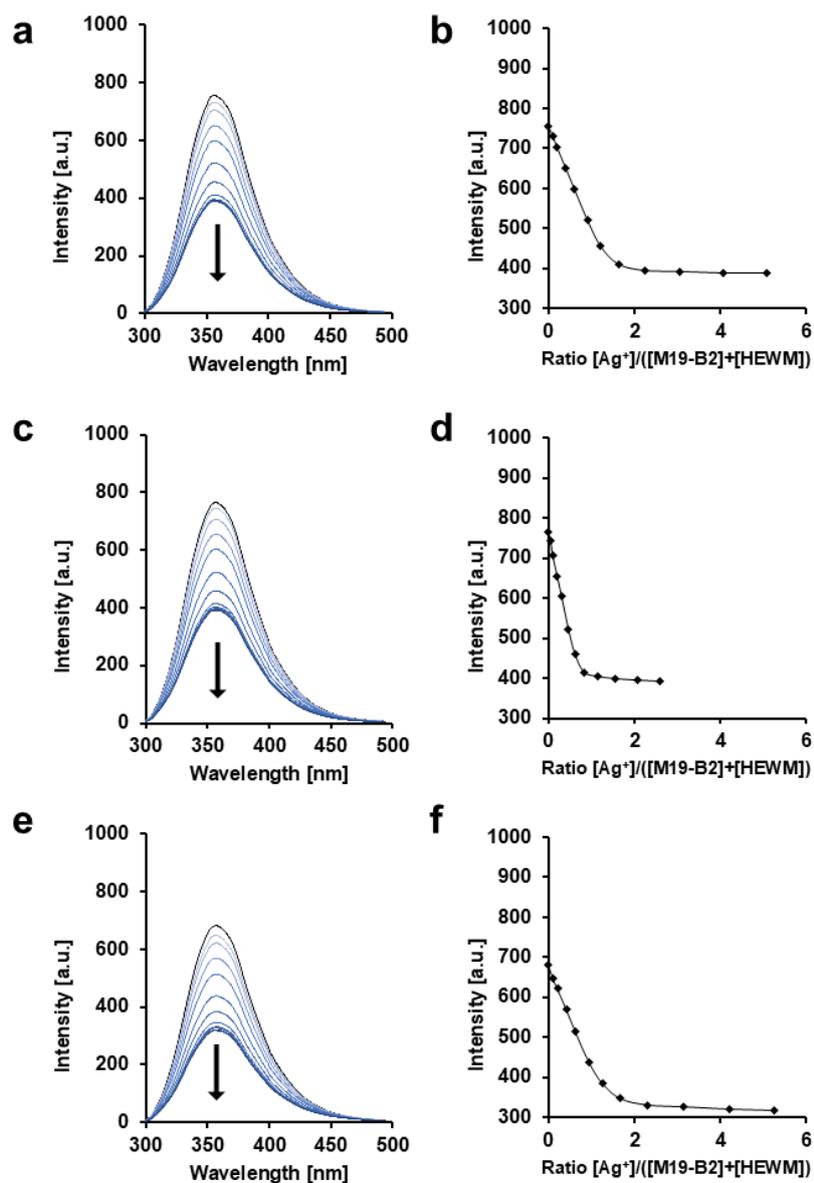
**Fig. S65** MKKMAEAHQH (M18-B2) / HEWM competition titrations, both at  $2 \cdot 10^{-5}$  M. (g, i & k) Tryptophan fluorescence ( $\lambda_{\text{ex}}$ :280 nm) quench by addition of  $\text{AgNO}_3$  (0 to 5.5 equivalents) to a solution of M18-B2 ( $2 \cdot 10^{-5}$  M) in competition with HEWM probe ( $2 \cdot 10^{-5}$  M), in MOPS buffer (20 equivalents, pH 7.4-7.5) at 25°C. (h, j & l) Plot of the maxima of fluorescence intensities. The solid line corresponds to the fit obtained using Dynafit software.<sup>9,10</sup>

**Table S20** Determination of the binding constants ( $\log(K_{b-1/b-2})$ ) of MKKMAEAHQH peptide

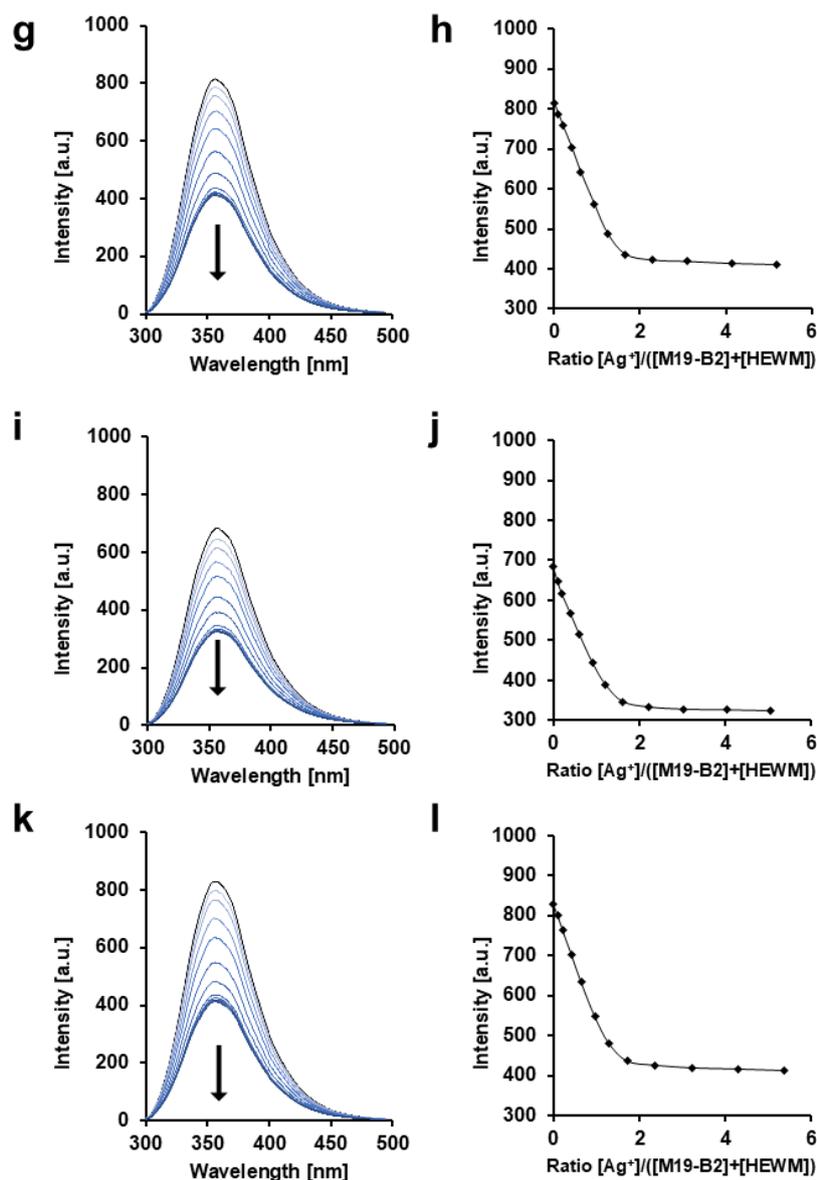
Model	$1 \cdot 10^{-5}$ M <sup>[a]</sup>		$2 \cdot 10^{-5}$ M <sup>[a]</sup>	
MKKMAEAHQH (M18-B2)	$\log(K_{b-1}) = 6.35 \pm 0.01$	$\log(K_{b-2}) = 5.08 \pm 0.06$	$\log(K_{b-1}) = 6.17 \pm 0.02$	$\log(K_{b-2}) = 4.76 \pm 0.15$
	$\log(K_{b-1}) = 6.75 \pm 0.05$	$\log(K_{b-2}) = 4.94 \pm 0.24$	$\log(K_{b-1}) = 6.05 \pm 0.04$	$\log(K_{b-2}) = 4.62 \pm 0.31$
	$\log(K_{b-1}) = 6.31 \pm 0.01$	$\log(K_{b-2}) = 5.06 \pm 0.06$	$\log(K_{b-1}) = 6.18 \pm 0.02$	$\log(K_{b-2}) = 4.93 \pm 0.10$
Average	$\log(K_{b-1}) = 6.30 \pm 0.24$		$\log(K_{b-2}) = 4.90 \pm 0.18$	

<sup>[a]</sup> The values correspond to the peptide and probe concentrations.

HQQHAAAHHQQH (M19-B2)



**Fig. S66** HQQHAAAHHQQH (M19-B2) / HEWM competition titrations, both at  $1 \cdot 10^{-5}$  M. (a, c & e) Tryptophan fluorescence ( $\lambda_{\text{ex}}$ :280 nm) quench by addition of  $\text{AgNO}_3$  (0 to 5.5 equivalents) to a solution of M19-B2 ( $1 \cdot 10^{-5}$  M) in competition with HEWM probe ( $1 \cdot 10^{-5}$  M), in MOPS buffer (20 equivalents, pH 7.4-7.5) at 25°C. (b, d & f) Plot of the maxima of fluorescence intensities. The solid line corresponds to the fit obtained using Dynafit software.<sup>9,10</sup>



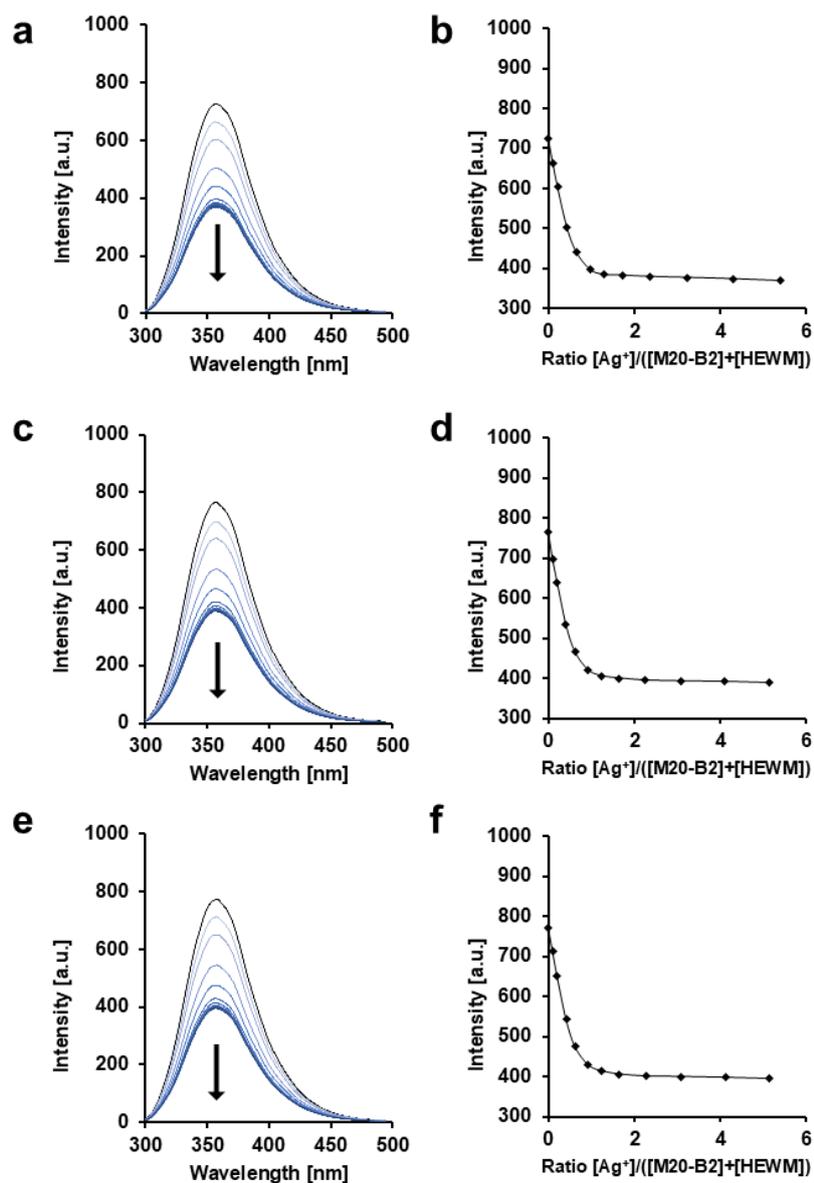
**Fig. S67** HQQHAAAHHQQH (M19-B2) / HEWM competition titrations, both at  $2 \cdot 10^{-5}$  M. (g, i & k) Tryptophan fluorescence ( $\lambda_{\text{ex}}$ :280 nm) quench by addition of  $\text{AgNO}_3$  (0 to 5.5 equivalents) to a solution of M19-B2 ( $2 \cdot 10^{-5}$  M) in competition with HEWM probe ( $2 \cdot 10^{-5}$  M), in MOPS buffer (20 equivalents, pH 7.4-7.5) at  $25^\circ\text{C}$ . (h, j & l) Plot of the maxima of fluorescence intensities. The solid line corresponds to the fit obtained using Dynafit software.<sup>9,10</sup>

**Table S21** Determination of the binding constants ( $\log(K_{b-1/b-2})$ ) of HQQHAAAHHQQH peptide

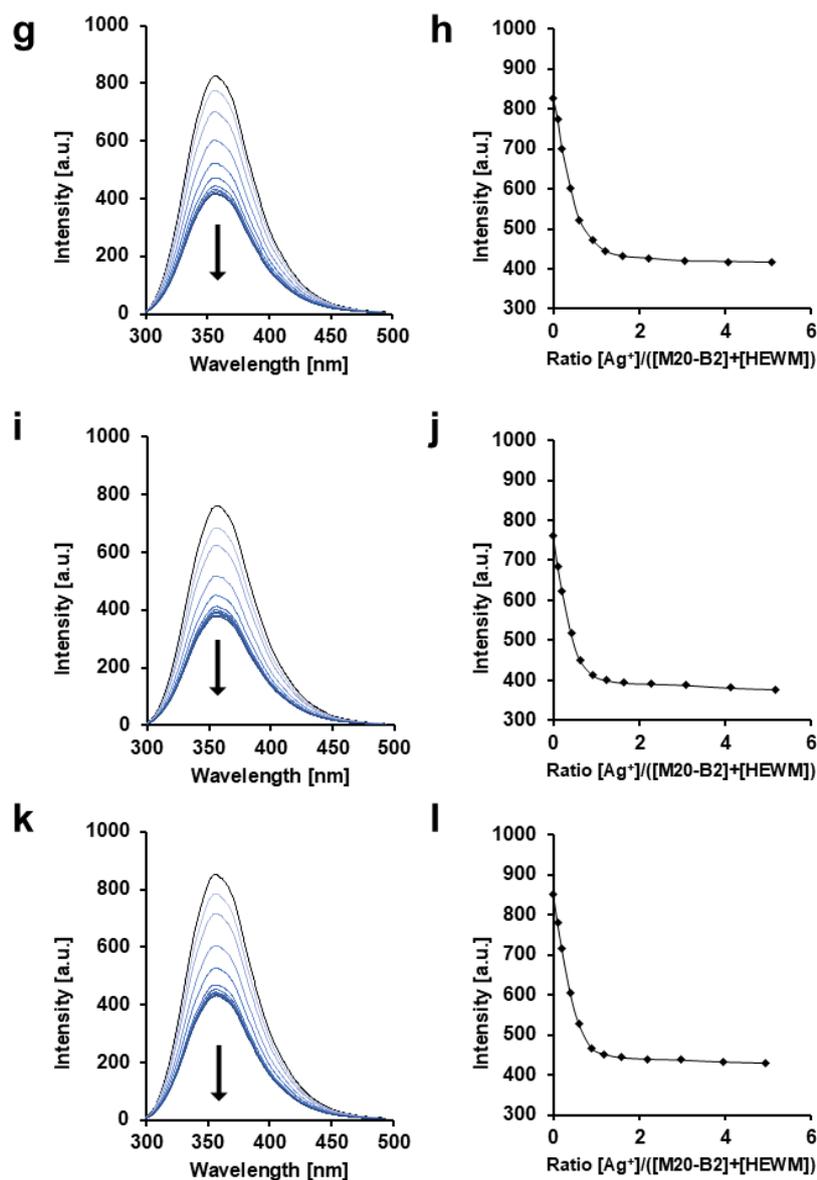
Model	$1 \cdot 10^{-5}$ M <sup>[a]</sup>		$2 \cdot 10^{-5}$ M <sup>[a]</sup>	
HQQHAAAHHQQH (M19-B2)	$\log(K_{b-1}) = 6.72 \pm 0.02$	$\log(K_{b-2}) = 5.88 \pm 0.03$	$\log(K_{b-1}) = 6.71 \pm 0.02$	$\log(K_{b-2}) = 6.01 \pm 0.03$
	$\log(K_{b-1}) = 6.66 \pm 0.06$	$\log(K_{b-2}) = 5.97 \pm 0.08$	$\log(K_{b-1}) = 6.45 \pm 0.05$	$\log(K_{b-2}) = 5.99 \pm 0.08$
	$\log(K_{b-1}) = 6.60 \pm 0.06$	$\log(K_{b-2}) = 5.95 \pm 0.11$	$\log(K_{b-1}) = 6.67 \pm 0.02$	$\log(K_{b-2}) = 5.85 \pm 0.03$
Average	$\log(K_{b-1}) = 6.63 \pm 0.10$		$\log(K_{b-2}) = 5.94 \pm 0.06$	

<sup>[a]</sup> The values correspond to the peptide and probe concentrations.

MKKMAAAMKKM (M20-B2)



**Fig. S68** MKKMAAAMKKM (M20-B2) / HEWM competition titrations, both at  $1 \cdot 10^{-5}$  M. (a, c & e) Tryptophan fluorescence ( $\lambda_{\text{ex}}$ :280 nm) quench by addition of  $\text{AgNO}_3$  (0 to 5.5 equivalents) to a solution of M20-B2 ( $1 \cdot 10^{-5}$  M) in competition with HEWM probe ( $1 \cdot 10^{-5}$  M), in MOPS buffer (20 equivalents, pH 7.4-7.5) at 25°C. (b, d & f) Plot of the maxima of fluorescence intensities. The solid line corresponds to the fit obtained using Dynafit software.<sup>9,10</sup>



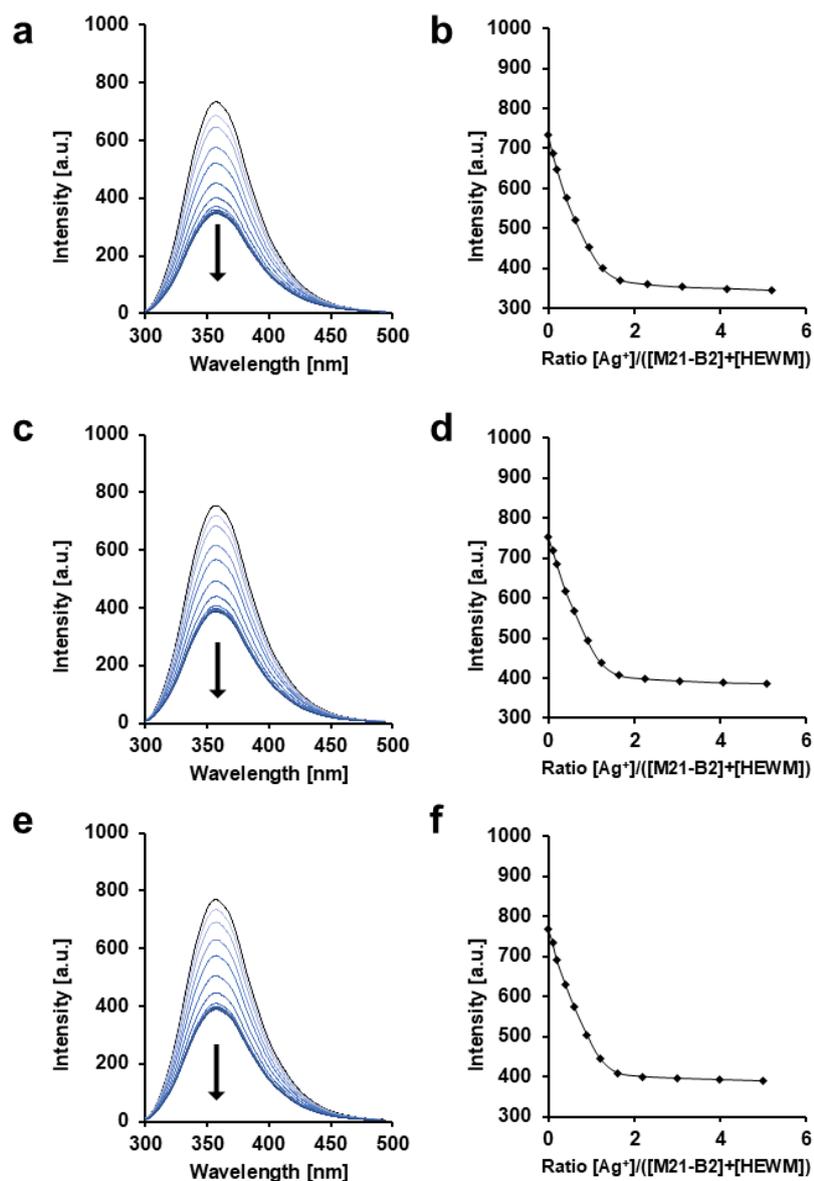
**Fig. S69** MKKMAAAMKKM (M20-B2) / HEWM competition titrations, both at  $2 \cdot 10^{-5}$  M. (g, i & k) Tryptophan fluorescence ( $\lambda_{\text{ex}}$ :280 nm) quench by addition of  $\text{AgNO}_3$  (0 to 5.5 equivalents) to a solution of M20-B2 ( $2 \cdot 10^{-5}$  M) in competition with HEWM probe ( $2 \cdot 10^{-5}$  M), in MOPS buffer (20 equivalents, pH 7.4-7.5) at  $25^\circ\text{C}$ . (h, j & l) Plot of the maxima of fluorescence intensities. The solid line corresponds to the fit obtained using Dynafit software.<sup>9,10</sup>

**Table S22** Determination of the binding constants ( $\log(K_{b-1/b-2})$ ) of MKKMAAAMKKM peptide

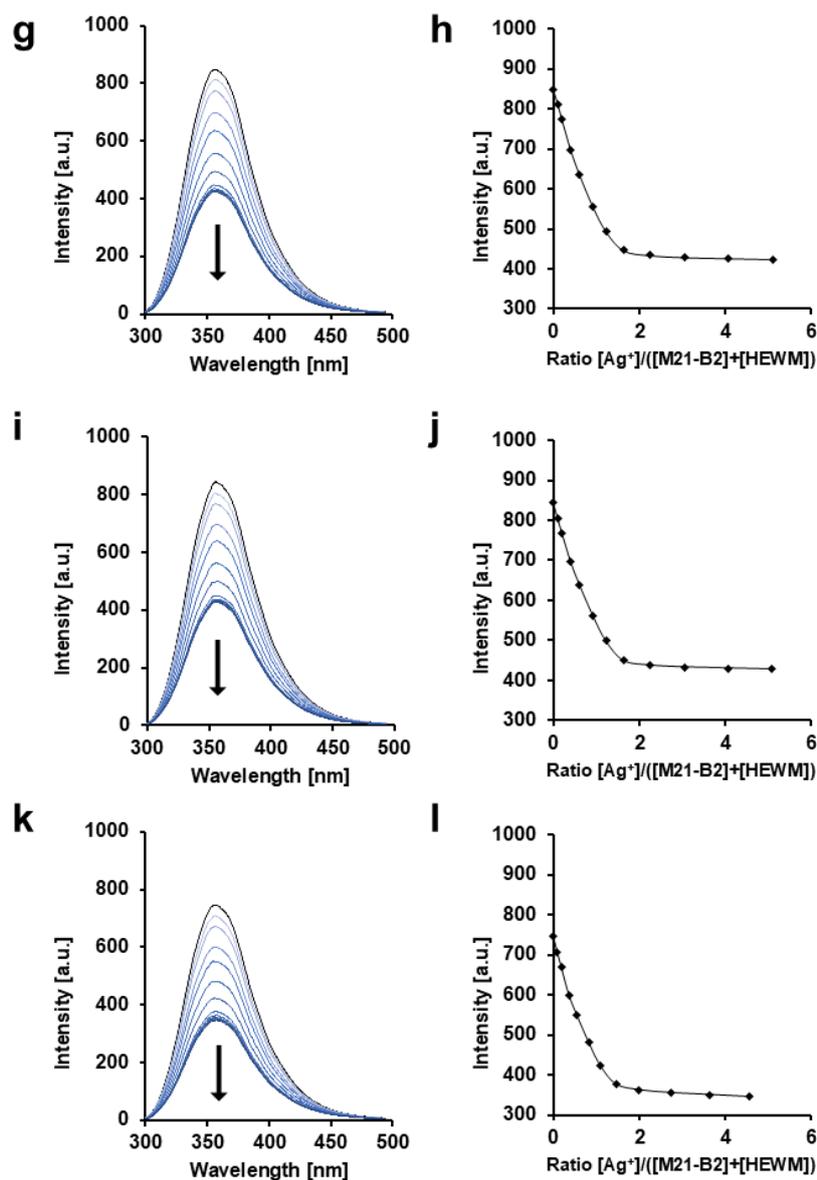
Model	$1 \cdot 10^{-5}$ M <sup>[a]</sup>		$2 \cdot 10^{-5}$ M <sup>[a]</sup>	
MKKMAAAMKKM (M20-B2)	$\log(K_{b-1}) = 5.61 \pm 0.04$	$\log(K_{b-2}) = 4.68 \pm 0.31$	$\log(K_{b-1}) = 5.74 \pm 0.07$	$\log(K_{b-2}) = 4.95 \pm 0.38$
	$\log(K_{b-1}) = 5.56 \pm 0.03$	$\log(K_{b-2}) = 4.71 \pm 0.19$	$\log(K_{b-1}) = 5.40 \pm 0.06$	$\log(K_{b-2}) = 4.85 \pm 0.34$
	$\log(K_{b-1}) = 5.63 \pm 0.03$	$\log(K_{b-2}) = 4.46 \pm 0.36$	$\log(K_{b-1}) = 5.56 \pm 0.02$	$\log(K_{b-2}) = 4.49 \pm 0.15$
Average	$\log(K_{b-1}) = 5.58 \pm 0.11$		$\log(K_{b-2}) = 4.69 \pm 0.19$	

<sup>[a]</sup> The values correspond to the peptide and probe concentrations.

MKKMAAAHQH (M21-B2)



**Fig. S70** MKKMAAAHQH (M21-B2) / HEWM competition titrations, both at  $1 \cdot 10^{-5}$  M. (a, c & e) Tryptophan fluorescence ( $\lambda_{\text{ex}}$ :280 nm) quench by addition of  $\text{AgNO}_3$  (0 to 5.5 equivalents) to a solution of M21-B2 ( $1 \cdot 10^{-5}$  M) in competition with HEWM probe ( $1 \cdot 10^{-5}$  M), in MOPS buffer (20 equivalents, pH 7.4-7.5) at 25°C. (b, d & f) Plot of the maxima of fluorescence intensities. The solid line corresponds to the fit obtained using Dynafit software.<sup>9,10</sup>



**Fig. S71** MKKMAAAHQH (M21-B2) / HEWM competition titrations, both at  $2 \cdot 10^{-5}$  M. (g, i & k) Tryptophan fluorescence ( $\lambda_{\text{ex}}$ :280 nm) quench by addition of  $\text{AgNO}_3$  (0 to 5.5 equivalents) to a solution of M21-B2 ( $2 \cdot 10^{-5}$  M) in competition with HEWM probe ( $2 \cdot 10^{-5}$  M), in MOPS buffer (20 equivalents, pH 7.4-7.5) at  $25^\circ\text{C}$ . (h, j & l) Plot of the maxima of fluorescence intensities. The solid line corresponds to the fit obtained using Dynafit software.<sup>9,10</sup>

**Table S23** Determination of the binding constants ( $\log(K_{b-1/b-2})$ ) of MKKMAAAHQH peptide

Model	$1 \cdot 10^{-5}$ M <sup>[a]</sup>		$2 \cdot 10^{-5}$ M <sup>[a]</sup>	
MKKMAAAHQH (M21-B2)	$\log(K_{b-1}) = 6.24 \pm 0.04$	$\log(K_{b-2}) = 5.90 \pm 0.06$	$\log(K_{b-1}) = 6.44 \pm 0.03$	$\log(K_{b-2}) = 5.80 \pm 0.05$
	$\log(K_{b-1}) = 6.42 \pm 0.04$	$\log(K_{b-2}) = 5.80 \pm 0.08$	$\log(K_{b-1}) = 6.41 \pm 0.02$	$\log(K_{b-2}) = 5.89 \pm 0.03$
	$\log(K_{b-1}) = 6.38 \pm 0.05$	$\log(K_{b-2}) = 5.85 \pm 0.09$	$\log(K_{b-1}) = 6.29 \pm 0.04$	$\log(K_{b-2}) = 5.77 \pm 0.07$
Average	$\log(K_{b-1}) = 6.36 \pm 0.08$		$\log(K_{b-2}) = 5.83 \pm 0.05$	

<sup>[a]</sup> The values correspond to the peptide and probe concentrations.

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