## **Supporting Information**

## Inhibitor-Assisted Synthesis of Silica-Core Microbeads with Pepsin-Imprinted Nanoshells

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Sample	C(1s) (%)	O(1s) (%)	N(1s) (%)	Si(2p) (%)
M1 (R <sub>AT</sub> = 0.40)	39.01	40.50	3.34	17.15
M2 (R <sub>AT</sub> = 0.80)	39.44	37.09	4.65	18.83

Table S1. Surface compositions (in atom%) for various samples determined via XPS



**Fig S1.** Nitrogen adsorption isotherm of silica samples prepared under  $R_{AT} = 0.40$  and  $R_{AT} = 0.80$ .



Fig S2. Synthesis scheme for the immobilization of pepstatin.



Fig. S3. XPS spectrum of M1.



Fig S4. XPS spectrum of Pep-M1.



Fig S5. XPS spectrum of M2.



Fig S6. XPS spectrum of Pep-M2.



Fig S7. SEM Image of (a) AFSS/M2 and (b) Pep-AFSS/M2.



**Fig S8.** SEM image of (a) Pep-M1/pAPBA-MIP, (b) Pep-M1/pAPBA-NIP, (c) Pep-M2/pAPBA-MIP and (d) Pep-M2/pAPBA-NIP. The SEM images of the microbeads after the grafting of pAPBA films onto the surface are shown. Compared to the images of AFFS and Pep-AFFS, these images confirm the formation of core–shell microbeads. The imprinted beads do not reveal a smooth surface anymore. All samples are rather described by a structured and rough surface. In addition, the rough surface of the imprinted microbeads could indicate that imprinted films have larger surface areas to interact with the pepsin.



**Fig S9.** Rebinding profile (n= 4) at MIP and NIP (40 mg). Extraction: at pH 6.0 sodium bicarbonate (0.1 M) containing sodium chloride (0.5 M) for 2 h. Rebinding: at pH 5.0 citrate buffer containing sodium chloride (0.3 M) for 60 min.



**Fig S10.** Elution profiles for pepsin, thermolysin, and trypsin (n= 3) on MIP and on NIP (cartridges containing 40 mg MIP or NIP sorbent, respectively). Binding buffer: 0.1 M citrate, 0.5 M sodium chloride, pH 4.5; washing buffer: 0.5 M sodium chloride; elution buffer: 0.1 M sodium bicarbonate, 0.5 M sodium chloride, pH 6.2.