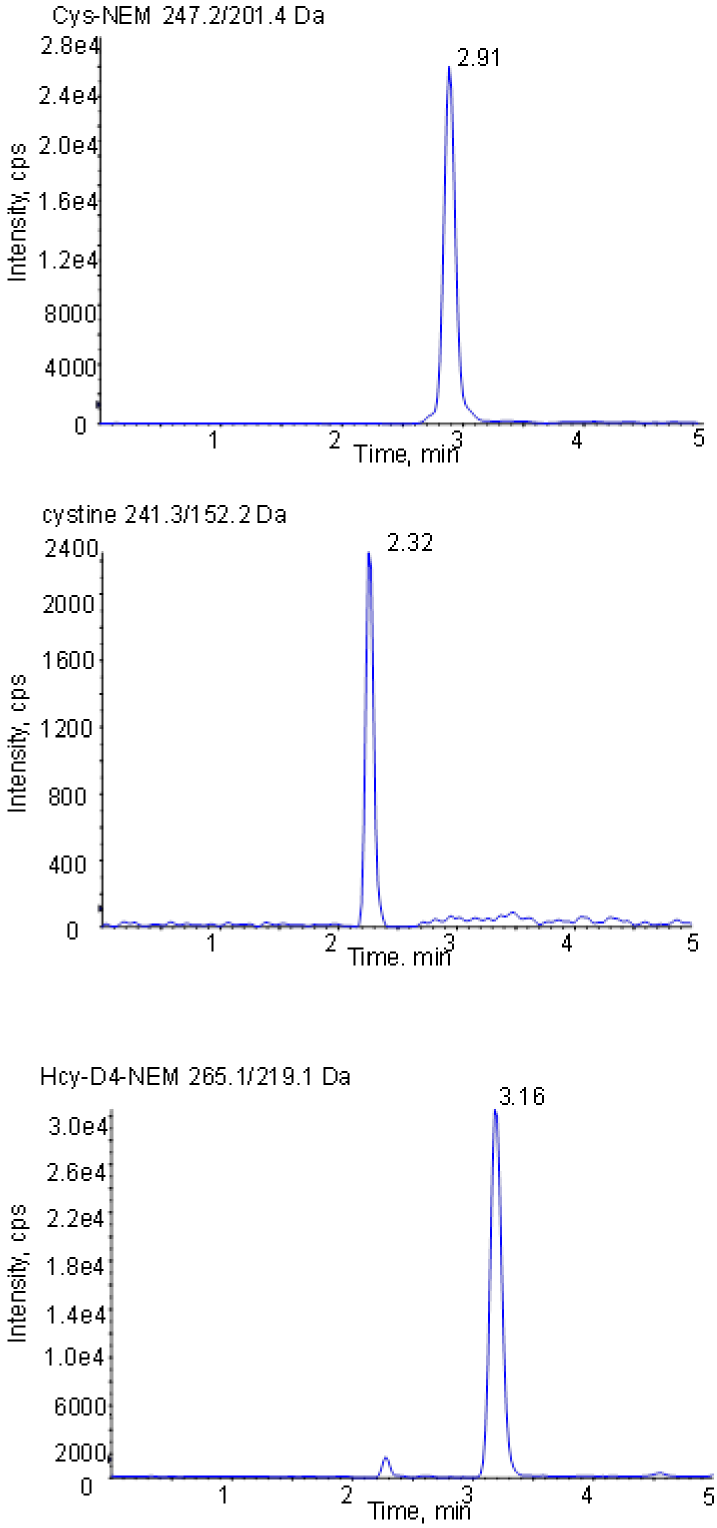
Supplementary Materials 1. Results of nonspecific binding for the analysis of Hcy-NEM, Cys-NEM, cystine and homocystine at three concentrations in PBS by HFCF-UF with polysulfone and polyacrylonitrile hollow fiber (*n*=5)

Analyte	Standard (μmol·L^{-1})	Obtained[1](μmol·L^{-1}) (mean±SD)	Obtained/Standard[1] (%, mean±SD	Obtained[2](μmol·L^{-1}) (mean±SD)	Obtained/Standar[2] (%, mean±SD)
Hcy-NEM	0.1	0.113±0.004	106±1.69	0.104±0.002	104±2.59
	1	0.995±0.118	95.5±6.41	1.06±0.042	105±4.20
	4	3.91±0.056	95.6±2.12	3.79±0.082	94.8±2.05
Cys-NEM	0.1	0.0906±0.004	89.3±2.26	0.106±0.008	114±5.04
	1	0.974±0.047	93.1±3.50	0.991±0.042	101±8.83
	4	3.49±0.112	94.3±3.31	4.02±0.100	109±2.71
cystine	0.04	0.0427±0.112	107±13.11	0.0413±0.003	103±8.23
	0.4	0.374±0.037	96.3±8.34	0.383±0.026	95.8±6.88
	1.6	1.71±0.048	97.9±1.53	1.59±0.067	99.1±4.21
homocystine	0.004	0.00423±0.164×10^{-3}	106±4.10	0.00401±0.329×10^{-3}	100±8.21
	0.04	0.0450±0.003	108±7.79	0.0381±0.001	95.3±2.97
	0.32	0.367±0.008	99.1±2.34	0.300±0.007	93.6±2.14
Hcy-D4-NEM	3.6	—	89.4±11.85	—	94.4±7.68

* 1 represent polysulfone hollow fiber and 2 is polyacrylonitrile hollow fiber



Supplementary materials 2: Representative MRM chromatograms of Cys-NEM, cystine, and internal standard in rat plasma sample.

Supplementary Material 3. Results of stability for the analysis of Hcy-NEM, Cys-NEM, cystine and homocystine in QC samples at three concentrations (*n*=3)

Analyte	Added concentration (μmol·L-1)	Room temperature, 26°C, 12 h		Freezing at -40 °C for 14 days		Freeze-thaw three cycles		After processing, 15°C, 24 h	
		Measured (μmol·L-1/ mean±SD)	RSD (%)	Measured (μmol·L-1/ mean±SD)	RSD (%)	Measured (μmol·L-1/ mean±SD)	RSD (%)	Measured (μmol·L-1/ mean±SD)	RSD (%)
Hcy-NEM	0.1	0.105±0.003	3.0	0.105±0.008	7.6	0.112±0.004	3.5	0.108±0.001	0.8
	1	1.02±0.079	7.8	1.01±0.033	3.3	1.01±0.026	2.5	1.07±0.008	0.8
	4	4.10±0.057	1.4	3.83±0.139	3.6	3.66±0.014	0.4	4.07±0.024	0.6
Cys-NEM	0.1	0.103±0.004	3.5	0.096±0.008	8.2	0.099±0.004	4.2	0.102±0.004	4.8
	1	1.04±0.022	2.1	0.977±0.048	5.0	0.891±0.011	1.2	1.06±0.012	1.2
	4	3.76±0.119	3.2	3.77±0.044	1.2	3.47±0.138	4.0	3.68±0.158	4.3
cystine	0.04	0.042±0.004	13.1	0.043±0.0003	0.7	0.042±0.005	12.3	0.044±0.005	11.1
	0.4	0.402±0.007	1.7	0.421±0.008	1.9	0.364±0.005	2.6	0.390±0.015	3.8
	1.6	1.65±0.036	2.2	1.69±0.039	2.3	1.56±0.051	3.3	1.71±0.146	8.5
homocystine	0.008	0.0088±0.0003	3.8	0.0089±0.0004	4.1	0.0090±0.0005	5.6	0.0090±0.0008	8.9
	0.08	0.0908±0.0025	2.8	0.0837±0.0078	9.4	0.0731±0.0047	6.5	0.0862±0.0078	9.0
	0.32	0.319±0.009	2.9	0.292±0.015	5.2	0.302±0.008	2.8	0.317±0.010	3.4

Supplementary Material 4

The formula derivation process was shown in detail, as below:

If we hypothesis the concentrations of Cys (C_{cys}) and Cyss (C_{cyss}) are both ten times of the concentrations of Hcy (C_{Hcy}) and HHcy (C_{HHcy}). $E0_{\text{HHcy/Hcy}}$ and $E0_{\text{Cyss/Cys}}$ are the standard potential of Hcy/HHcy and Cys/Cyss, respectively.

Before the REDOX reaction, the potential of the REDOX reaction pair of Hcy/HHcy and Cys/Cyss are $E1_{\text{HHcy/Hcy}}$ and $E1_{\text{Cyss/Cys}}$.

$$E1_{HHcy/Hcy} = E0_{HHcy/Hcy} + \frac{RT}{nF} ln \frac{c_{HHcy}}{c_{Hcy}} \quad (2)$$

$$E1_{Cyss/Cys} = E0_{Cyss/Cys} + \frac{RT}{nF} ln \frac{c_{Cyss}}{c_{Cys}} \quad (3)$$

After peroxide [O] is reacting with Hcy and Cys, the potential of the REDOX reaction pair of Hcy/HHcy and Cys/Cyss are $E2_{\text{HHcy/Hcy}}$ and $E2_{\text{Cyss/Cys}}$.

$$E2_{HHcy/Hcy} = E0_{HHcy/Hcy} + \frac{RT}{nF} ln \frac{c'_{HHcy}}{c'_{Hcy}} \quad (4)$$

$$E2_{Cyss/Cys} = E0_{Cyss/Cys} + \frac{RT}{nF} ln \frac{c'_{Cyss}}{c'_{Cys}} \quad (5)$$

Since the reactions is according to the concentration ratio of 2:1, as below:

$$2Hcy + [O] = HHcy + \mathrm{H_2O} \quad (6)$$

If there is $\frac{1}{2}C_{Hcy}$ reacted [O] to generate $\frac{1}{4}C_{HHcy}$, After the reactions, the concentrations of Hcy and HHcy are $C'_{Hcy}$and C'_{HHcy}, then:

$$C'_{Hcy} = \frac{1}{2}C_{Hcy} \quad (7)$$

$$C'_{HHcy} = C_{HHcy} + \frac{1}{4}C_{HHcy} = \frac{5}{4}C_{HHcy} \quad (8)$$

The Equation 4 could be show as:

$$E2_{HHcy/Hcy} = E0_{HHcy/Hcy} + \frac{RT}{nF} ln \frac{\frac{5}{4}C_{HHcy}}{\frac{1}{2}C_{Hcy}} = E0_{HHcy/Hcy} + \frac{RT}{nF} ln \frac{5C_{HHcy}}{2C_{Hcy}} \quad (9)$$

The same goes for Cys/Cyss in the Equation 5:

$$E2_{Cyss/Cys} = E0_{Cyss/Cys} + \frac{RT}{nF} ln \frac{C_{Cyss} + \frac{1}{4}C_{HHcy}}{C_{cys} - \frac{1}{2}C_{Hcy}} \quad (10)$$

From Table 6, we hypothesis that:

$$C_{Cyss} = 10C_{HHcy}; \quad C_{Cys} = 10C_{Hcy} \quad (11)$$

Then the Equation 10 could be show as：

$$E2_{Cyss/Cys} = E0_{Cyss/Cys} + \frac{RT}{nF} ln \frac{10C_{HHcy} + \frac{1}{4}C_{HHcy}}{10C_{Hcy} - \frac{1}{2}C_{Hcy}}$$

$$= E0_{Cyss/Cys} + \frac{RT}{nF} ln \frac{41C_{HHcy}}{38C_{Hcy}} \quad (12)$$

The difference of $E_{HHcy/Hcy}$ after and before the reaction is $\Delta E_{HHcy/Hcy}$:

$$\Delta E_{HHcy/Hcy} = E2_{HHcy/Hcy} - E1_{HHcy/Hcy}$$

$$\Delta E_{HHcy/Hcy} = E0_{HHcy/Hcy} + \frac{RT}{nF} ln \frac{5C_{HHcy}}{2C_{Hcy}} - E0_{HHcy/Hcy} - \frac{RT}{nF} ln \frac{C_{HHcy}}{C_{Hcy}} = \frac{RT}{nF} ln \frac{5}{2}$$

(13)

The difference of $E_{Cyss/Cys}$ before and after the reactionis $\Delta E_{Cyss/Cys}$:

$$\Delta E_{Cyss/Cys} = E2_{Cyss/Cys} - E1_{Cyss/Cys}$$

$$\Delta E_{Cyss/Cys} = E0_{Cyss/Cys} + \frac{RT}{nF} ln \frac{41C_{HHcy}}{38C_{Hcy}} - E0_{Cyss/Cys} - \frac{RT}{nF} ln \frac{C_{Cyss}}{C_{Cys}}$$

$$= \frac{RT}{nF} ln \frac{41C_{HHcy}}{38C_{Hcy}} - \frac{RT}{nF} ln \frac{10C_{HHcy}}{10C_{Hcy}} = \frac{RT}{nF} ln \frac{41}{38} \quad (14)$$

The ratio of Equation 13 to Equation 14 is *R:*

$$R = \frac{\Delta E_{HHcy/Hcy}}{\Delta E_{Cyss/Cys}} = \frac{\frac{RT}{nF} ln \frac{5}{2}}{\frac{RT}{nF} ln \frac{41}{38}} = 12.06 \quad (15)$$