Imaging of Drug Loading Distributions in Individual Microsphere of Calcium Silicate Hydrate - An X-ray Spectromicroscopic Study

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1. STXM images and XANES analysis of multiple mesoporous CSH microspheres before and after IBU loading:
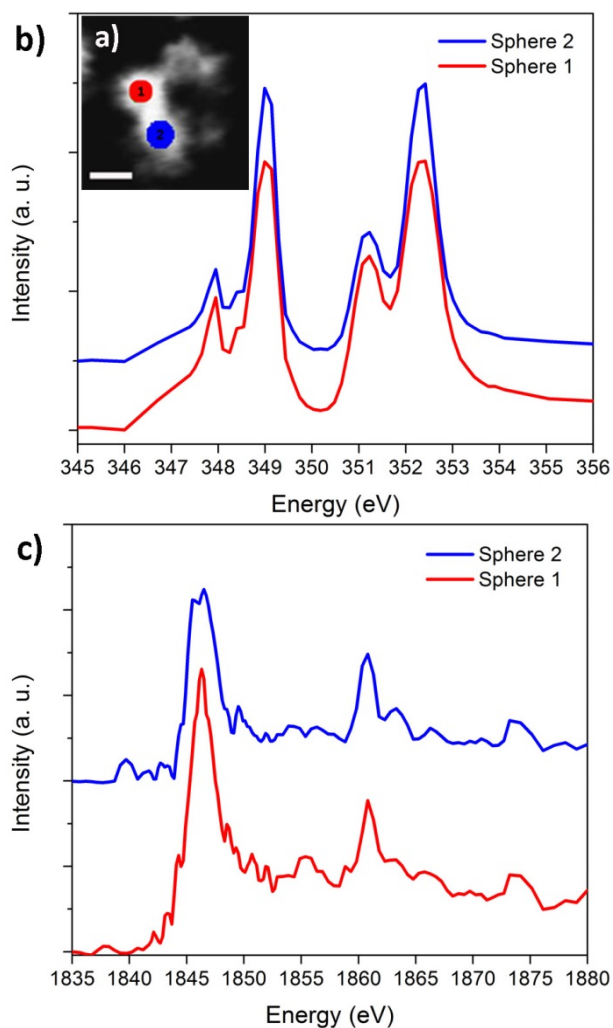

Figure S1 (a) STXM images of CSH microspheres before IBU loading: two ROIs were selected which represented different CSH microspheres; Red: Sphere-1, Blue: Sphere-2. Scale bar in (a) is 1µm. (b,c) XANES spectra from each ROI displayed at the Ca $L_{3,2}$-edge (b) and the Si K-edge (c).
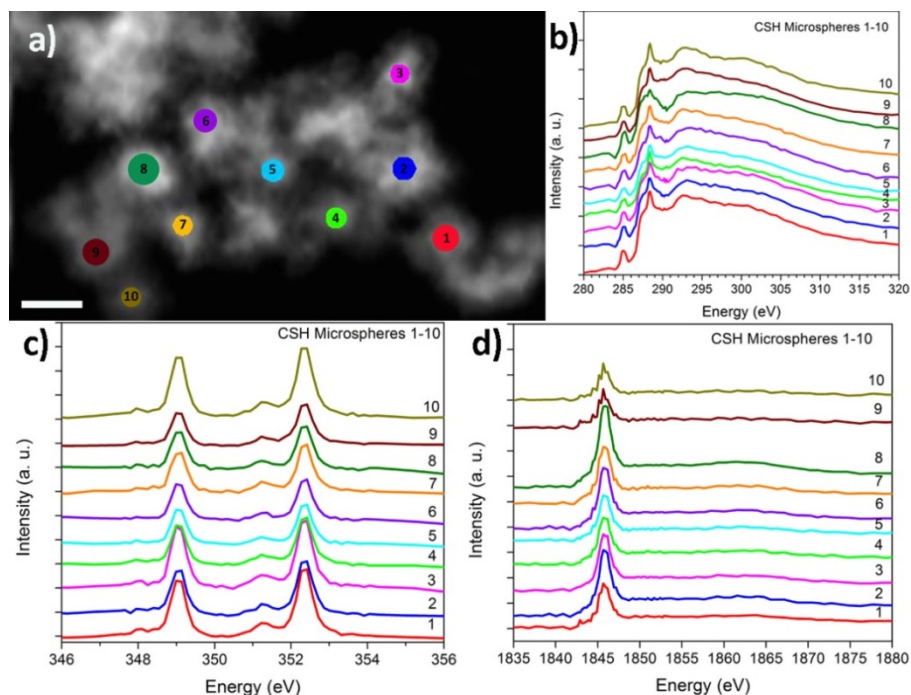
Figure S2 (a) STXM images of CSH microspheres after IBU loading: 10 ROIs were selected which represented different CSH microspheres. Scale bar in (a) is 1µm. XANES spectra from each ROI displayed at (b) the C K-edge, (c) the Ca $L_{3,2}$-edge and (d) the Si K-edge.

2. STXM images and XANES analysis of individual mesoporous CSH microsphere before IBU loading:

Figure S3 shows the STXM images and XANES spectra taken from different regions of interests (ROIs) of individual CSH microsphere before IBU loading at Ca $L_{3,2}$-edge, O K-edge and Si K-edge, respectively. Several interesting features are apparent. First, at the Ca $L_{3,2}$-edge (Figure S3c), no significant changes were observed in the XANES spectra of different ROIs, except that the peaks taken in the thick region (ROI-4) are broaden and the intensity ratios of a_1/a_2 and b_1/b_2 increase a lot due to the thickness effects (saturation phenomenon). At all the edges, we do not observe any significant changes in spectral features in the spectra of different ROIs, indicating that there are no chemical differences in the condensed and the relatively thin areas.
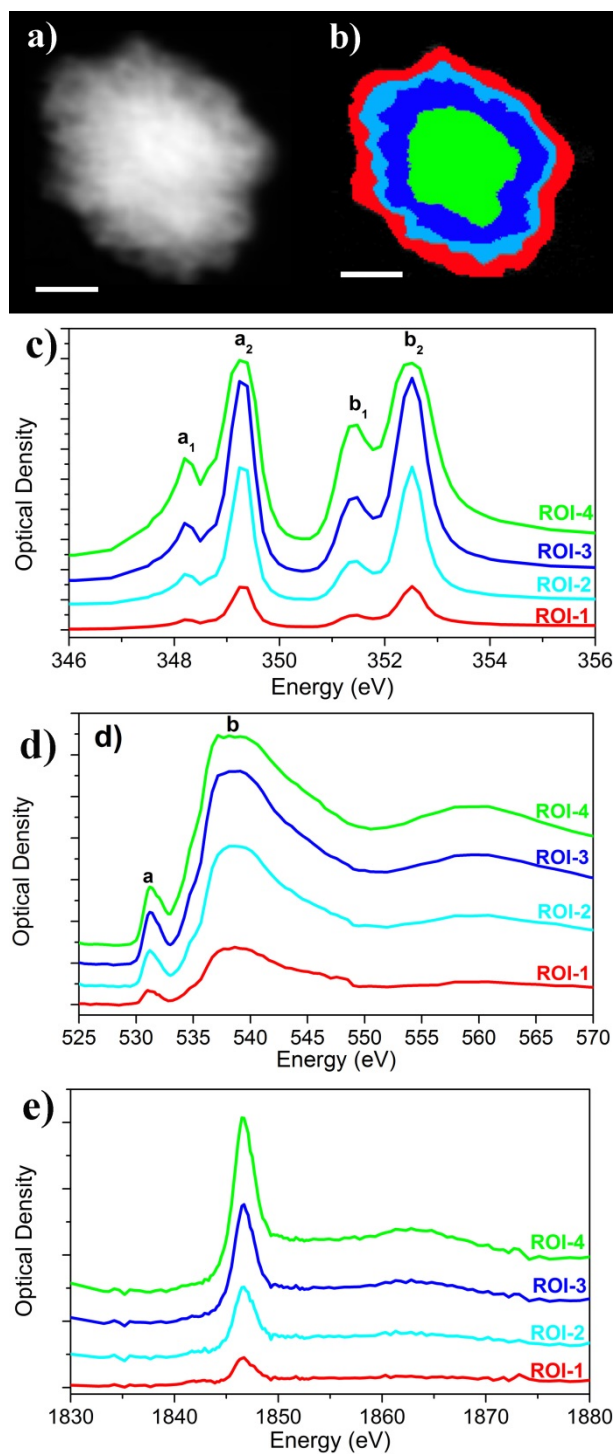
Figure S3 STXM images and XANES spectra of individual CSH microsphere before IBU loading, a) STXM image of individual CSH microsphere (average: 346-1890 eV); b) 4 ROIs taken from the CSH microsphere: Red: ROI-1, Cyan: ROI-2, Blue: ROI-3, Green: ROI-4. Scale bars in a) and b) are 600 nm; c), d) e) are isolated XANES spectra of each ROIs displayed in b) at Ca $L_{3,2}$-edge , O K-edge and Si K-edge, respectively.

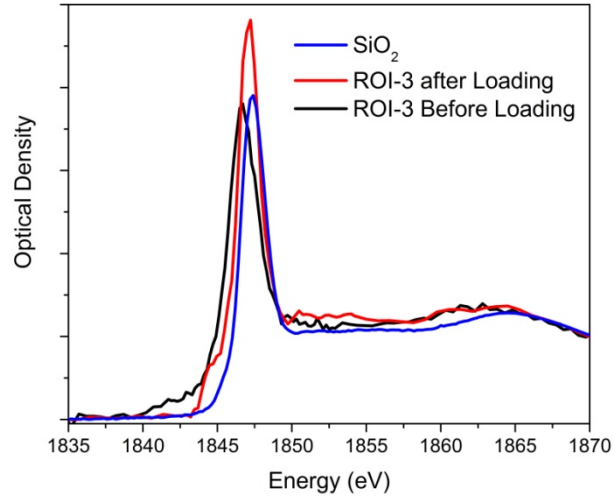## 3. XANES comparison of SiO$_2$ at Si K-edge

Figure S4 XANES spectra comparisons of individual mesoporous CSH microsphere before/after IBU loading and SiO$_2$

4. Thickness modelling of individual CSH microsphere before and after IBU loading

In the data analysis procedure, XANES spectra were obtained by converting the signal to optical density (OD) based on Beer-Lambert Law:

$$OD = -\ln\left(\frac{I}{I_0}\right) = \mu \cdot \rho \cdot t \quad (1)$$

where I_0 and I are the incident and transmitted X-ray photon flux (photons), respectively. μ is the energy dependent mass absorption coefficient (cm^2/g), ρ is the density (g/cm^3) of the material, and t is the sample thickness (nm). Then these spectra were converted to absolute linear absorbance scales (optical density per nm thickness sample). The elemental linear X-ray absorption, which neglects interactions such as bonding among the atoms, is calculated by aXis2000 using equation (1) and (2):

$$\mu = \frac{N_A}{MM}\sum_i x_i \cdot \sigma_{ai} \quad (2)$$

where N_A is the Avogadro's number, MM is the molecular weight of a compound containing x_i atoms of type i, σ_{ai} is the atomic photo-absorption cross section (cm^2/atom) for type i atom. Then, the thickness was obtained by comparing the OD of each pixel in a STXM image and reference spectra. In this study, silicon and carbon reference spectra were obtained by fitting the original XANES spectra to match its calculated elemental linear X-ray absorption profile: calcium silicate (CaSiO$_3$: density = 2.900 g/cm^3, and thickness = 1 nm, ibuprofen (C$_{12}$H$_{18}$O$_2$: density = 1.030 g/cm^3, and thickness = 1 nm) in the pre-edge and continuum.
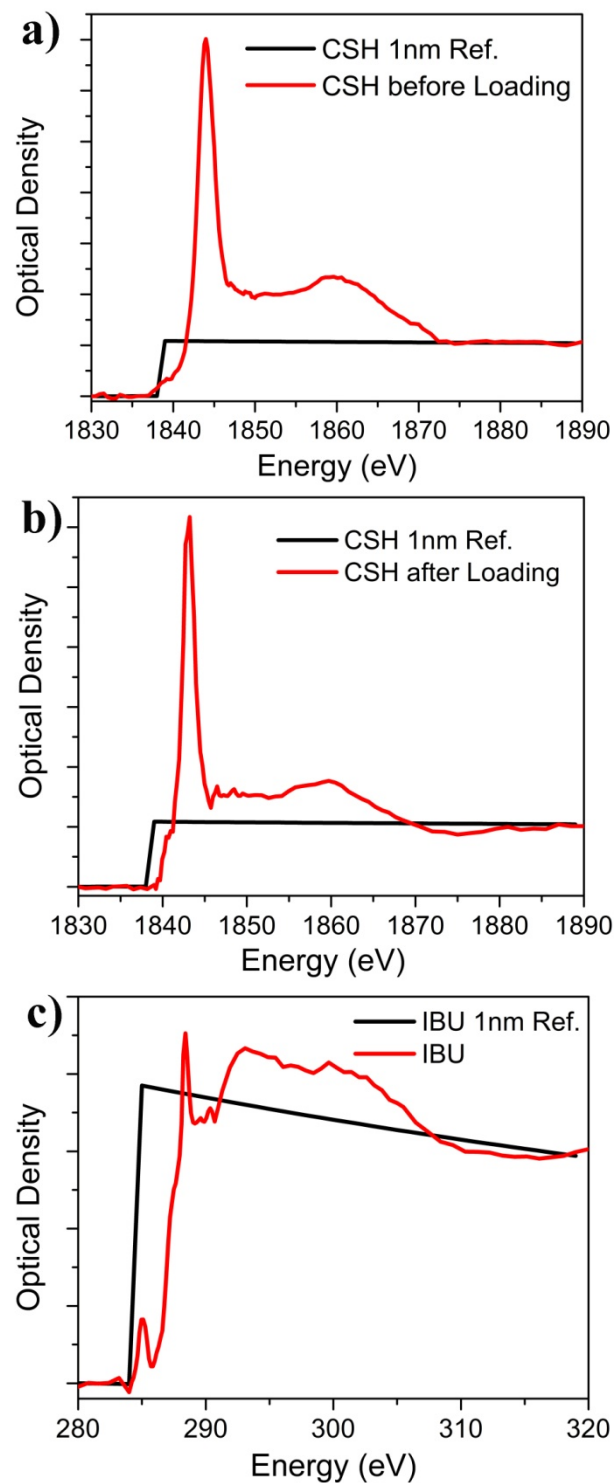
Figure S5 Reference spectra and elemental linear X-ray absorption profiles of CSH and IBU. a) and b) CSH Si K-edge before and after IBU loading (black profile: optical density spectrum of 1 nm thickness; red profile: elemental linear X-ray absorption profile based on formula $CaSiO_3$); c) IBU C K-edge (black profile: optical density spectrum of 1 nm thickness; red profile: elemental linear X-ray absorption profile based on formula $C_{12}H_{18}O_2$)

In Figure S6, the stripes across the microsphere which are due to the beam vibration during the STXM measurement are not real structures of individual CSH microsphere. The thickness was obtained from stack fitting with the quantitatively scaled reference spectra of 1 nm thickness. The thickness of the condensed core of the CSH microsphere is determined to be about 235 nm, while the thickness of the outer surface area is around 24 nm (± 10 %). This result confirms that under the ultrasonic irradiation, the CSH first forms a condensed core by stacking up nanosheets as building blocks, then more nanosheets aggregate and self-assemble to bird-nest like 3D hierachical networks with mesopores and macropores.
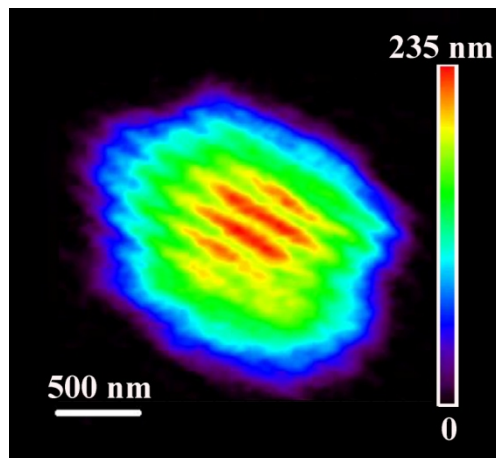

Figure S6 Thickness distribution of individual CSH microsphere at the Si K-edge; the vertical color bar illustrates the thickness of the microsphere.