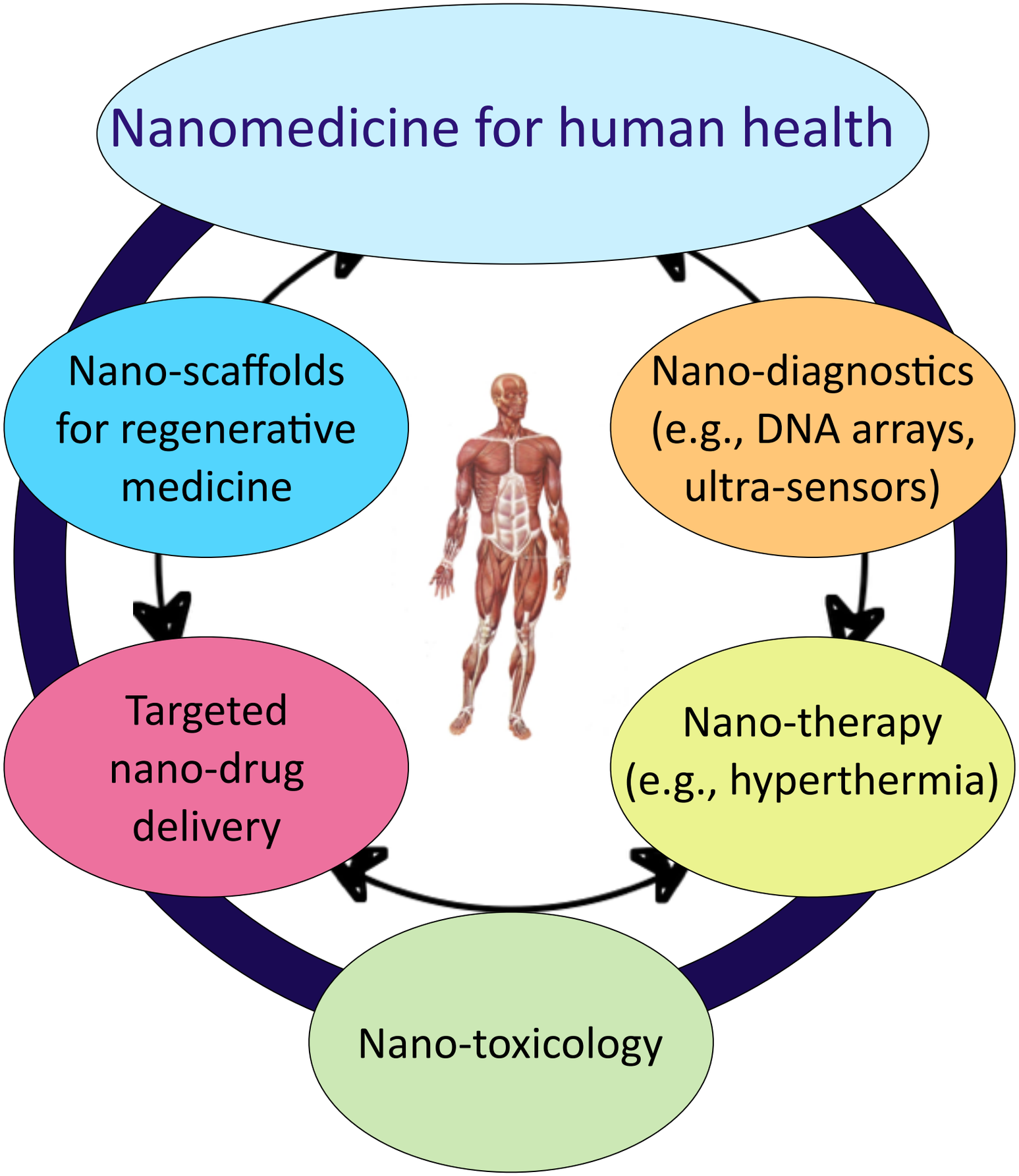
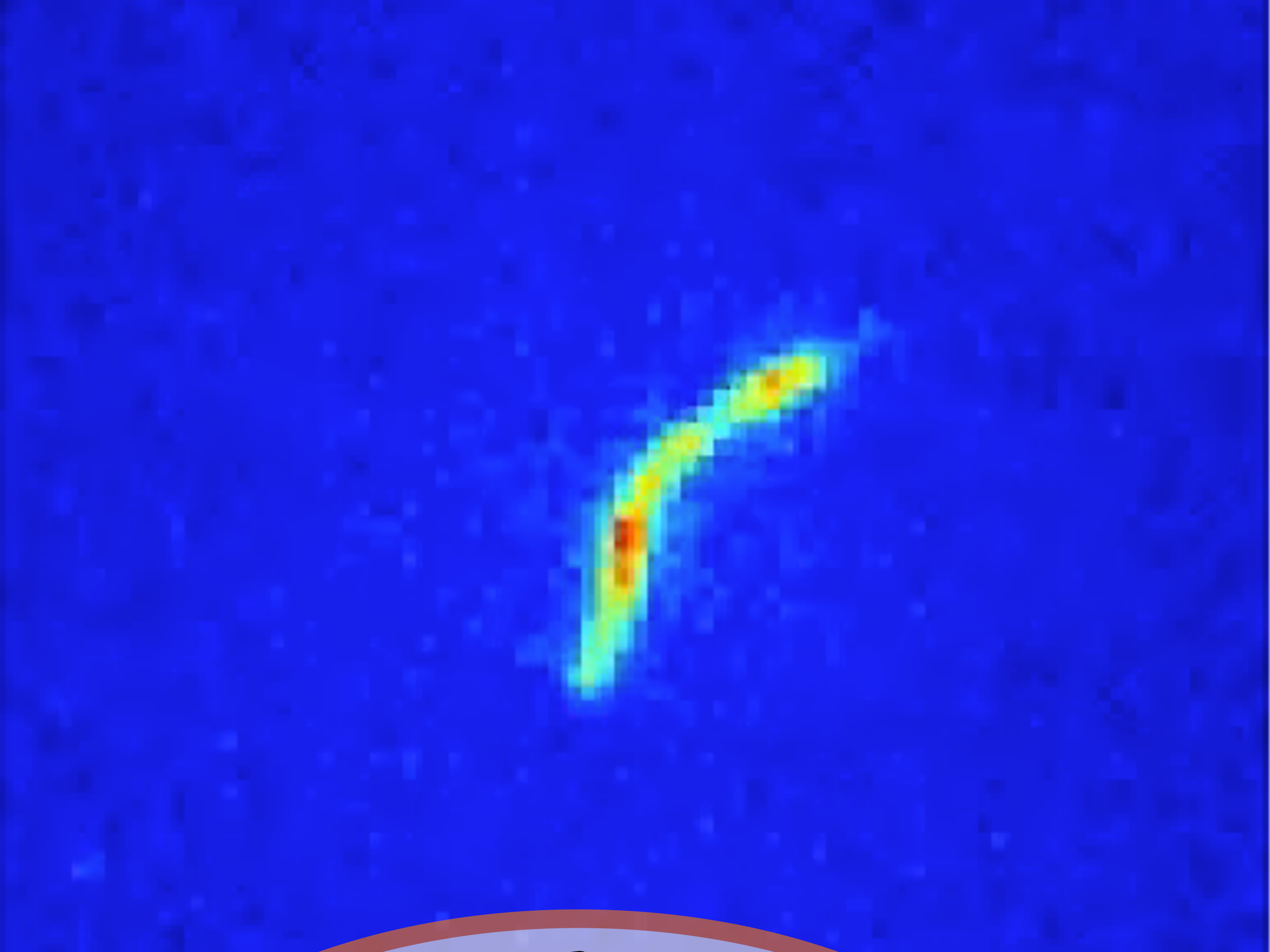
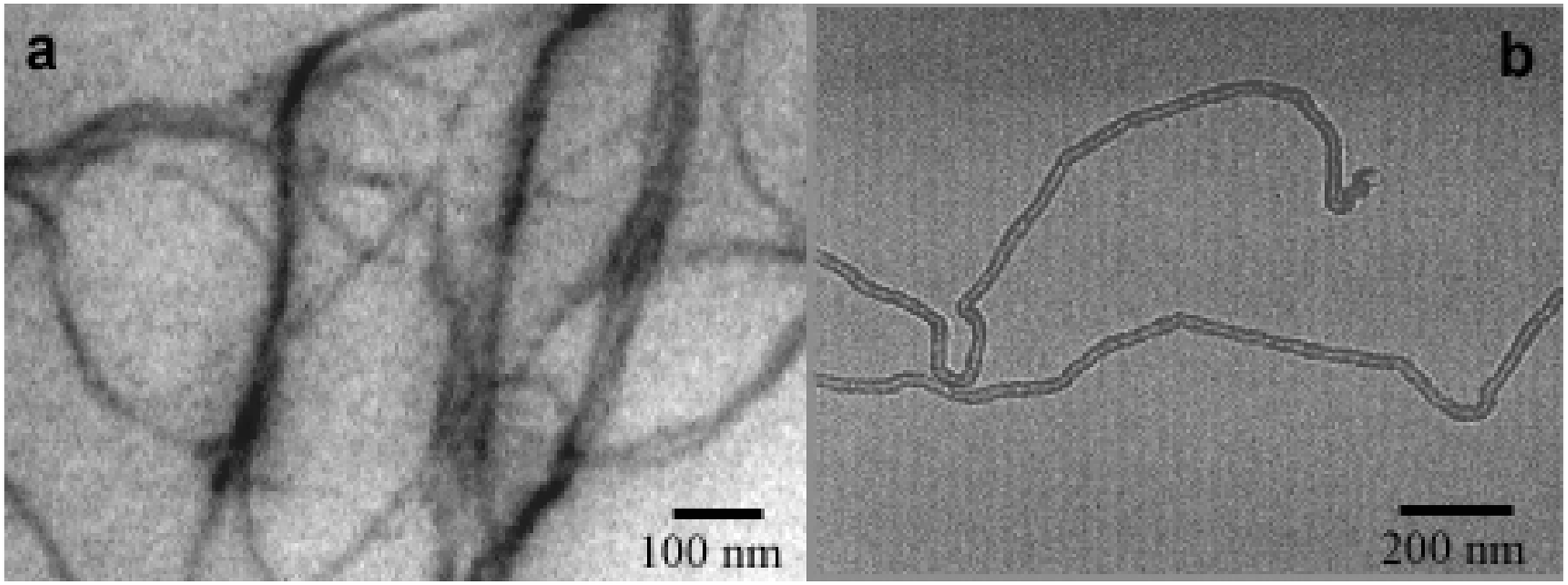
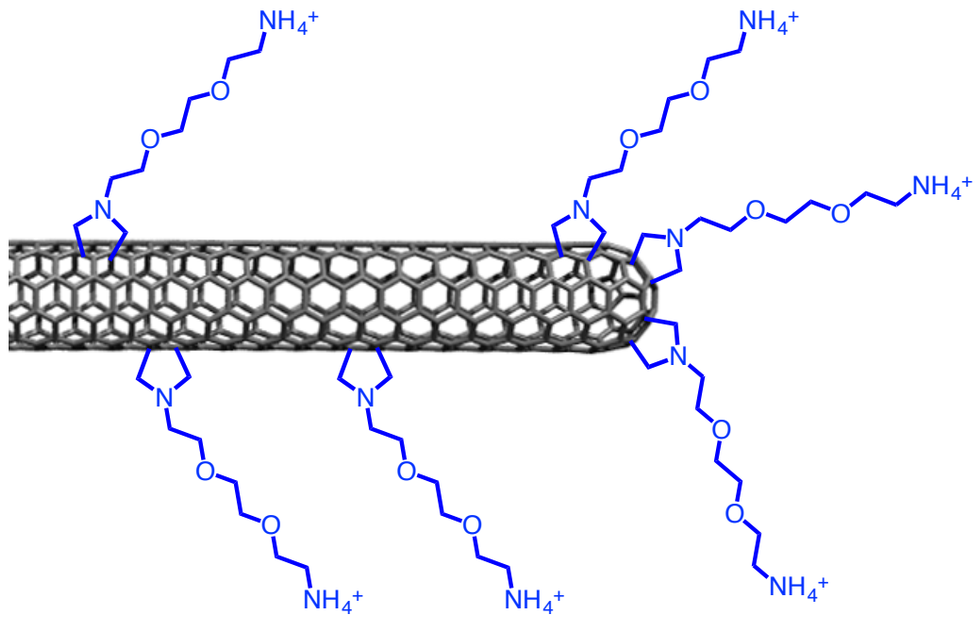

Nanomedicine for human health
Nano-scaffolds for regenerative medicine
Nano-diagnostics (e.g., DNA arrays, ultra-sensors)
Targeted nano-drug delivery
Nano-therapy (e.g., hyperthermia)
Nano-toxicology



TEM OF WATER SOLUBLE SWNT AND MWNT

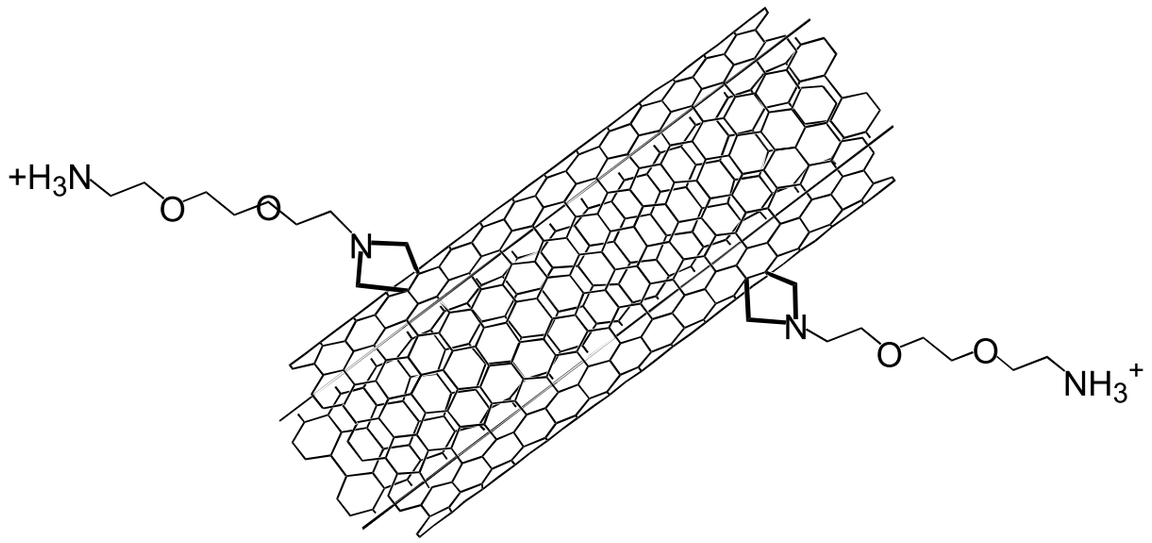




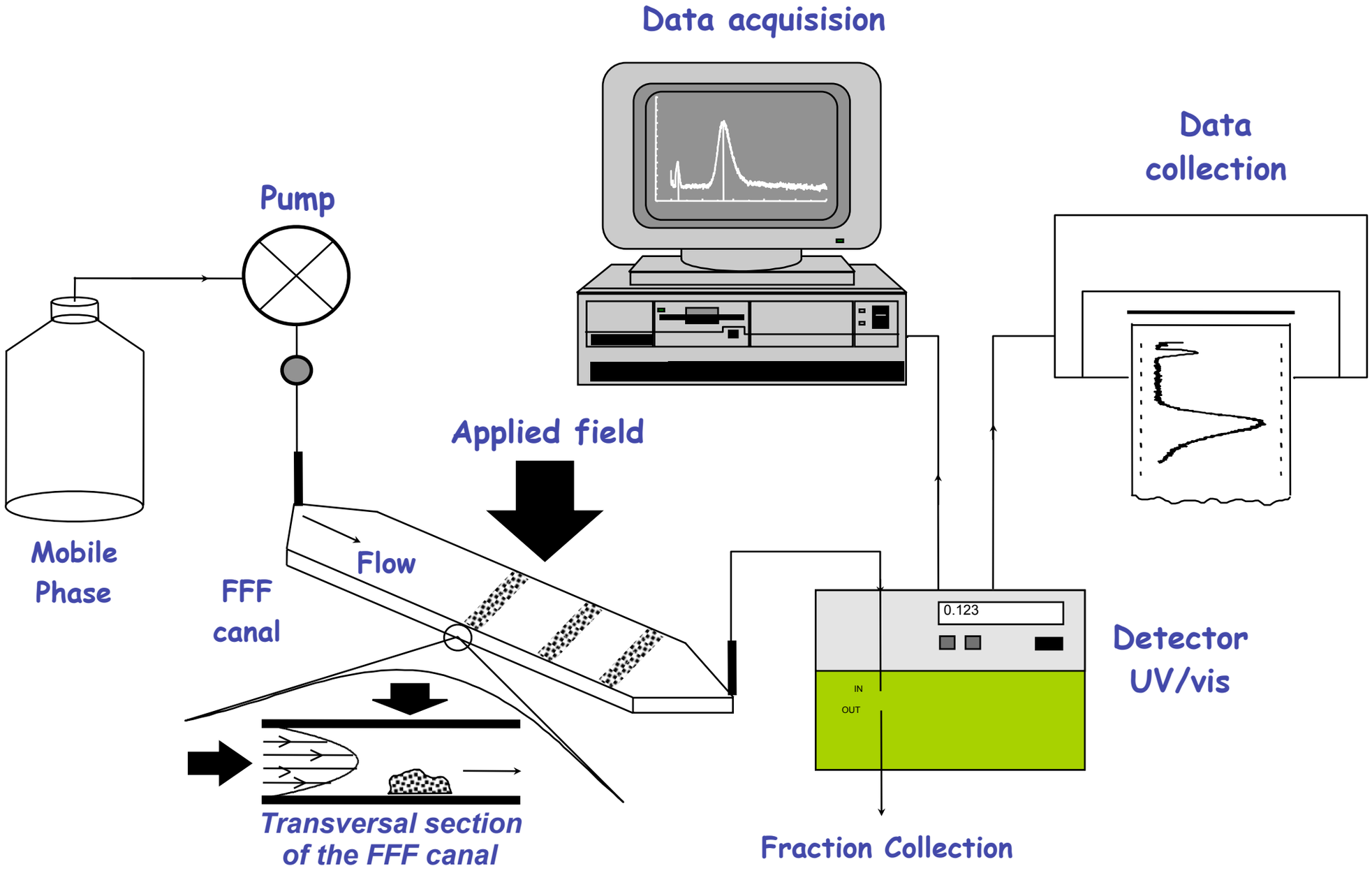
Chem. Commun. **2002**, 3050-3051

TEM Water-Soluble MWNTs-NH_3^+

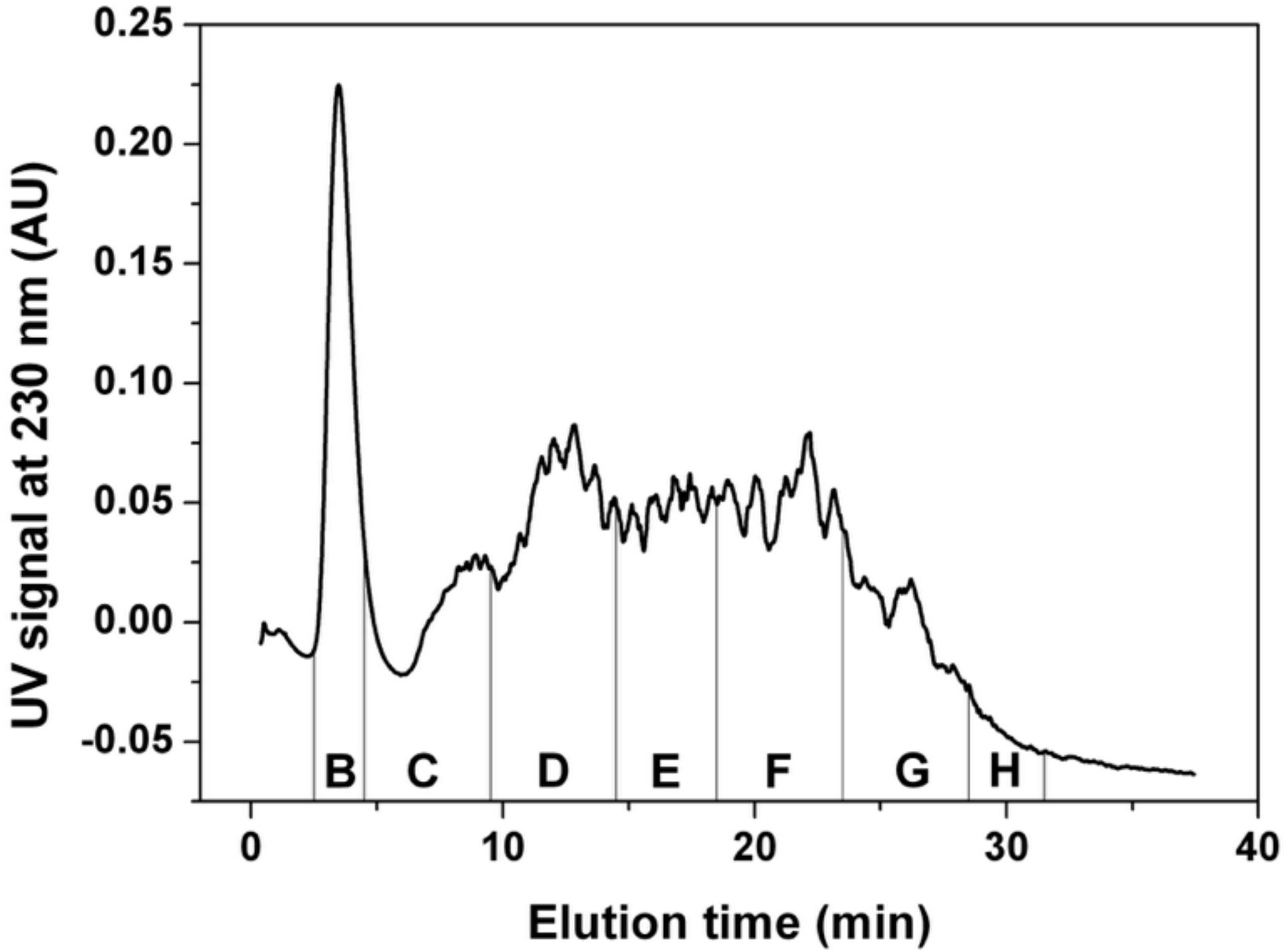
250 nm



FFF instrumentation



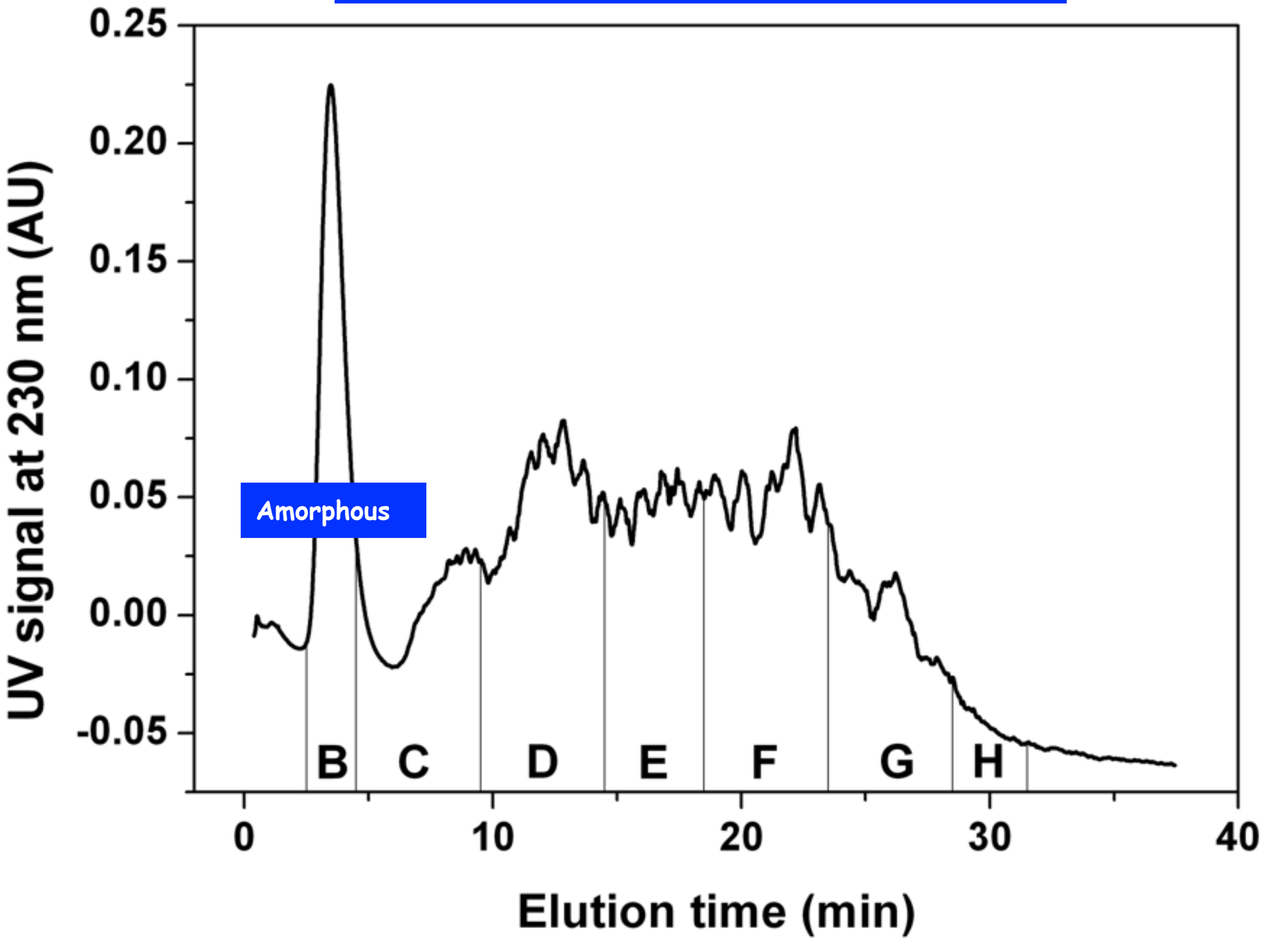
Length Separation of Water-Soluble MWNT-NH_3^+ by Field Flow Fractionation (FFF)



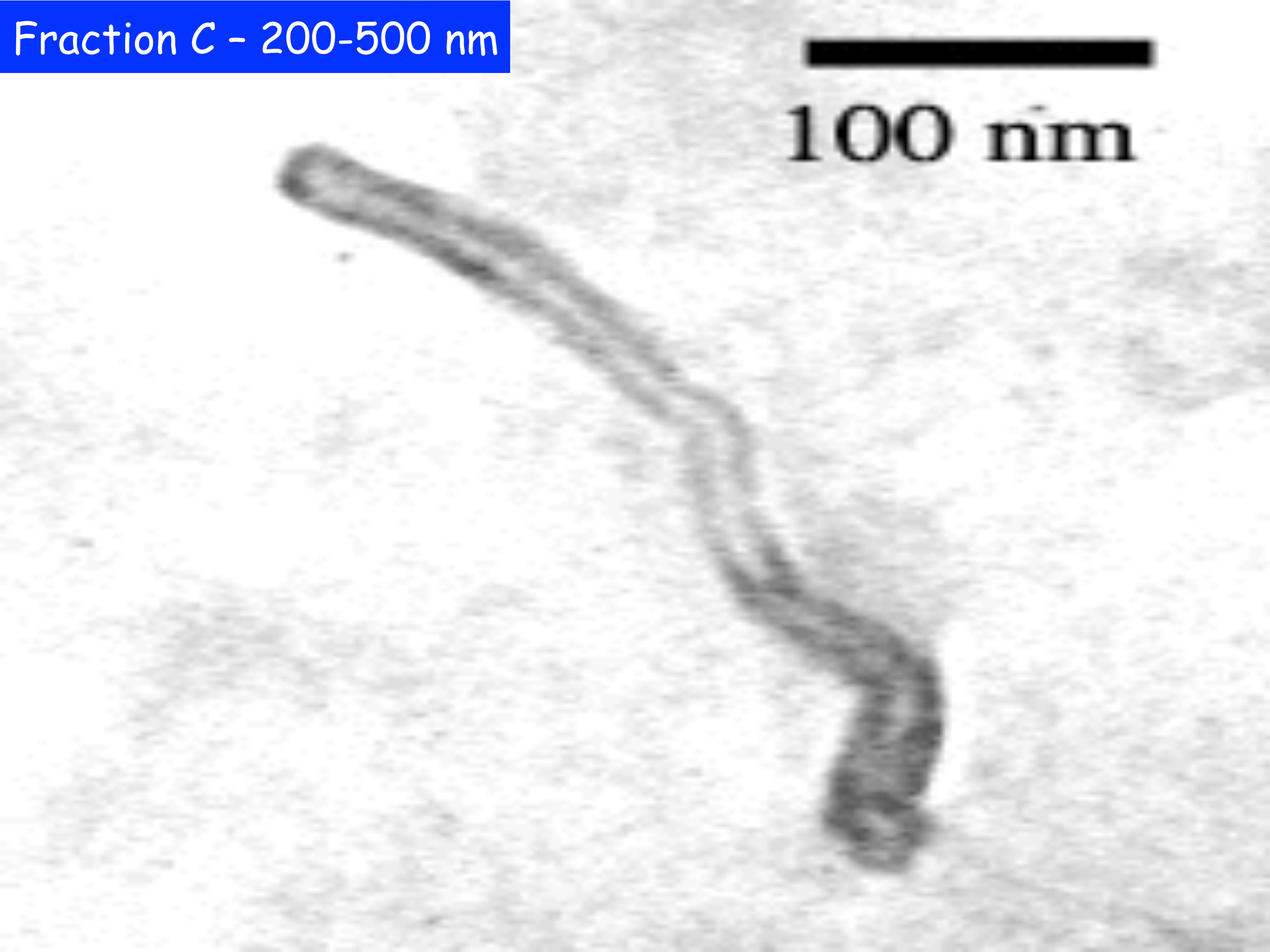
Fraction B – Amorphous material

100 nm

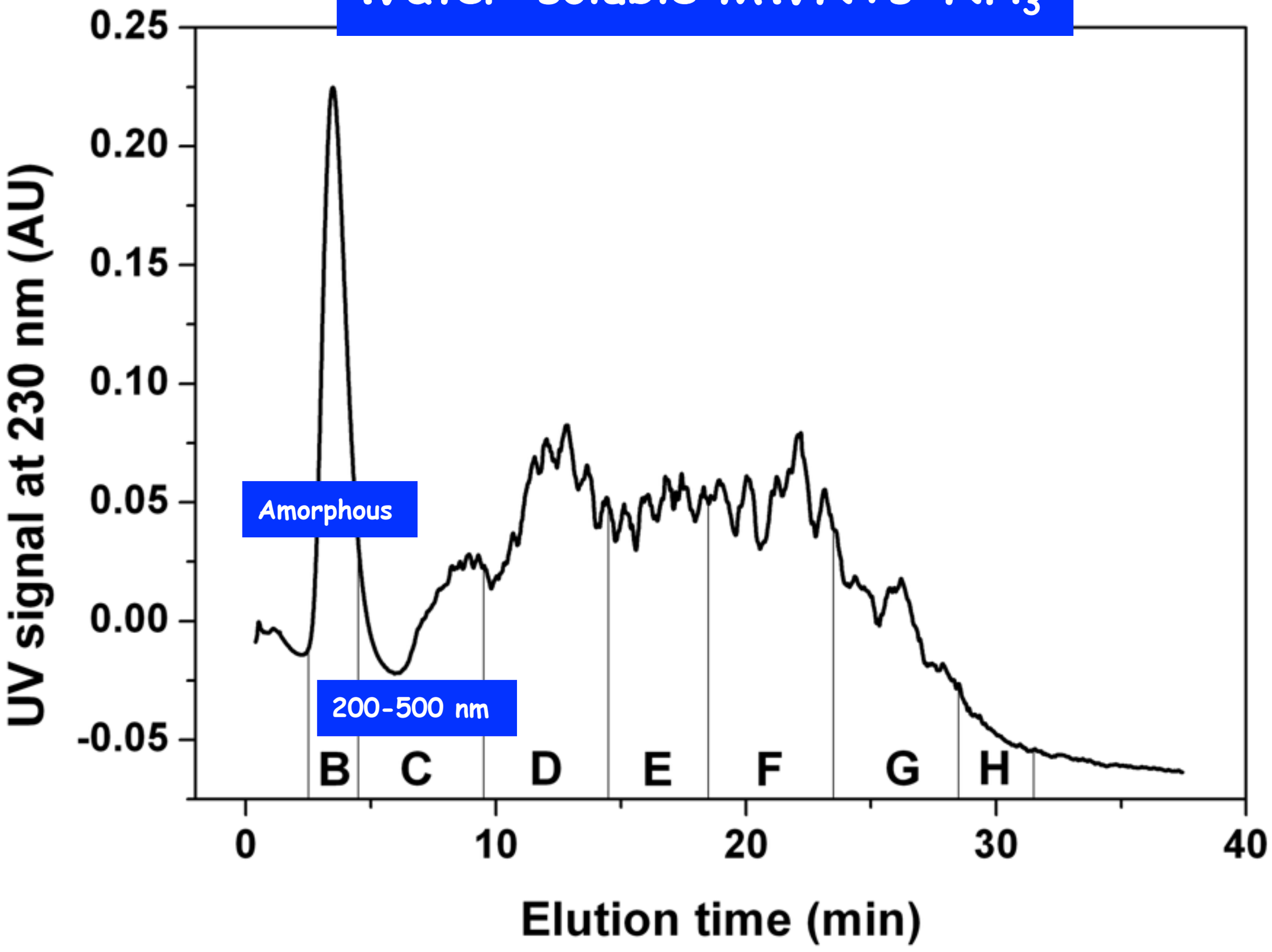
FFF Fractogram of Water-soluble MWNTs-NH_3^+



Fraction C - 200-500 nm



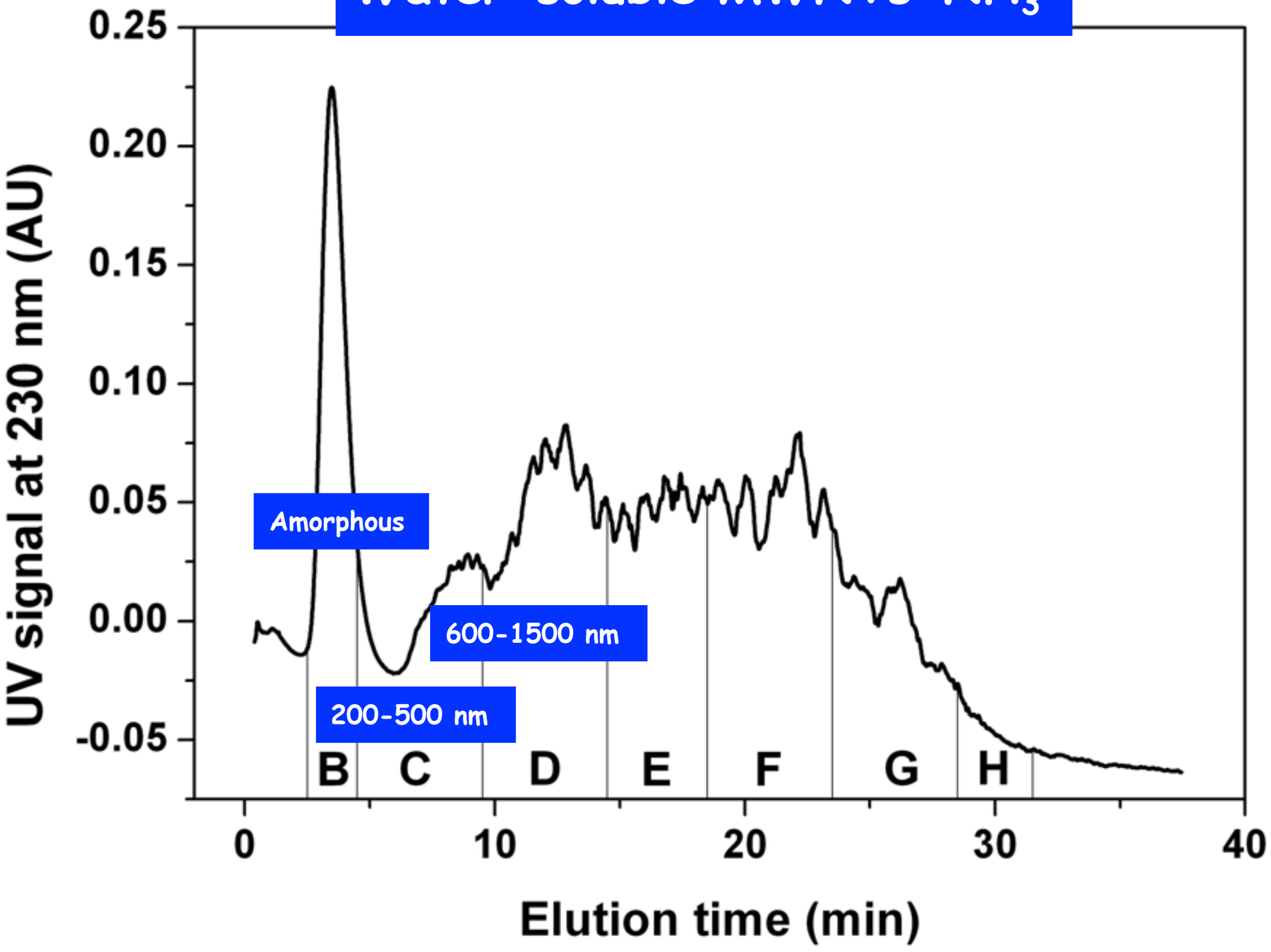
FFF Fractogram of Water-soluble MWNTs-NH_3^+



Fraction D - 600-1500 nm

100 nm

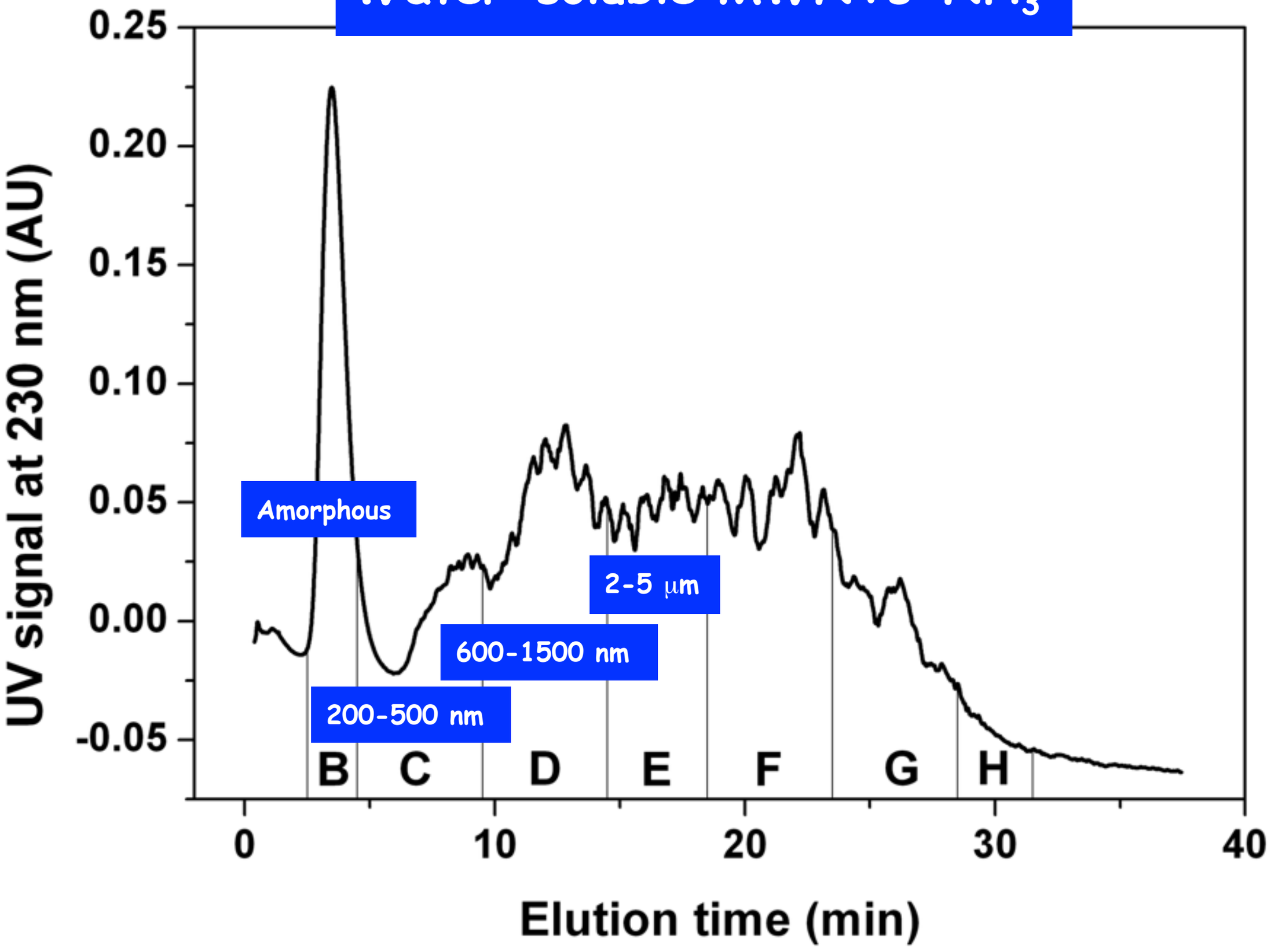
FFF Fractogram of Water-soluble MWNTs-NH_3^+



Fraction E - 2-5 μm

500 nm

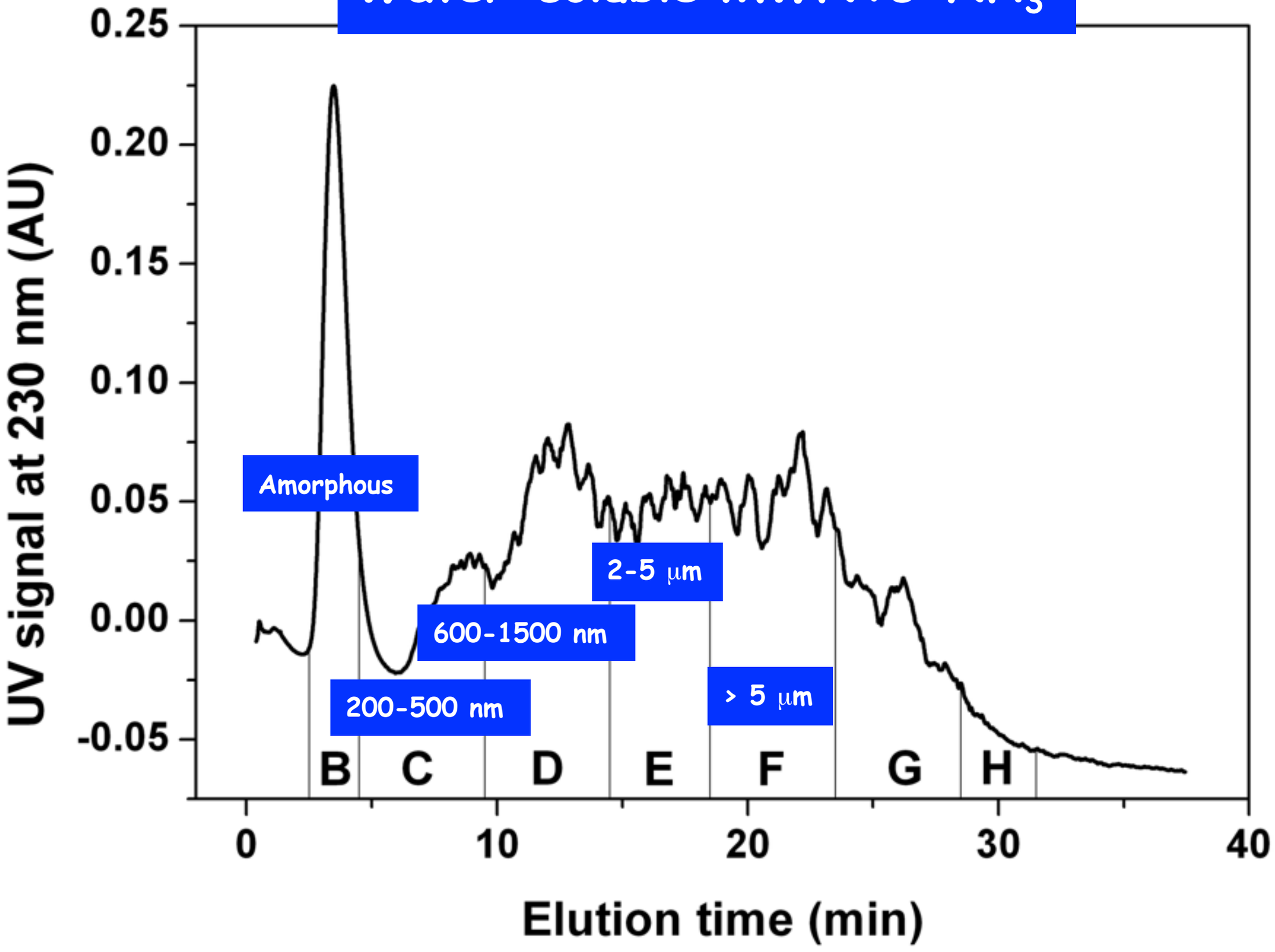
FFF Fractogram of Water-soluble MWNTs-NH_3^+

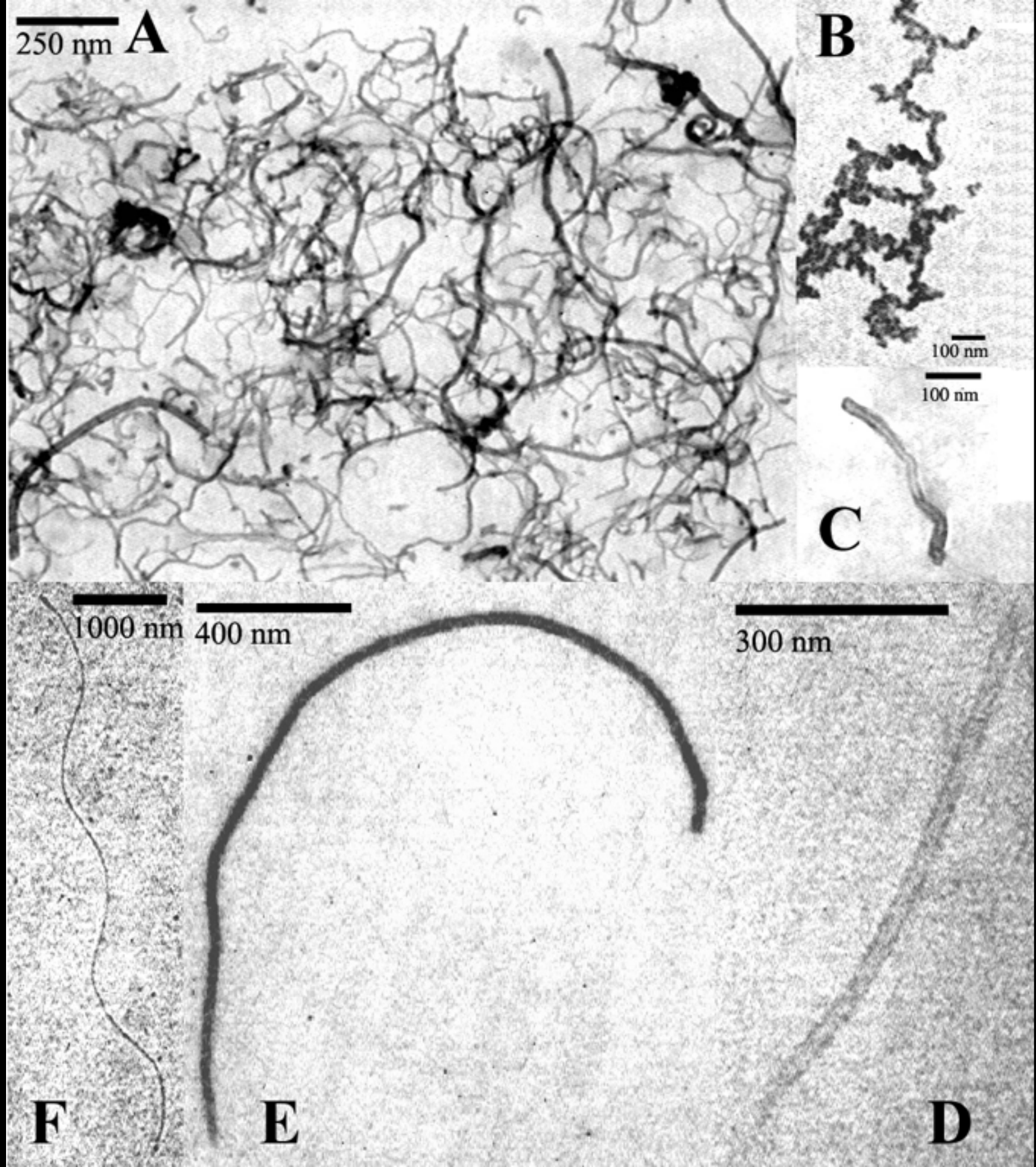


Fraction F > 5 μm

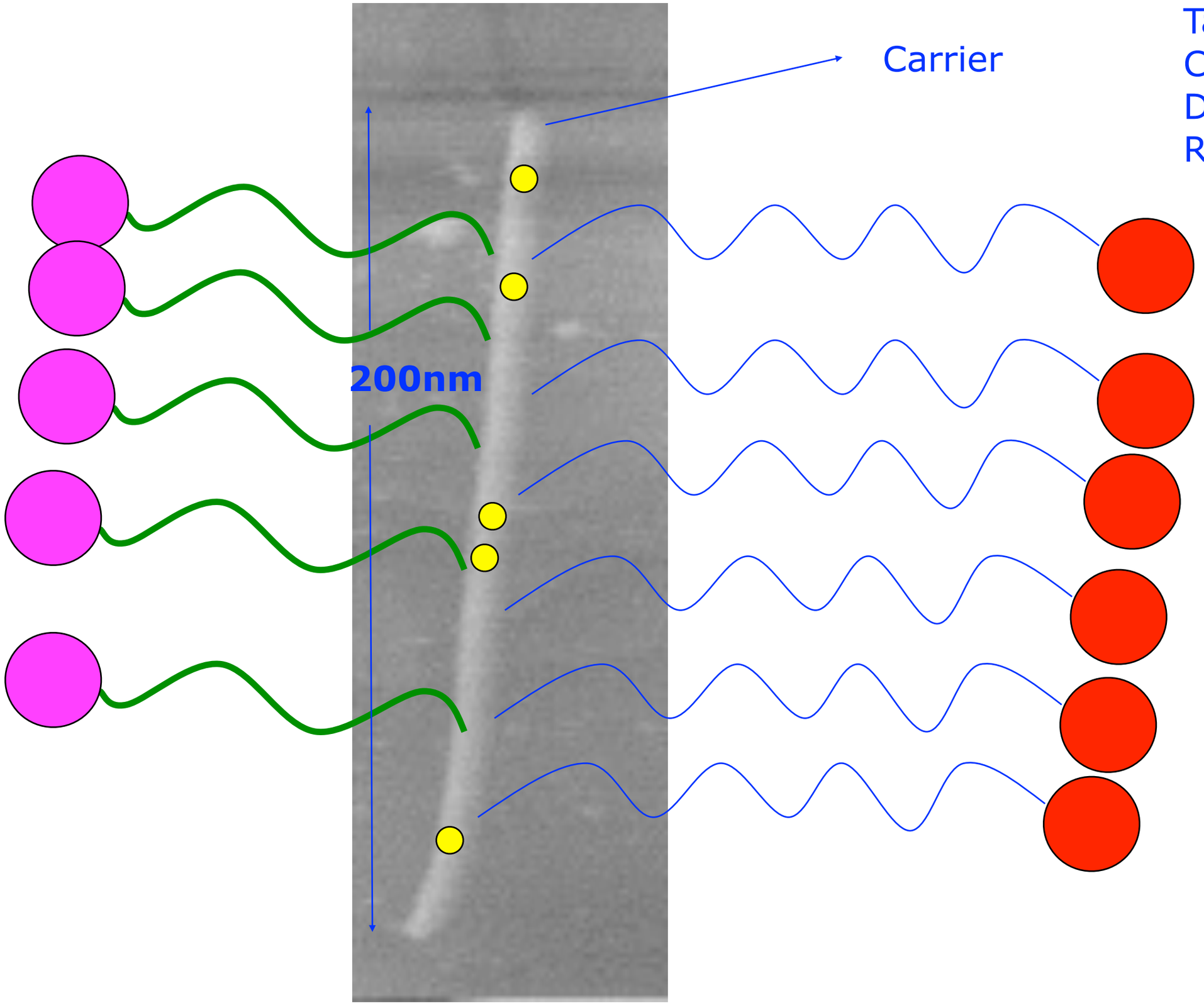
1000 nm

FFF Fractogram of Water-soluble MWNTs-NH_3^+

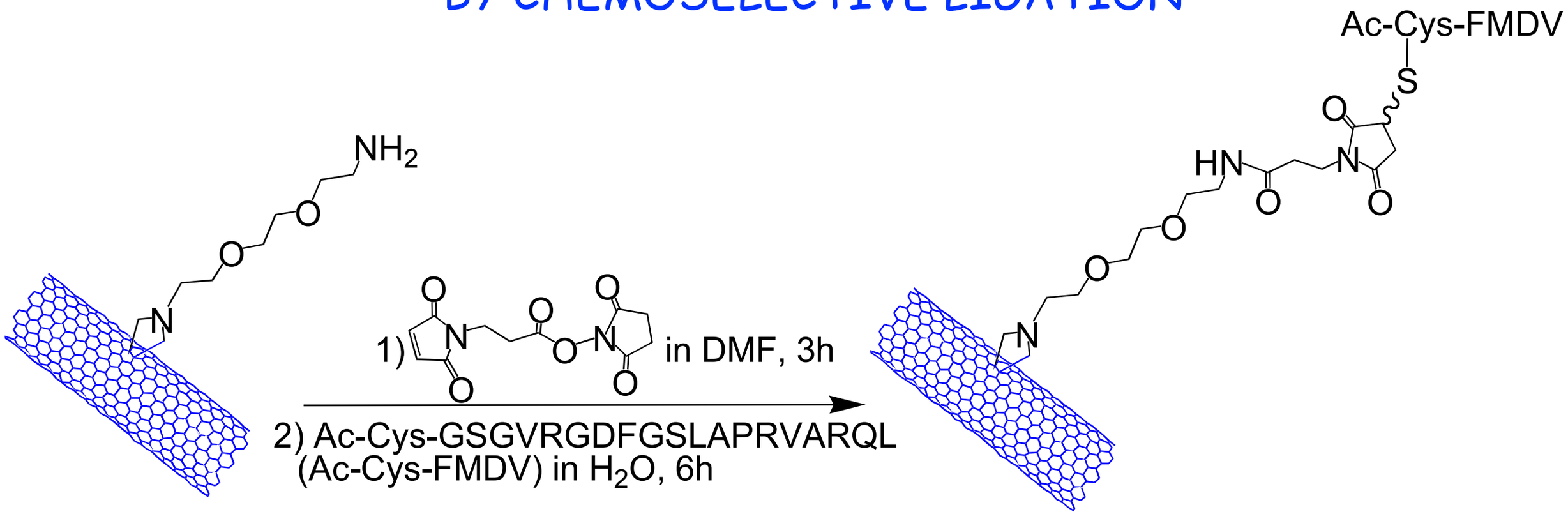



250 nm
A
B
100 nm
100 nm
C
1000 nm
400 nm
300 nm
F
E
D

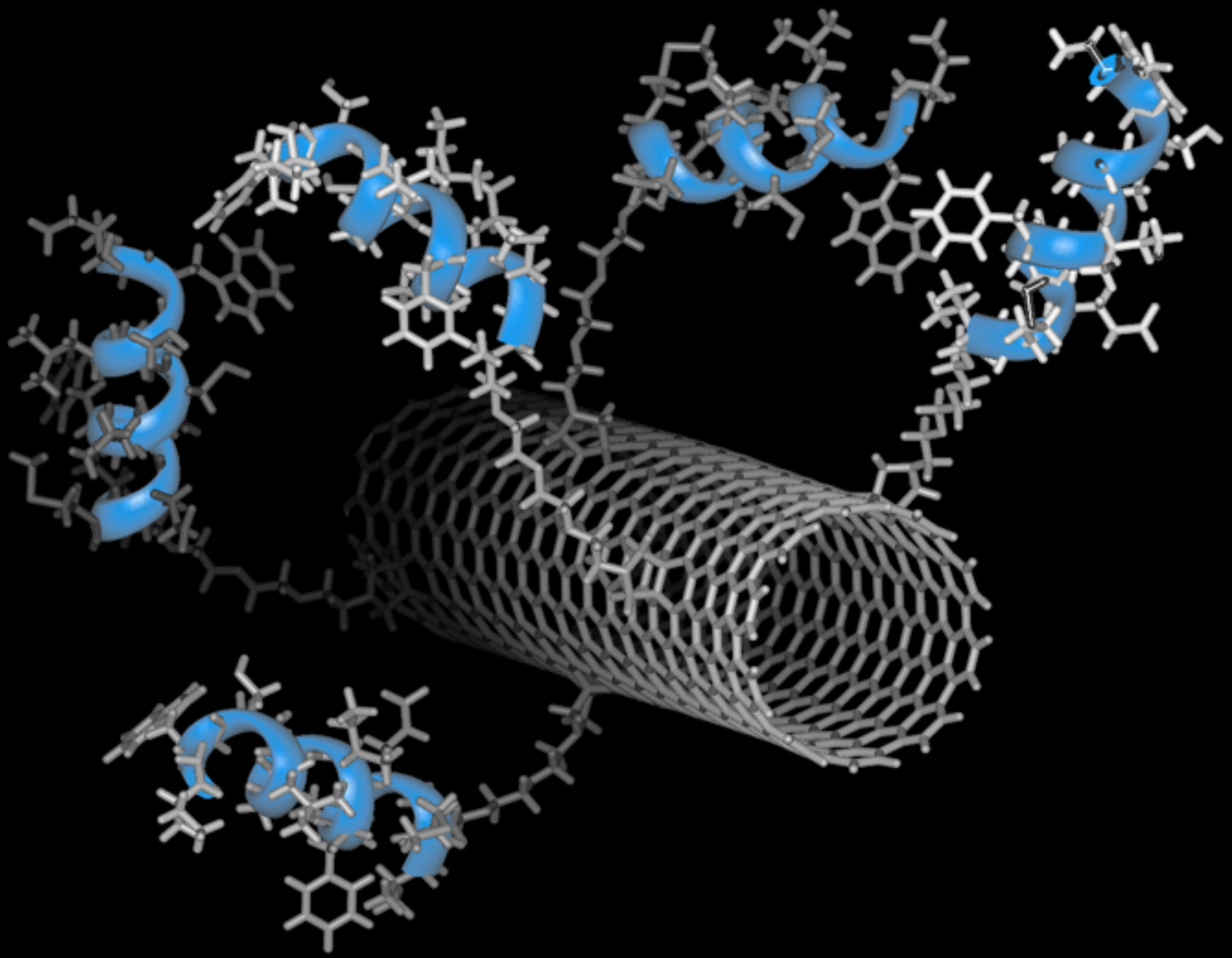
Approach to “Smart” Therapy



SYNTHESIS OF A BIOACTIVE SWNT EICOSAPEPTIDE BY CHEMOSELECTIVE LIGATION

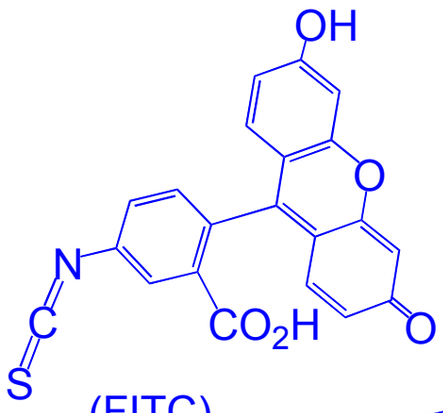


1) B-cell epitope from the foot-and-mouth disease virus (FMDV);
2) This peptide elicits neutralizing antibody response for protection;
3) On SWNT, this peptide keeps the same conformational behavior;
4) Antibodies recognize the FMDV peptide attached to SWNT;
5) No anti-SWNT antibodies are induced;
6) In vivo experiments demonstrate that peptide-nanotube conjugates are immunogenic, eliciting antibody responses of the right specificity.

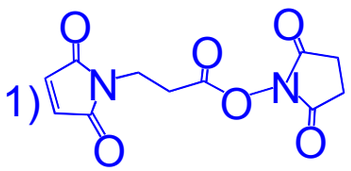


These findings highlight the potential use of peptide-carbon nanotube conjugates for diagnostic purposes and pave the way for their application in vaccine delivery

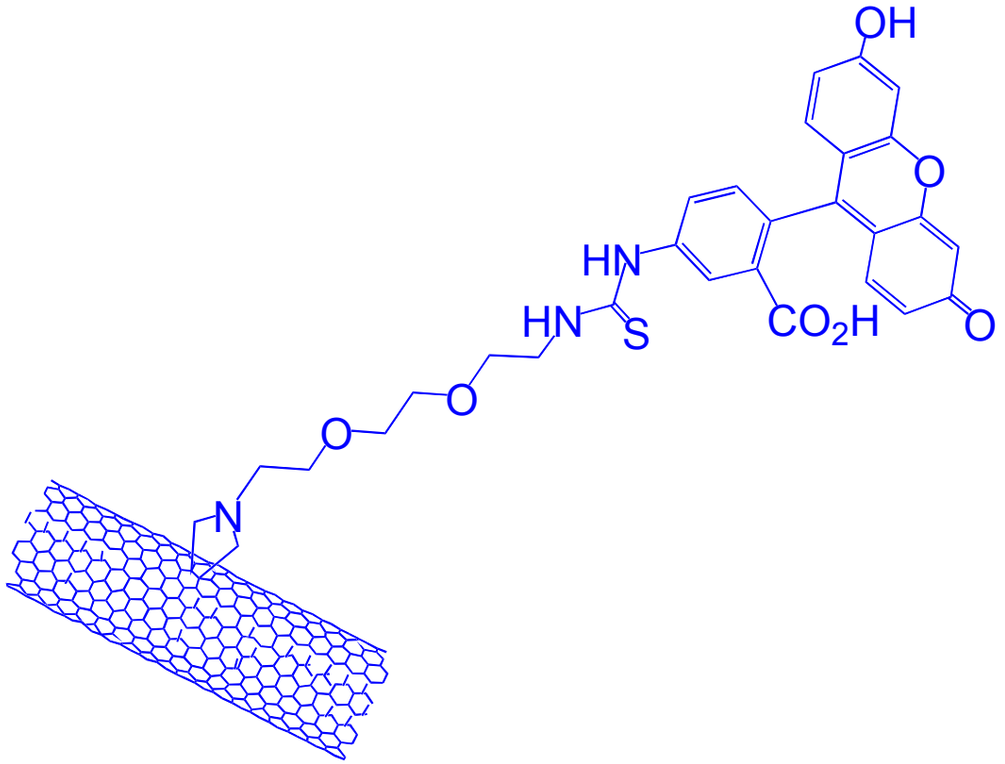
Can these monster molecules
pass through cell membranes???



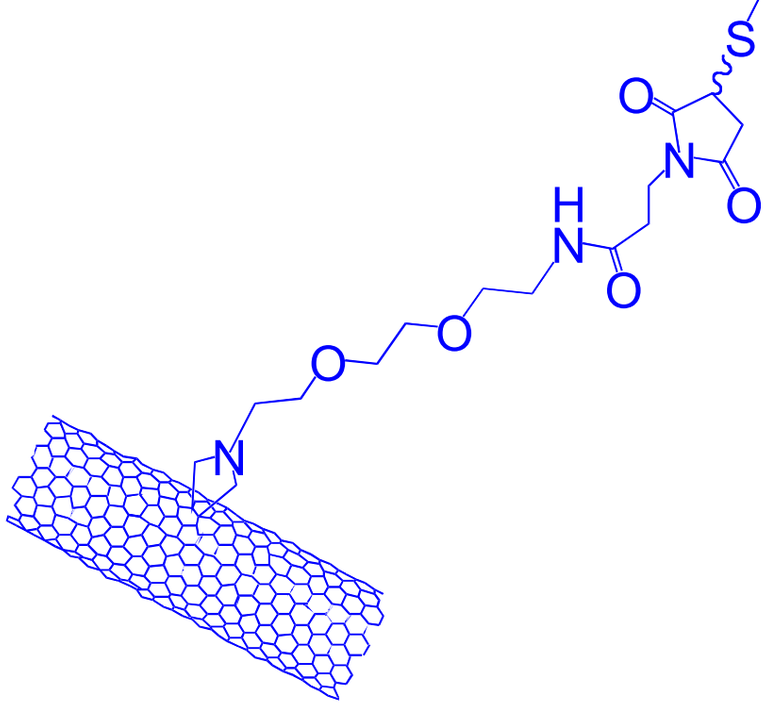
(FITC)

1)  in DMF, 3h

2) H-Lys-(FITC)-QRMHLRQYELLC
in H_2O, 6h

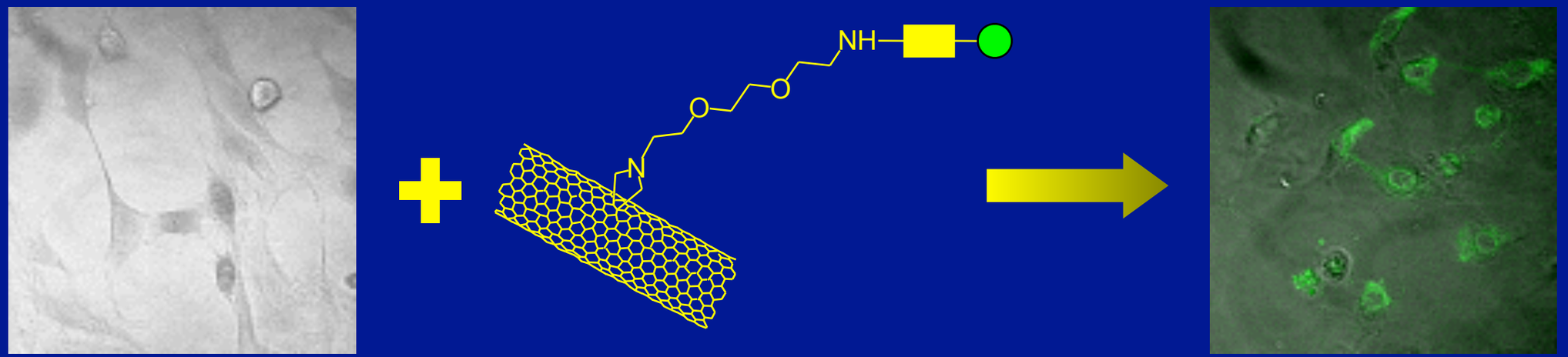


H-Lys(FITC)-(α_s384-394)-Cys-OH

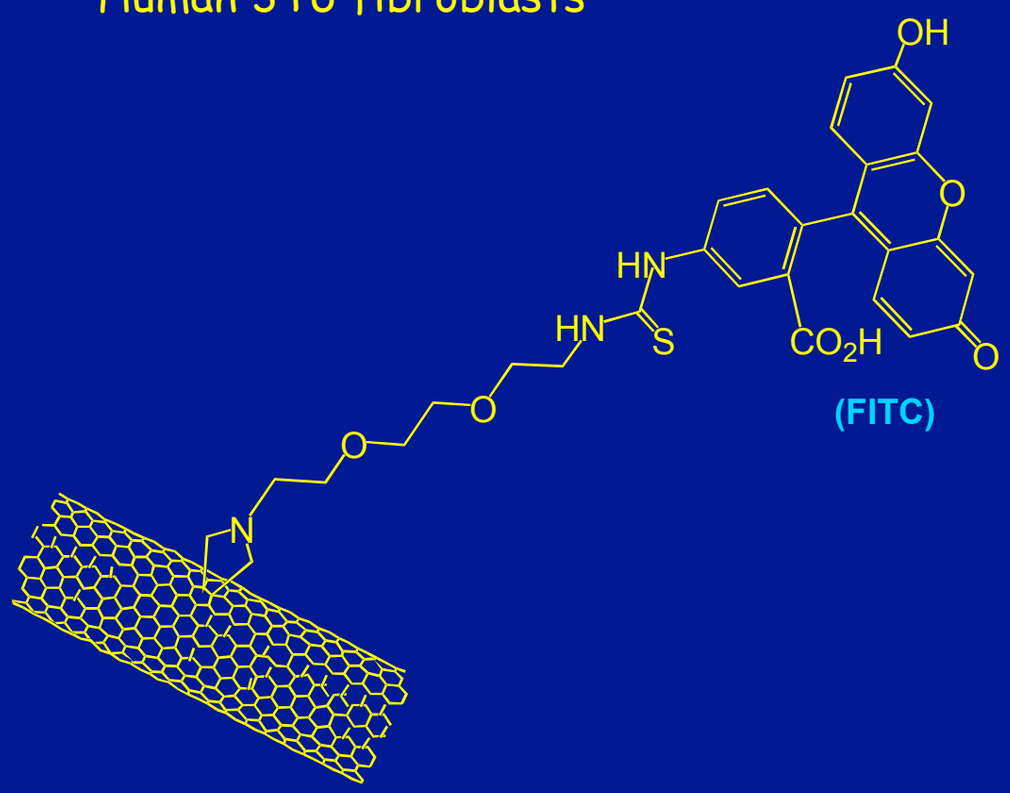


Shown to block β-adrenergic activation
of adenyl cyclase in permeable cells

Cell Uptake of Fluorescent Carbon Nanotubes

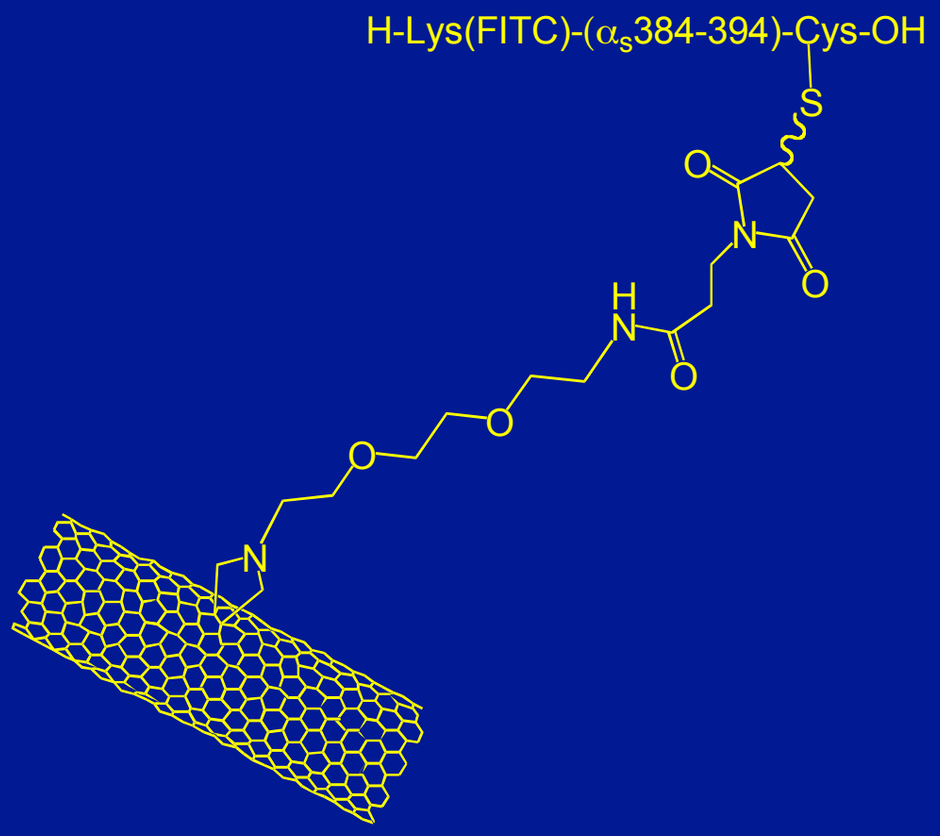


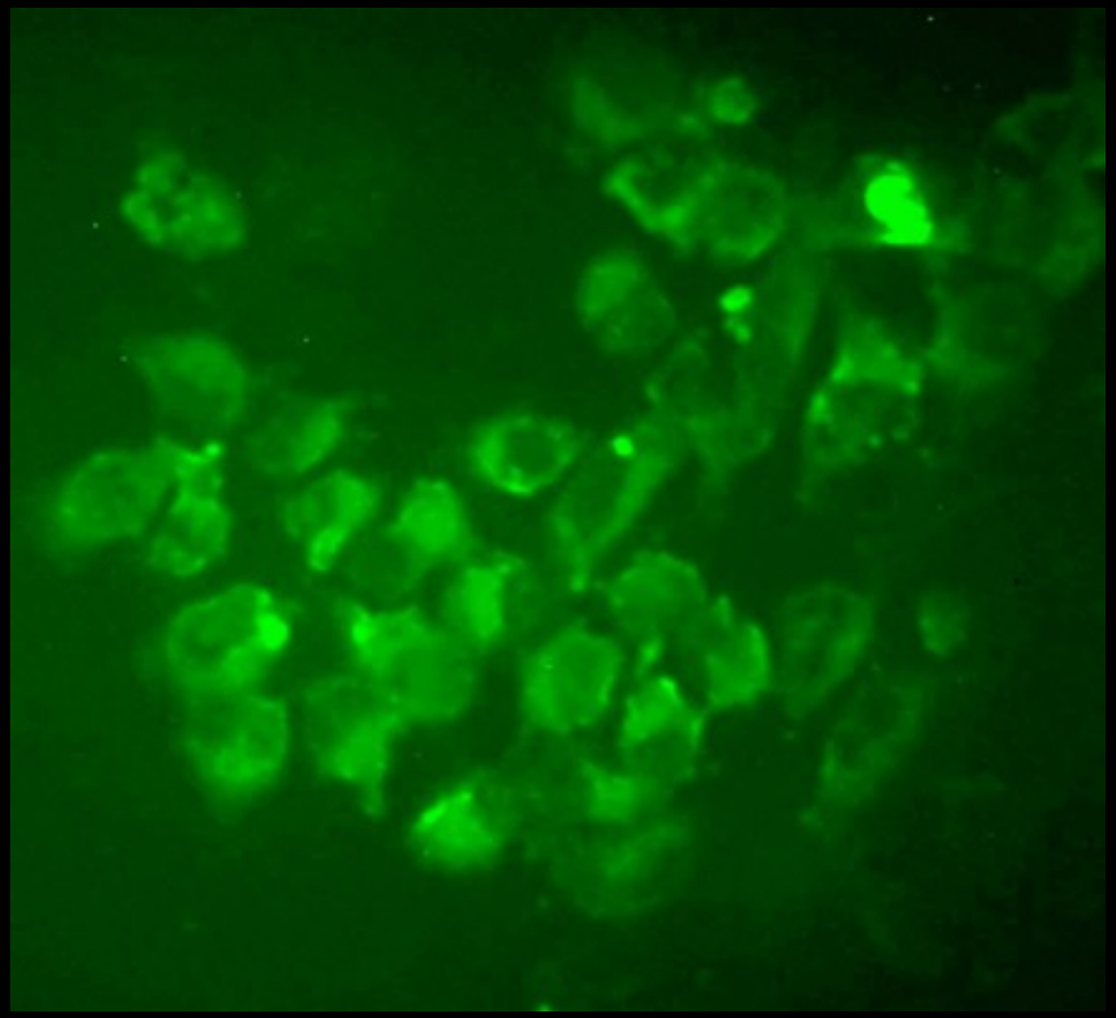
Human 3T6 fibroblasts

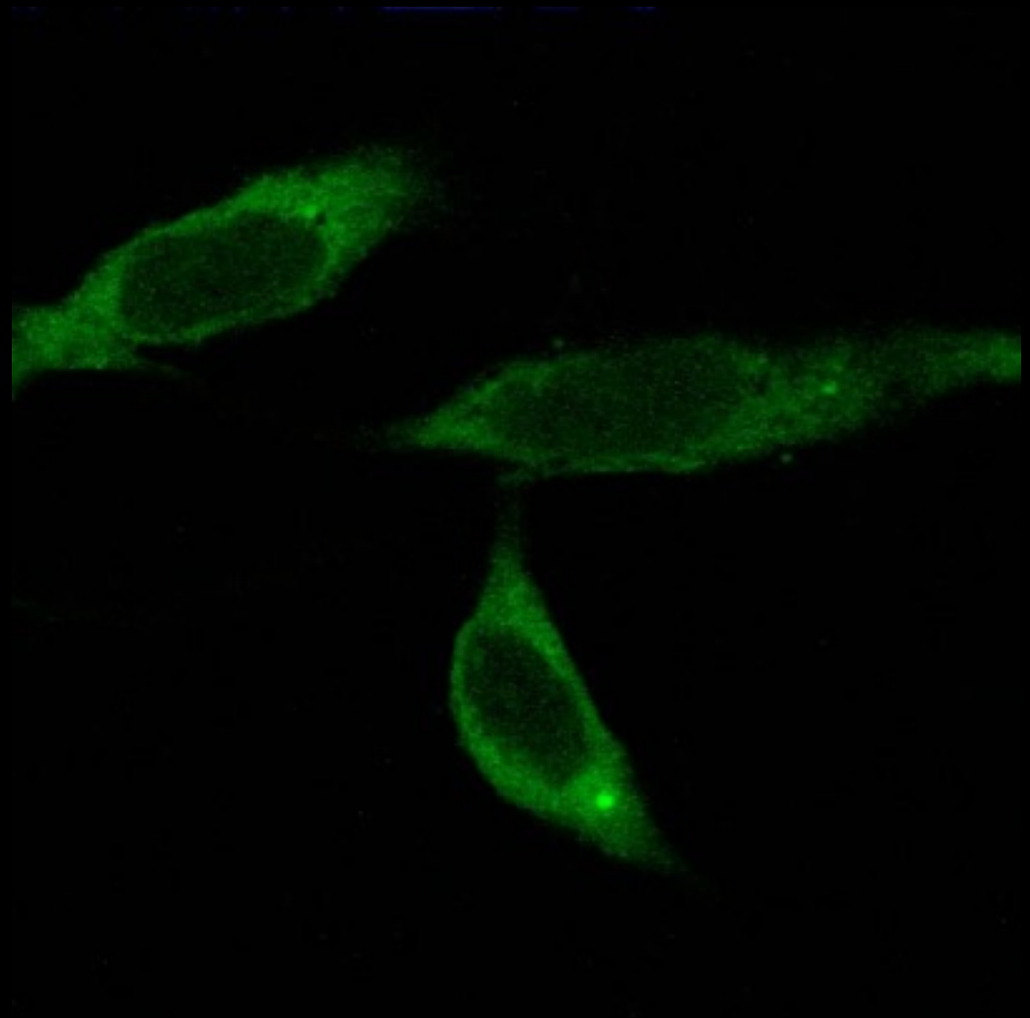


(FITC)

H-Lys(FITC)-(α_s384-394)-Cys-OH

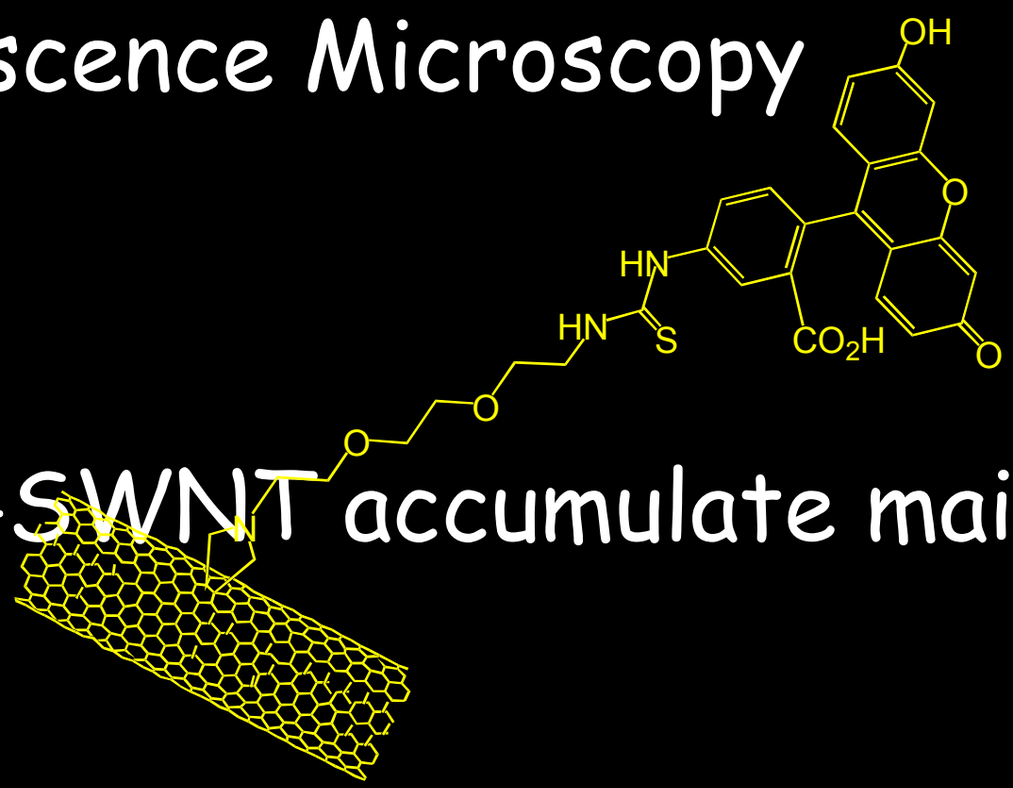






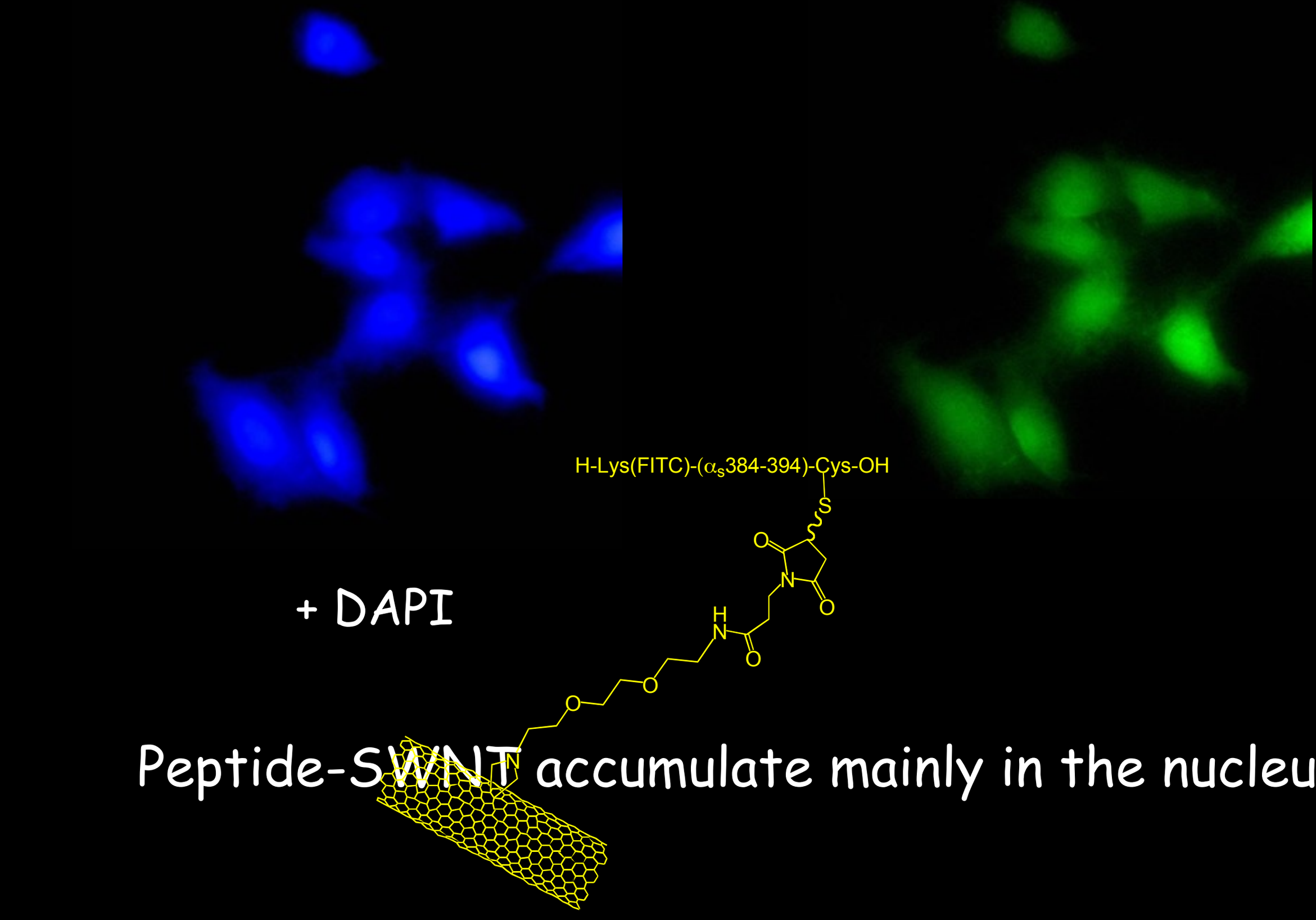
Epifluorescence Microscopy

Confocal Microscopy



FITC-SWNT accumulate mainly in the cytoplasm

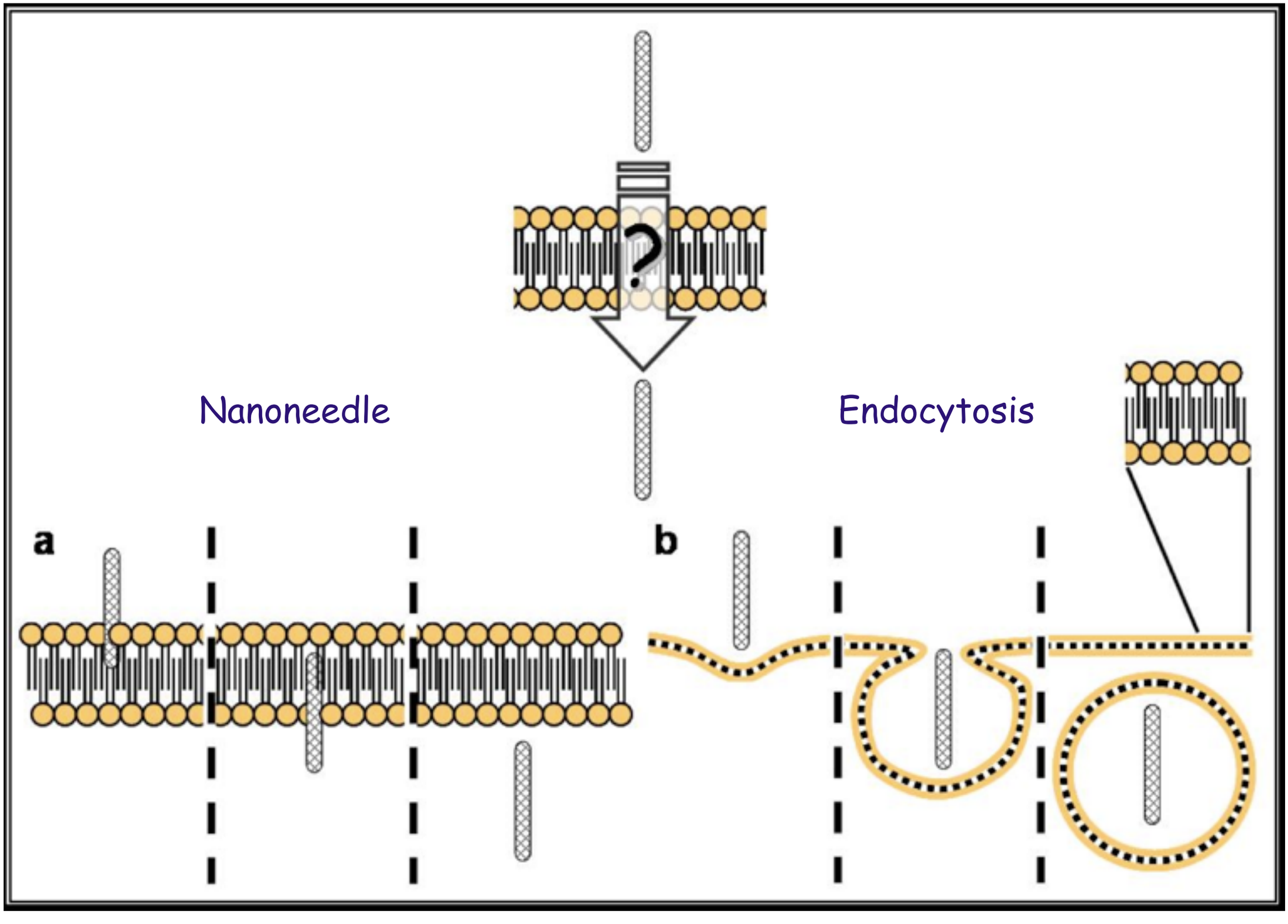
Epifluorescence Microscopy



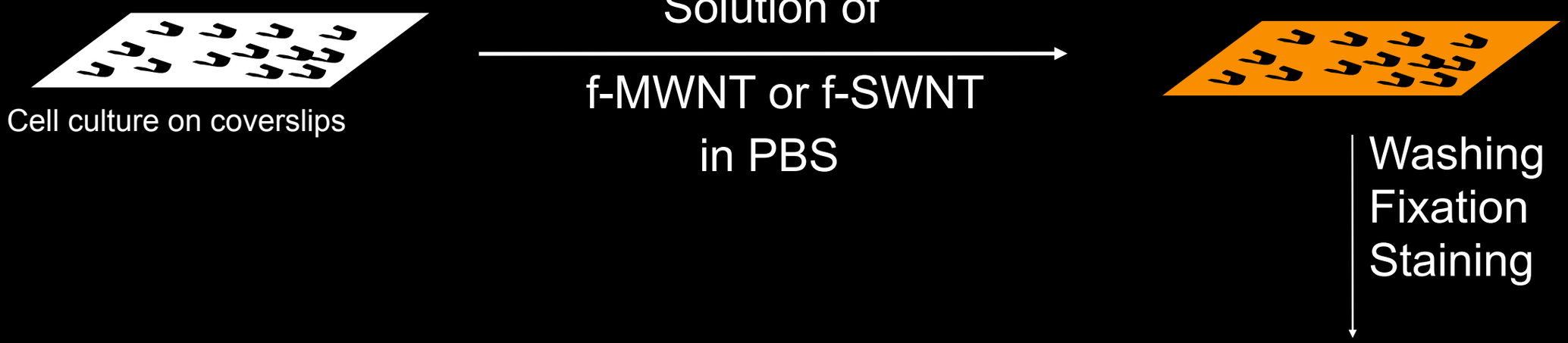
+ DAPI

Peptide-SWNT accumulate mainly in the nucleus

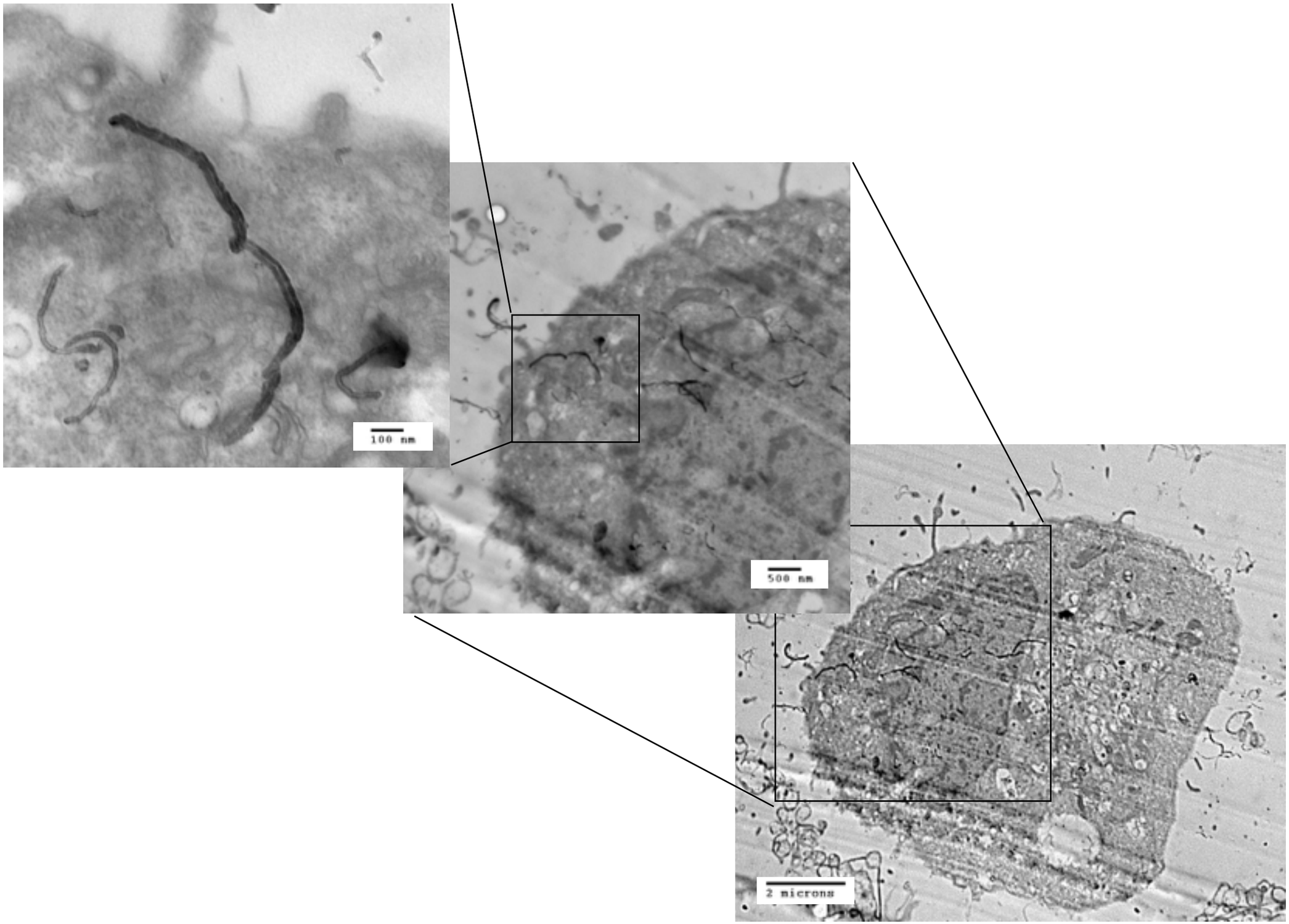
Possible mechanisms of membrane trespassing



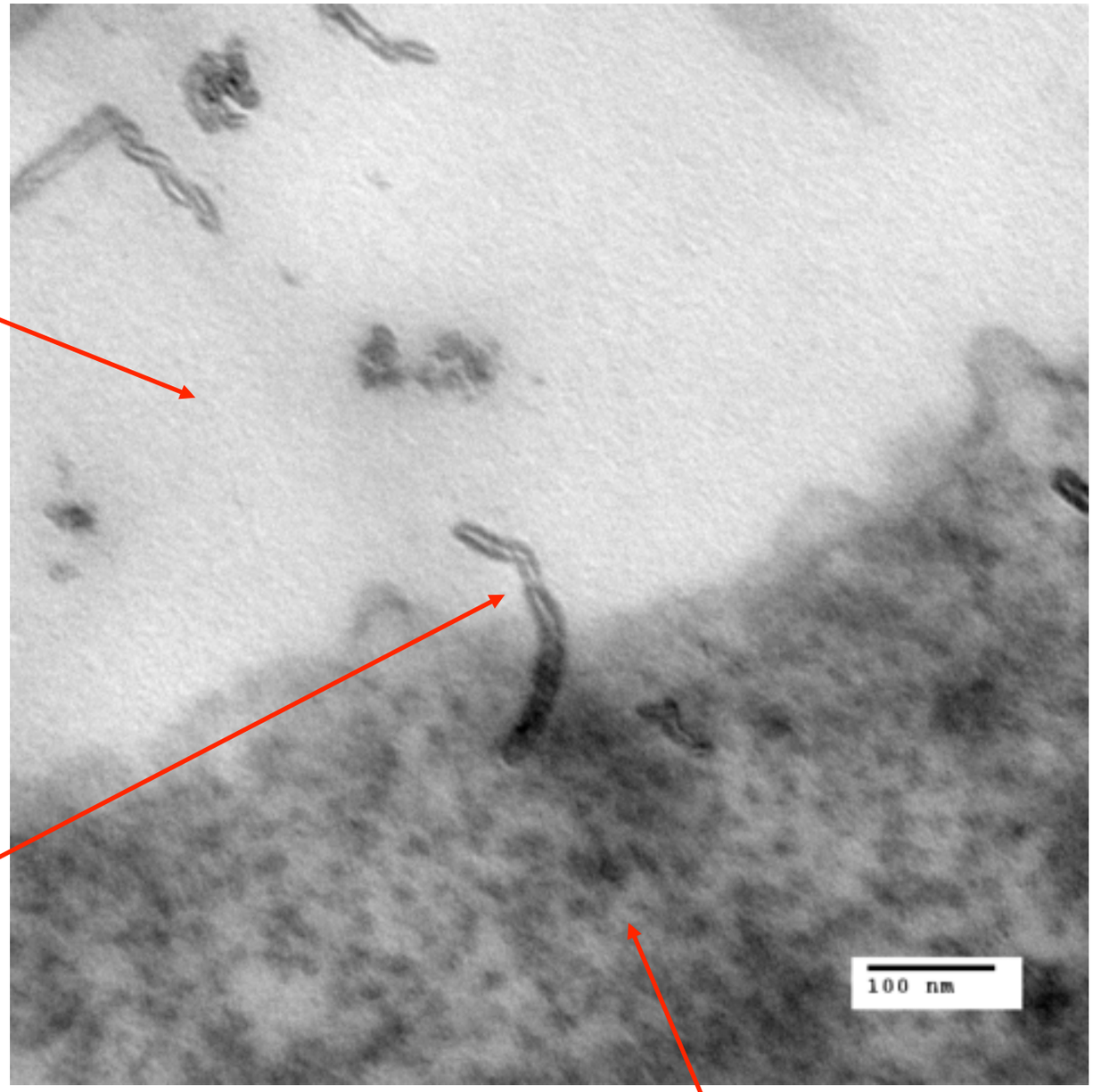
Cells Cut with a Microtome Knife



HeLa cells incubated with 10μM MWNT-$NH_3^+Cl^-$ washed, fixed, stained, embedded, sectioned and analysed by TEM (75 kV).



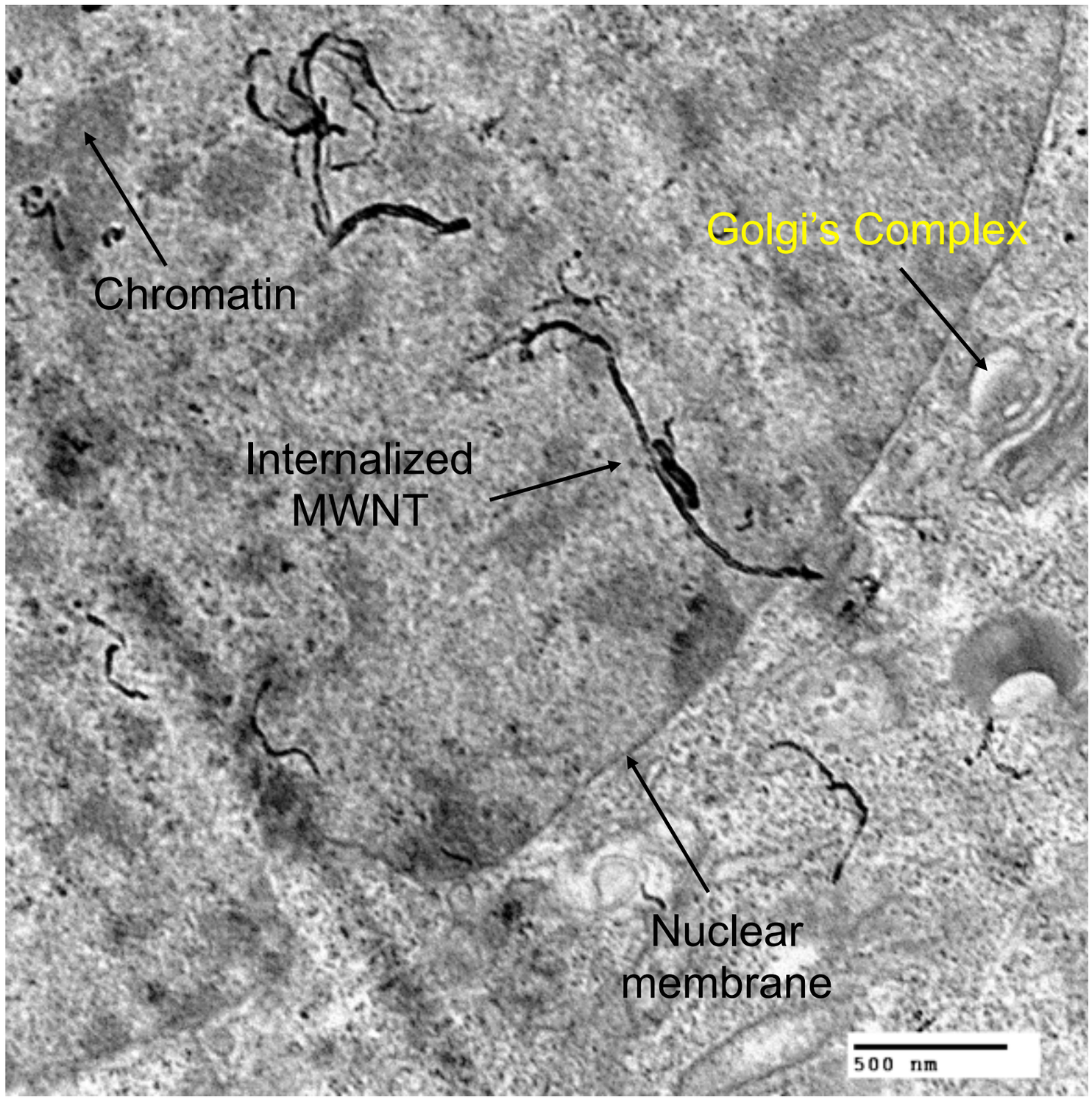
Outside the cell

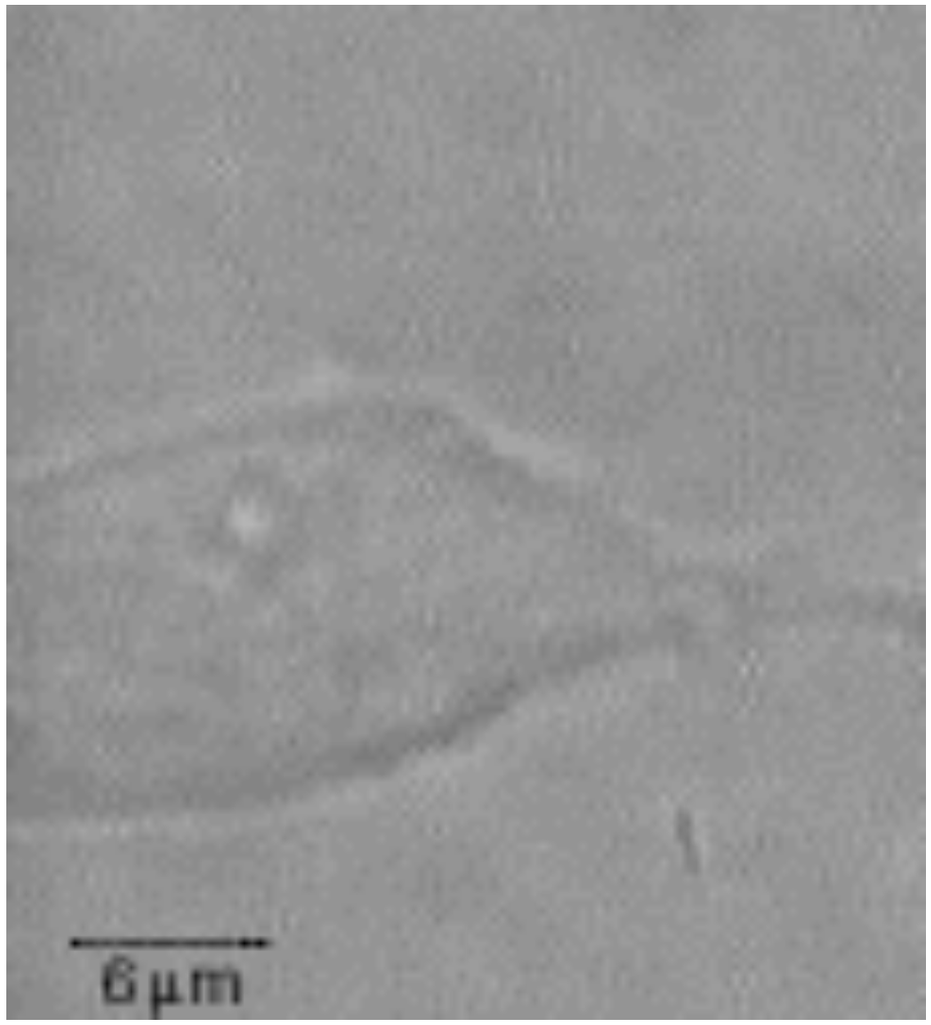


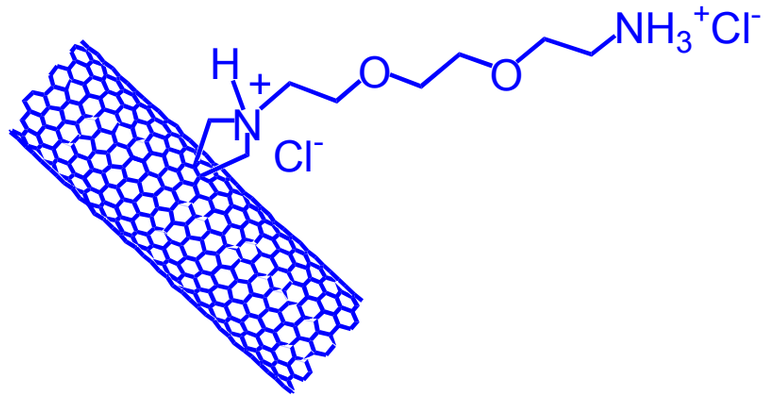
A MWNT is crossing the cell membrane

Inside the cell

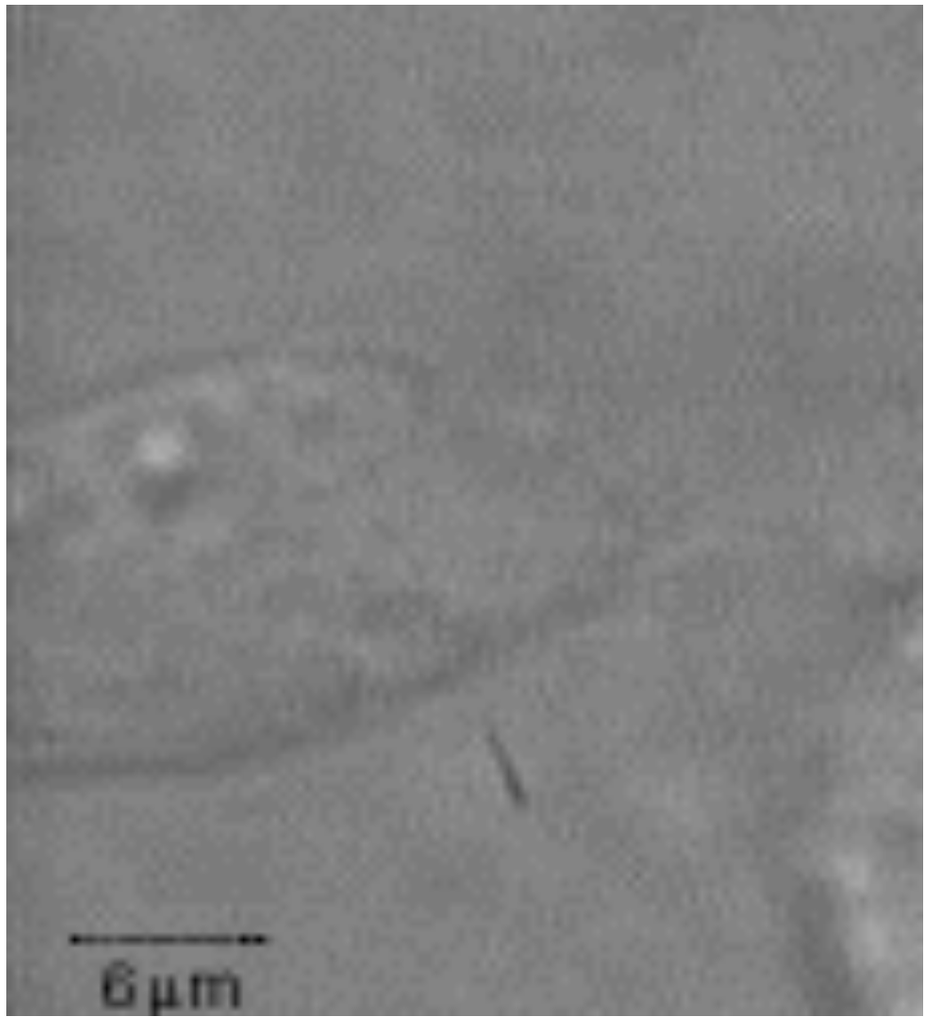
Cell Uptake of Carbon Nanotubes

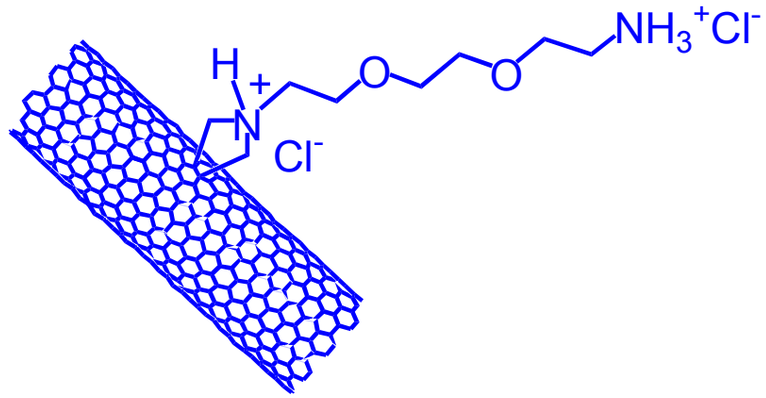




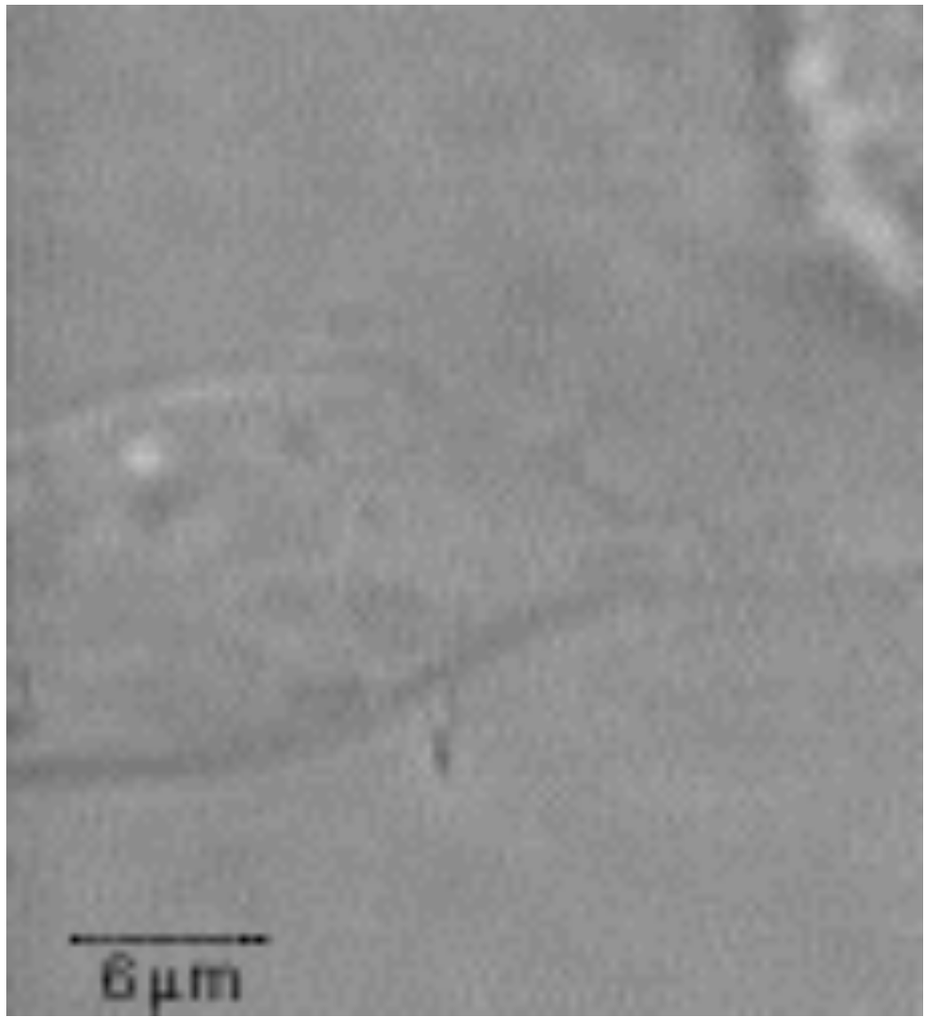


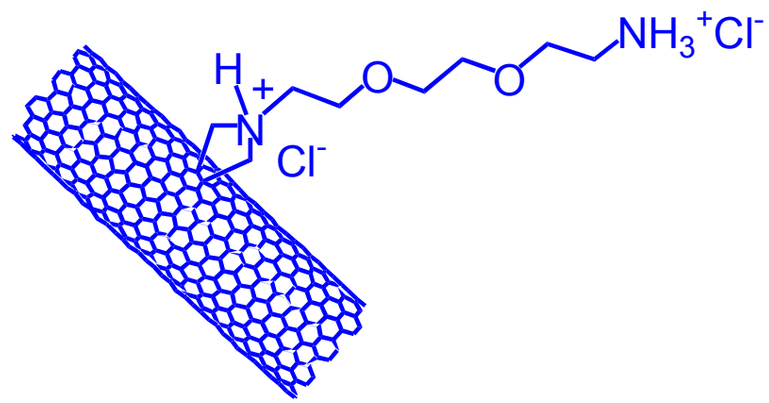
Optical videomicroscopy images showing interaction between MWCNT-NH_3 and human kidney epithelial 293 (HEK293) cells immediately after addition of CNT onto a cell culture.

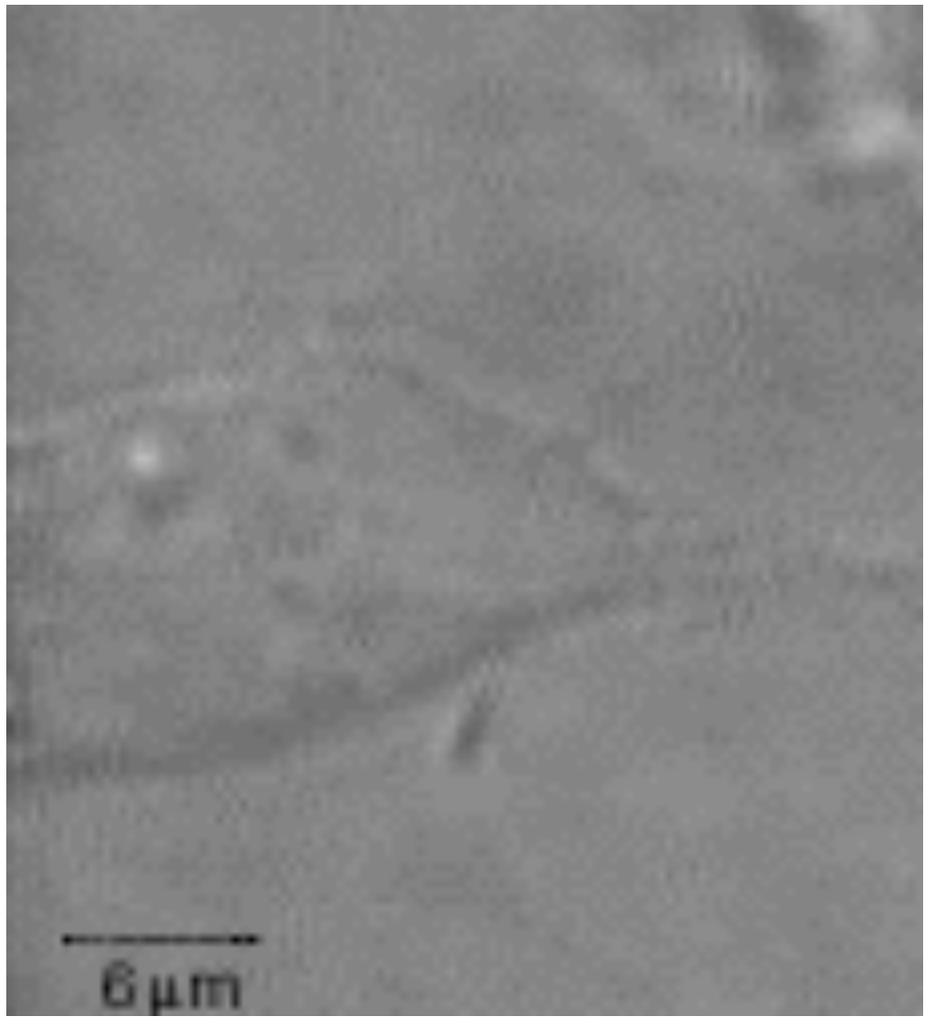


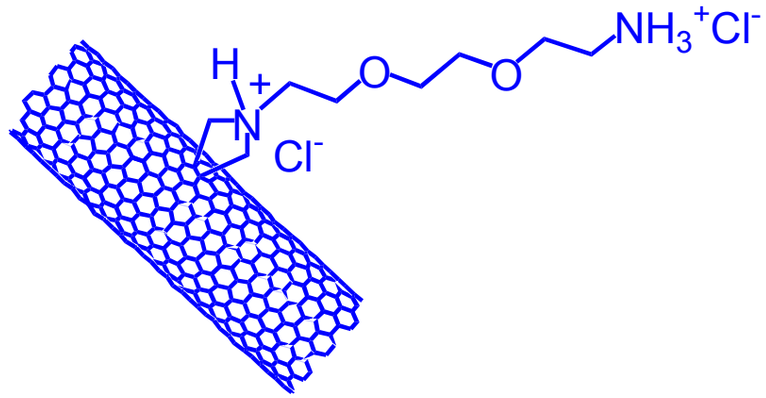


The CNT is approaching the cell surface moving on a perpendicular axis to the plasma membrane…

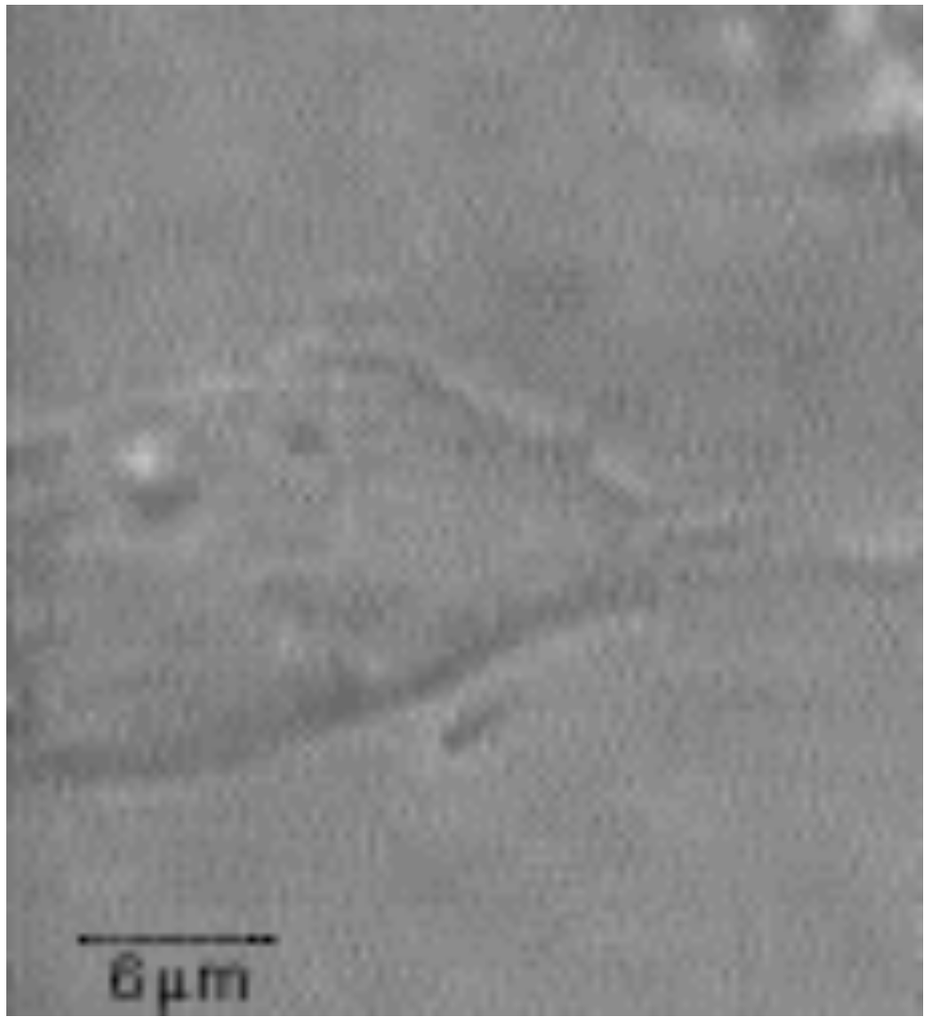

6 µm

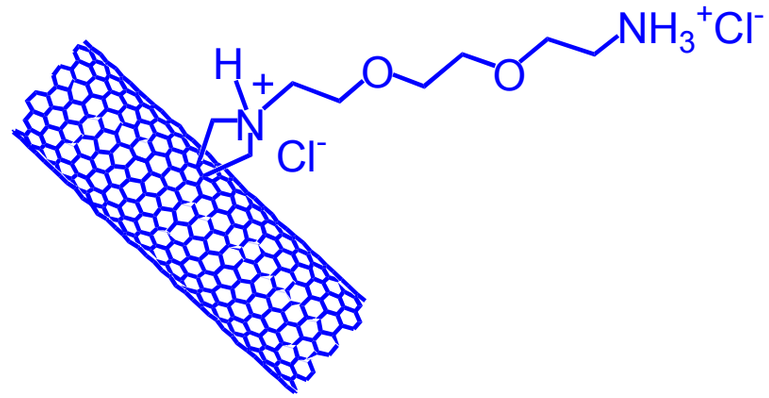

H
+
N
Cl-
O
O
NH3+Cl-



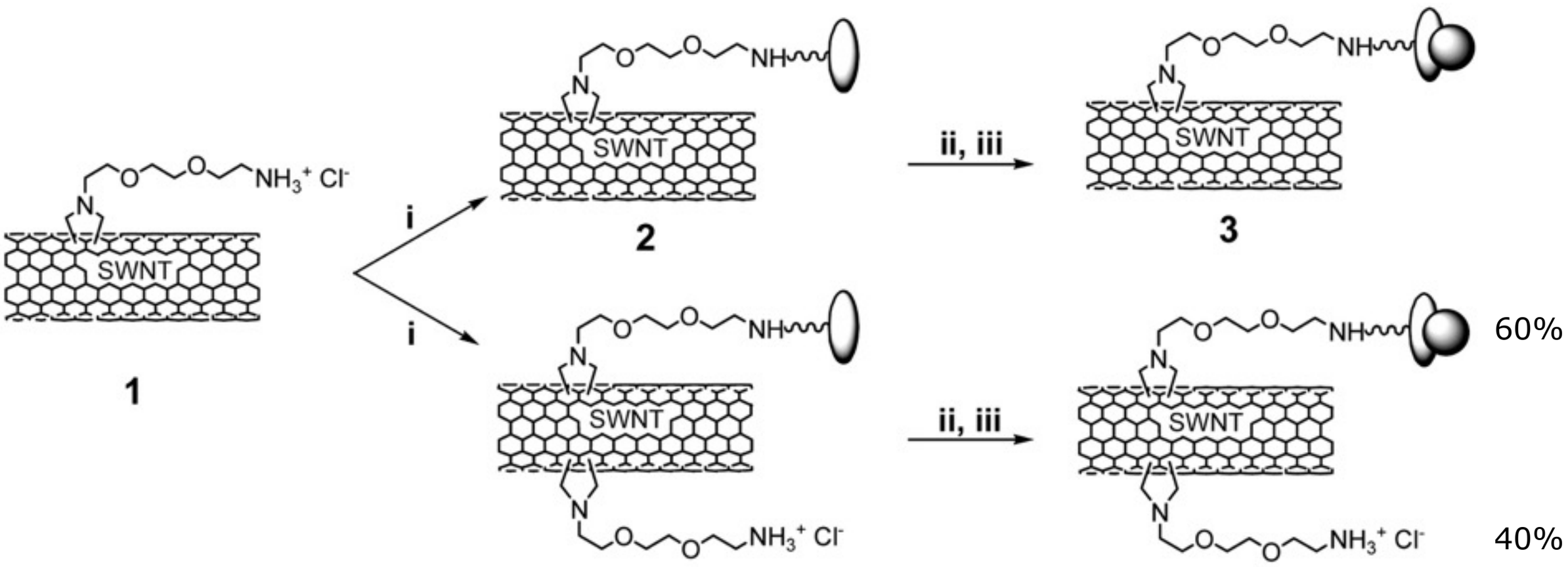


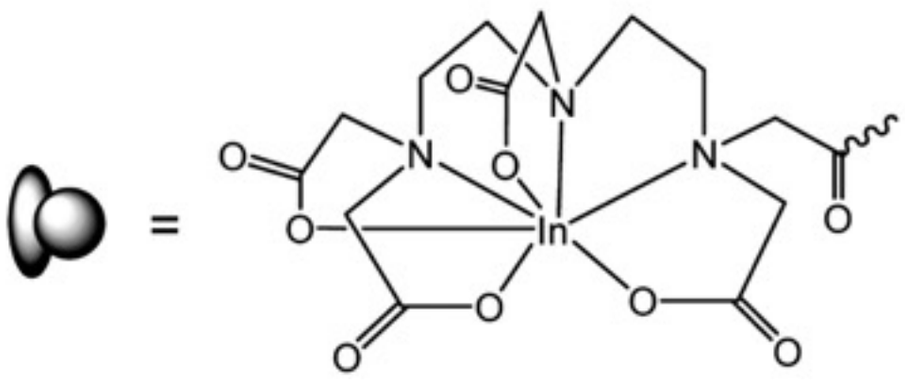
…and then re-aligning its position on a plane parallel to the plasma membrane


6 µm


H
+
N
Cl-
O
O
NH3+Cl-

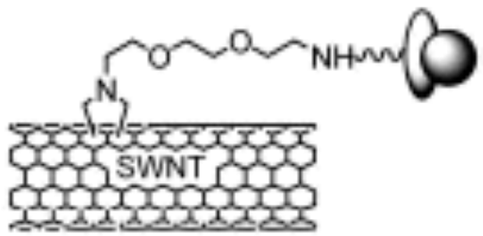
Preparation of [^{111}In]DTPA-SWNT for (i.v.) administration

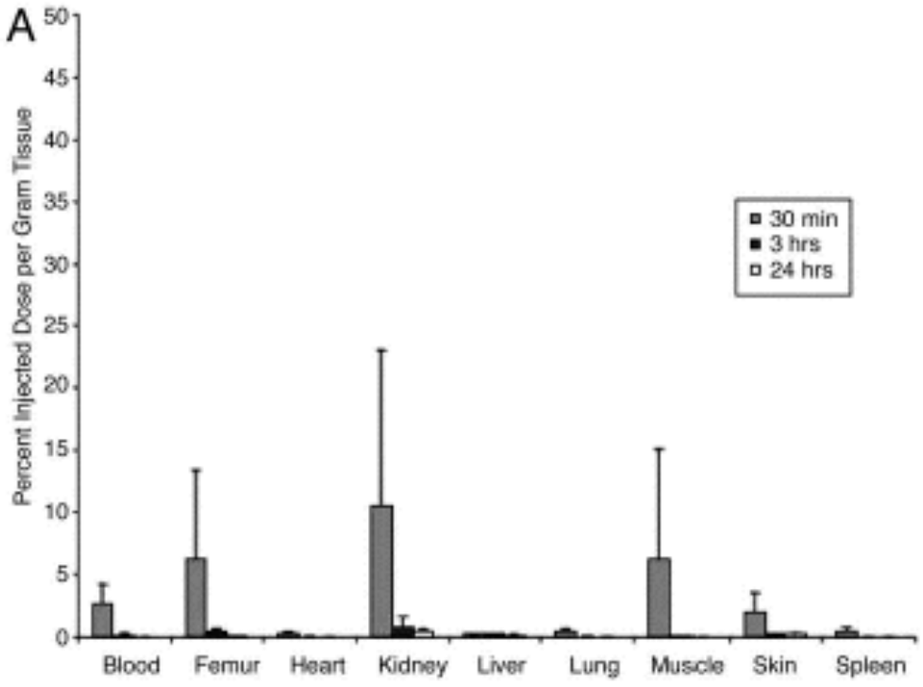


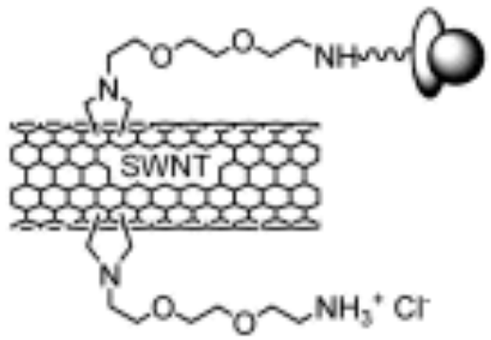


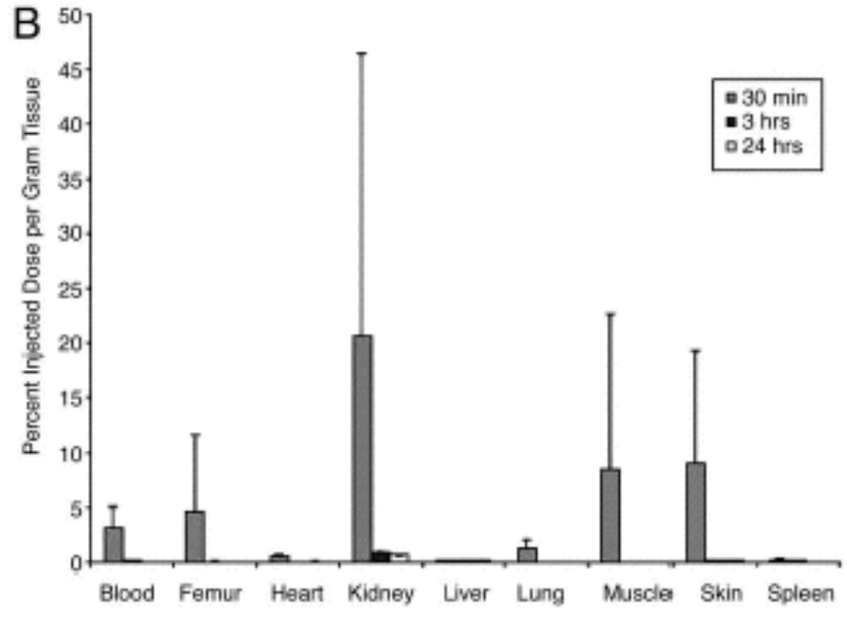
= [^{111}In]DTPA

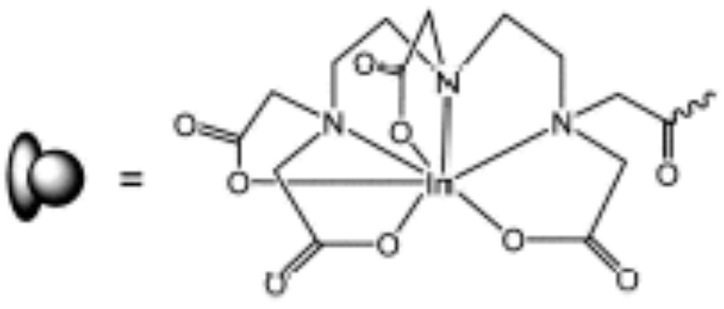
Biodistribution per collected gram of tissue of [^{111}In]DTPA-SWNT (i.v.)



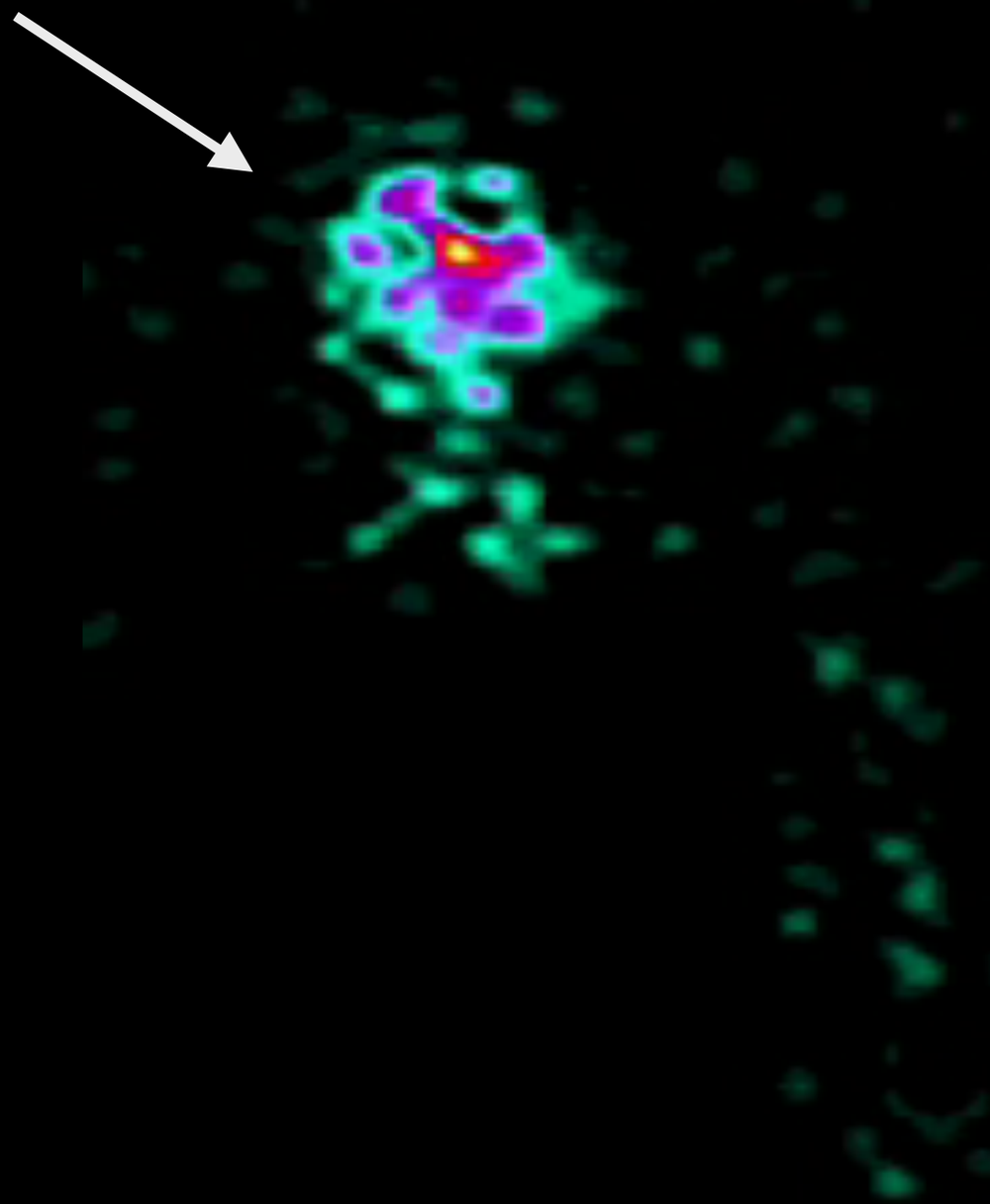




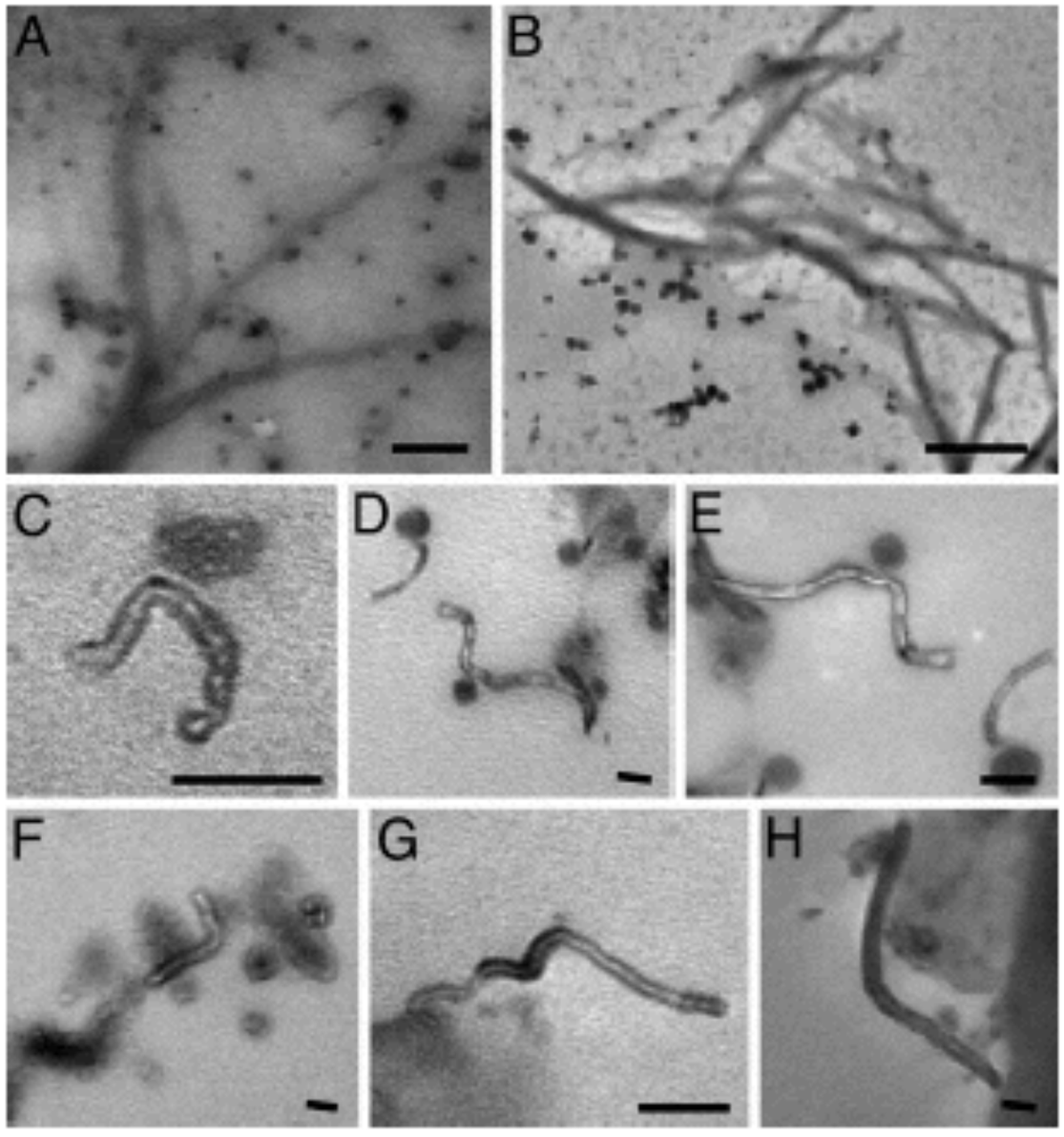




external reference



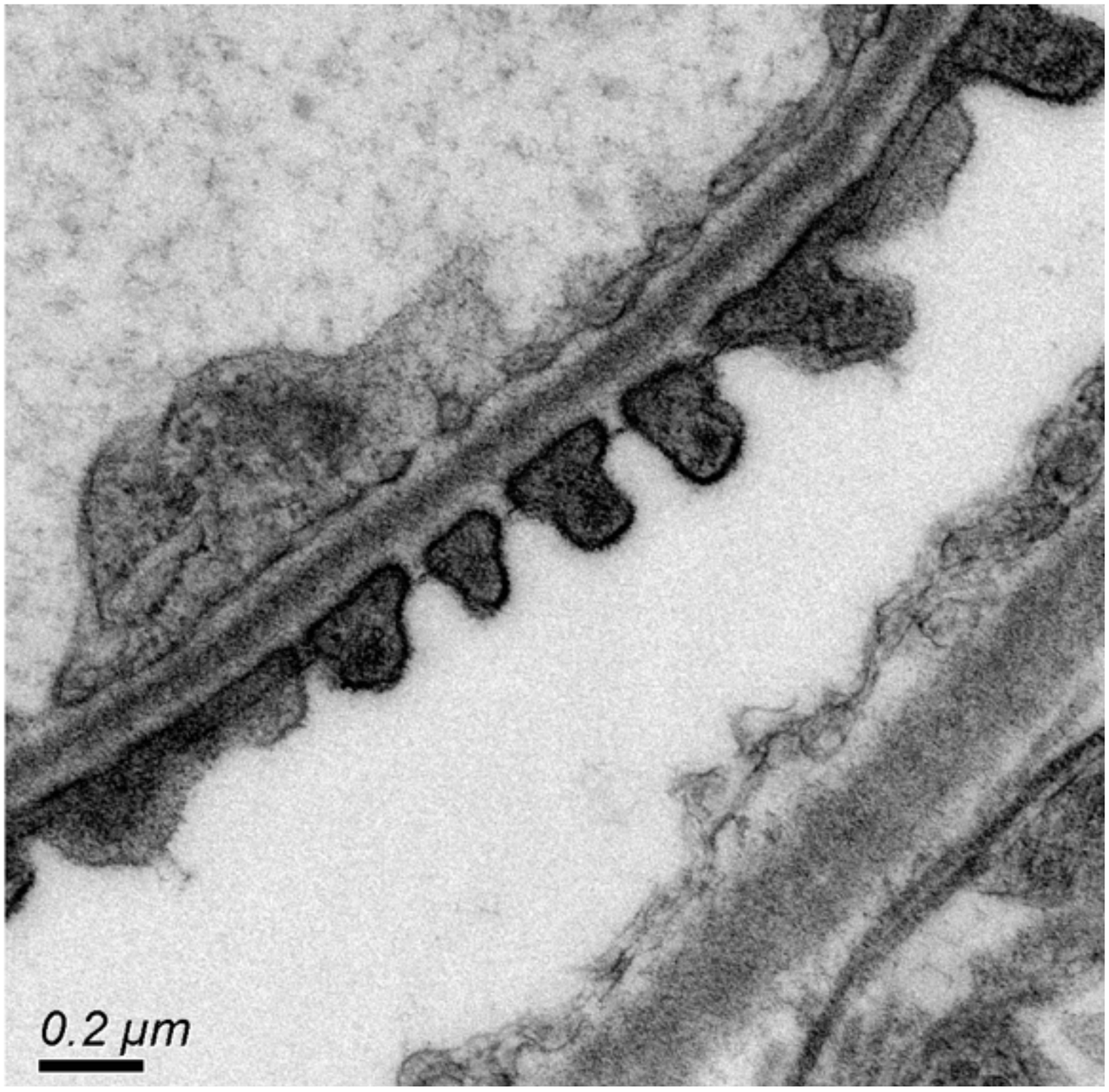
TEM images of excreted urine samples containing SWNT and MWNT DTPA



The urine samples were centrifuged, and both the supernatant and the precipitate were analyzed.
A-B: DTPA-SWNT from the supernatant (scale bar 500 nm); C-E DTPA-MWNT in the supernatant;
F-H: DTPA-MWNT from the precipitate (scale bars 100 nm).

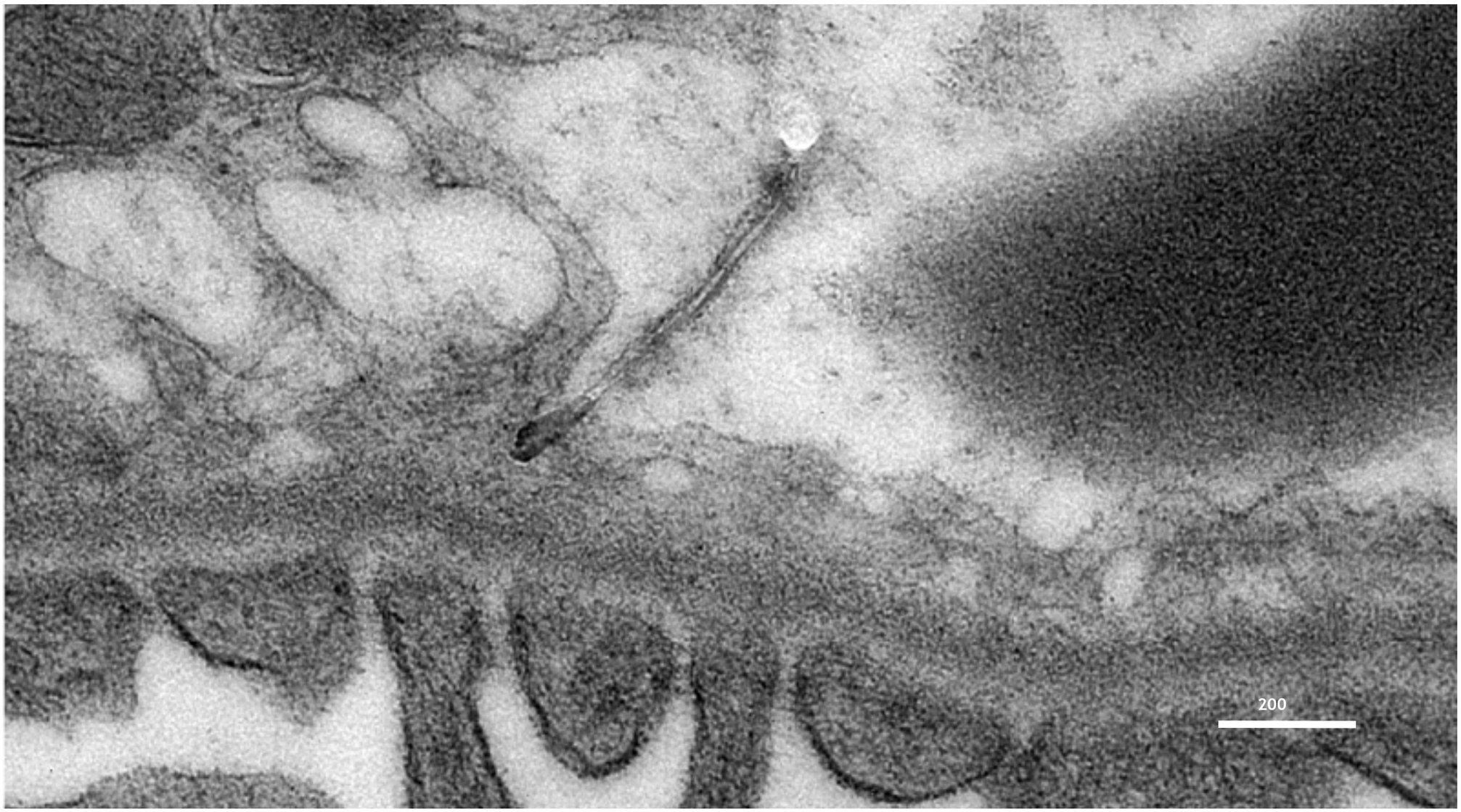
PNAS 2006

Mechanism of CNT Renal Excretion

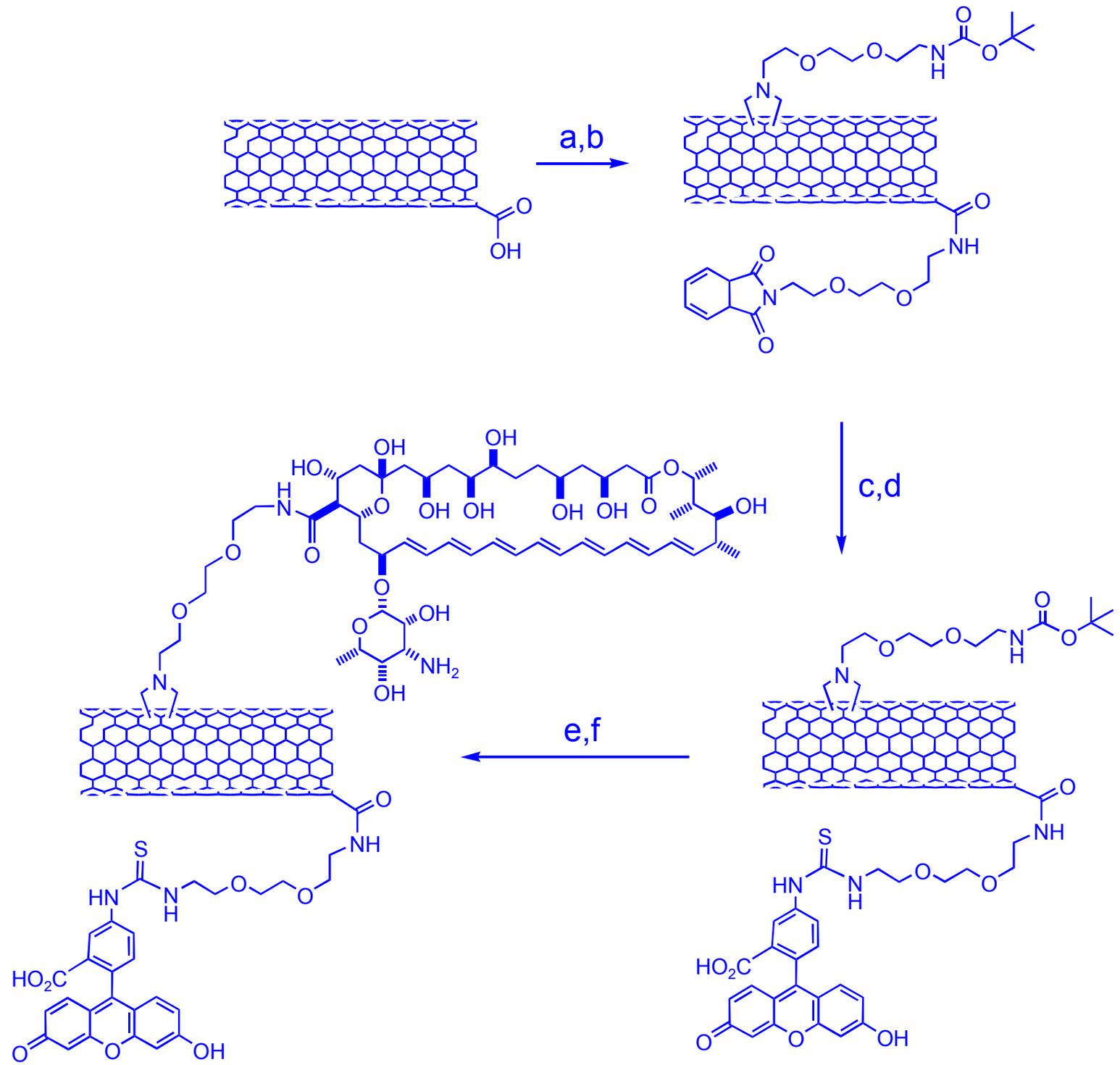


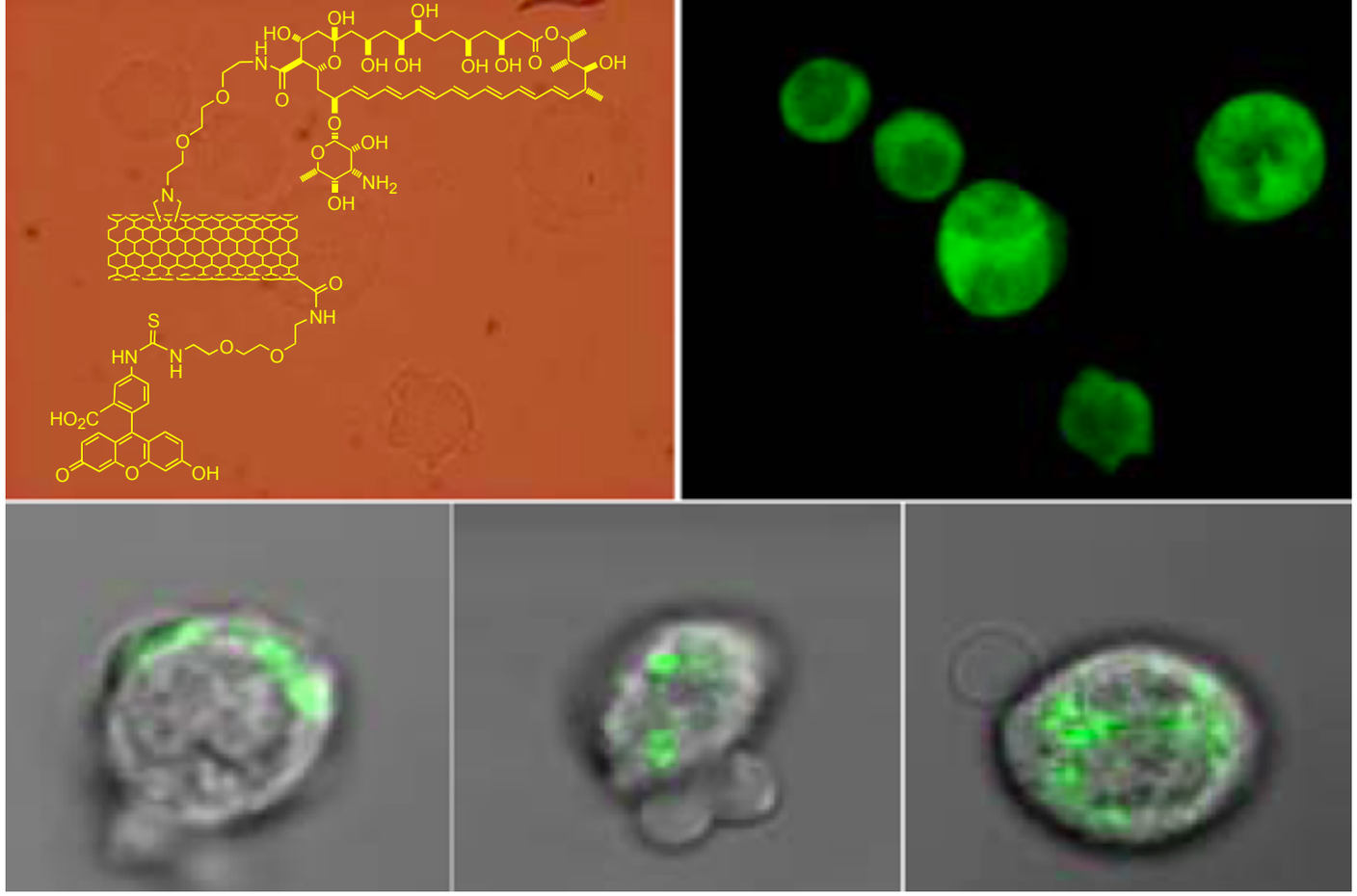
Mechanism of CNT Renal Excretion

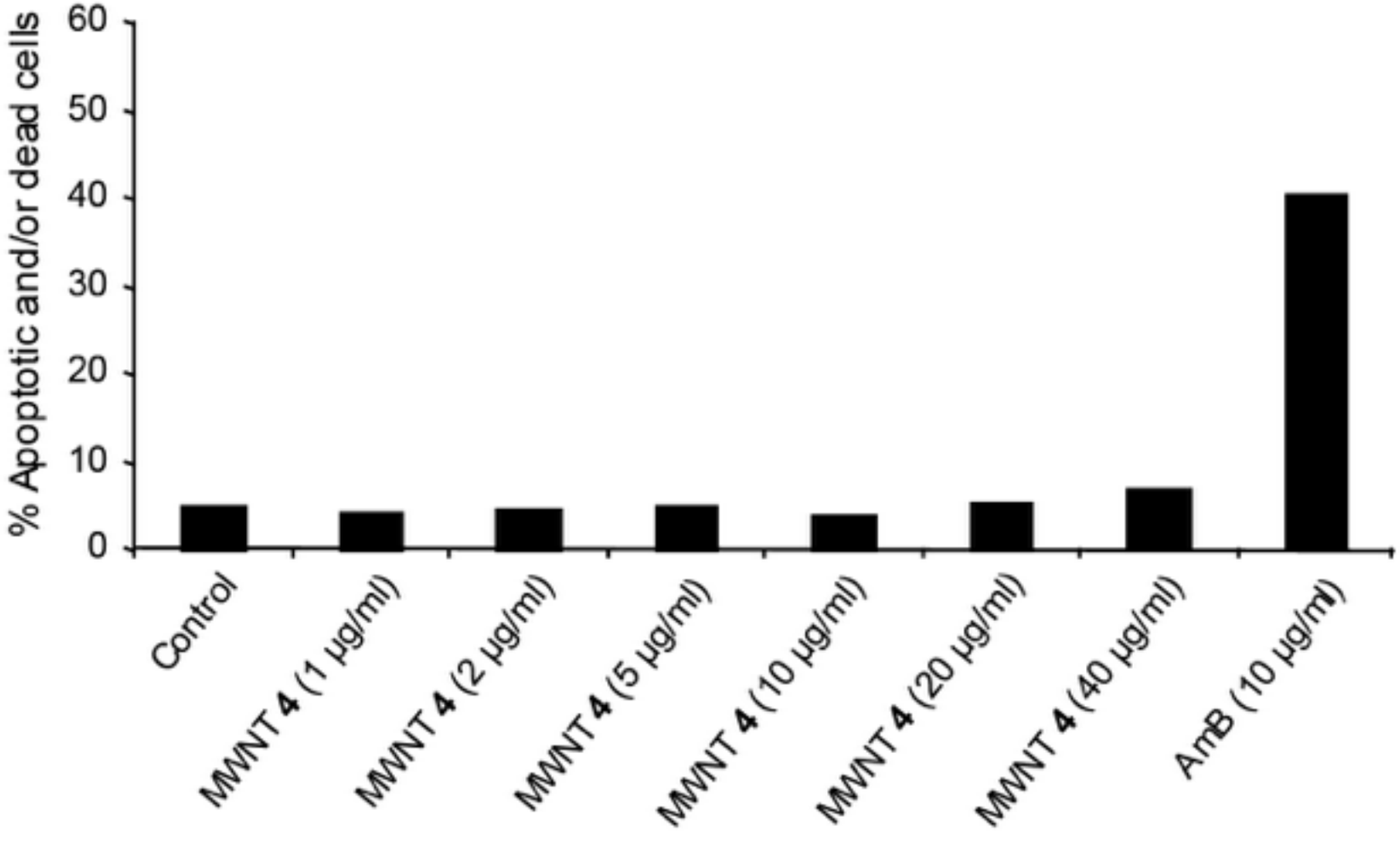
f-MWNT crossing the glomerular filter



Both amphotericin and a fluorophore on *f*-CNT




OH
HO
OH
OH OH
OH OH
O
OH
NH
O
O
O
O
OH
NH2
OH
N
O
S
HN
N
H
O
O
NH
HO2C
O
O
OH


% Apoptotic and/or dead cells
60
50
40
30
20
10
0
Control
MWNT 4 (1 μg/ml)
MWNT 4 (2 μg/ml)
MWNT 4 (5 μg/ml)
MWNT 4 (10 μg/ml)
MWNT 4 (20 μg/ml)
MWNT 4 (40 μg/ml)
AmB (10 μg/ml)

	Cryptococcus neoformans	Candida albicans	Saccharomyces cerevisiae	Rhodotorula rubra
1	**2.5**	**> 80**	**2.5**	**20**
2	**> 80**	**> 80**	**> 80**	**>80**
3	**2.5**	**20**	**2.5**	**5**
4	**2.5**	**40**	**5**	**5**

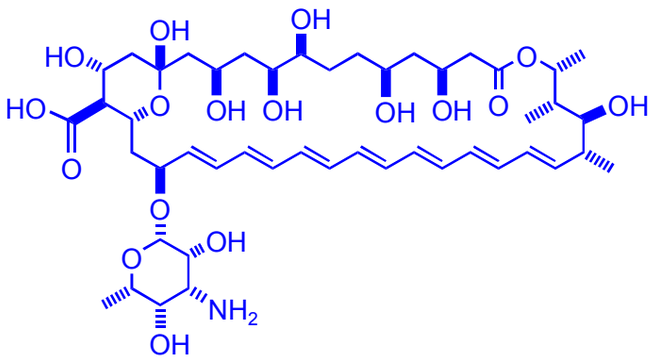
All the values are given in μg/mL and represent the MIC (minimal inhibitory concentration**)**

1 = AmB

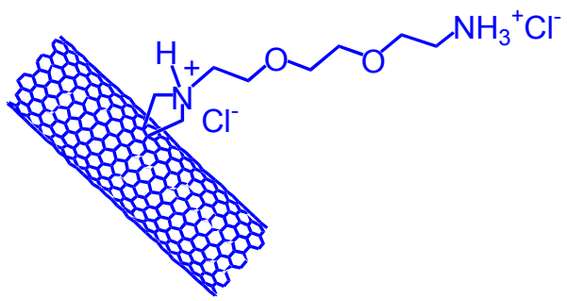
2 = SWNT-NH_3Cl

3 = MWNT-AmB; 2.6 mg loading 0.6 mmol/g, AmB about 25% of weight of MWNT-AmB

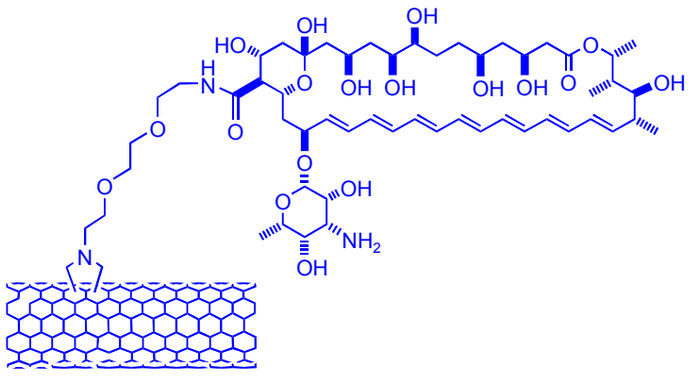
4 = SWNT-AmB; 2.3 mg loading 0.5 mmol/g, AmB about 25% of weight of SWNT-AmB



1



2



3,4

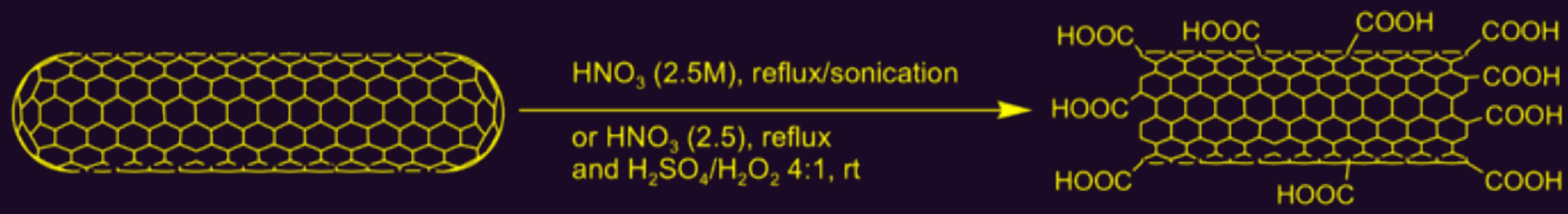
Angew. Chem. 2005

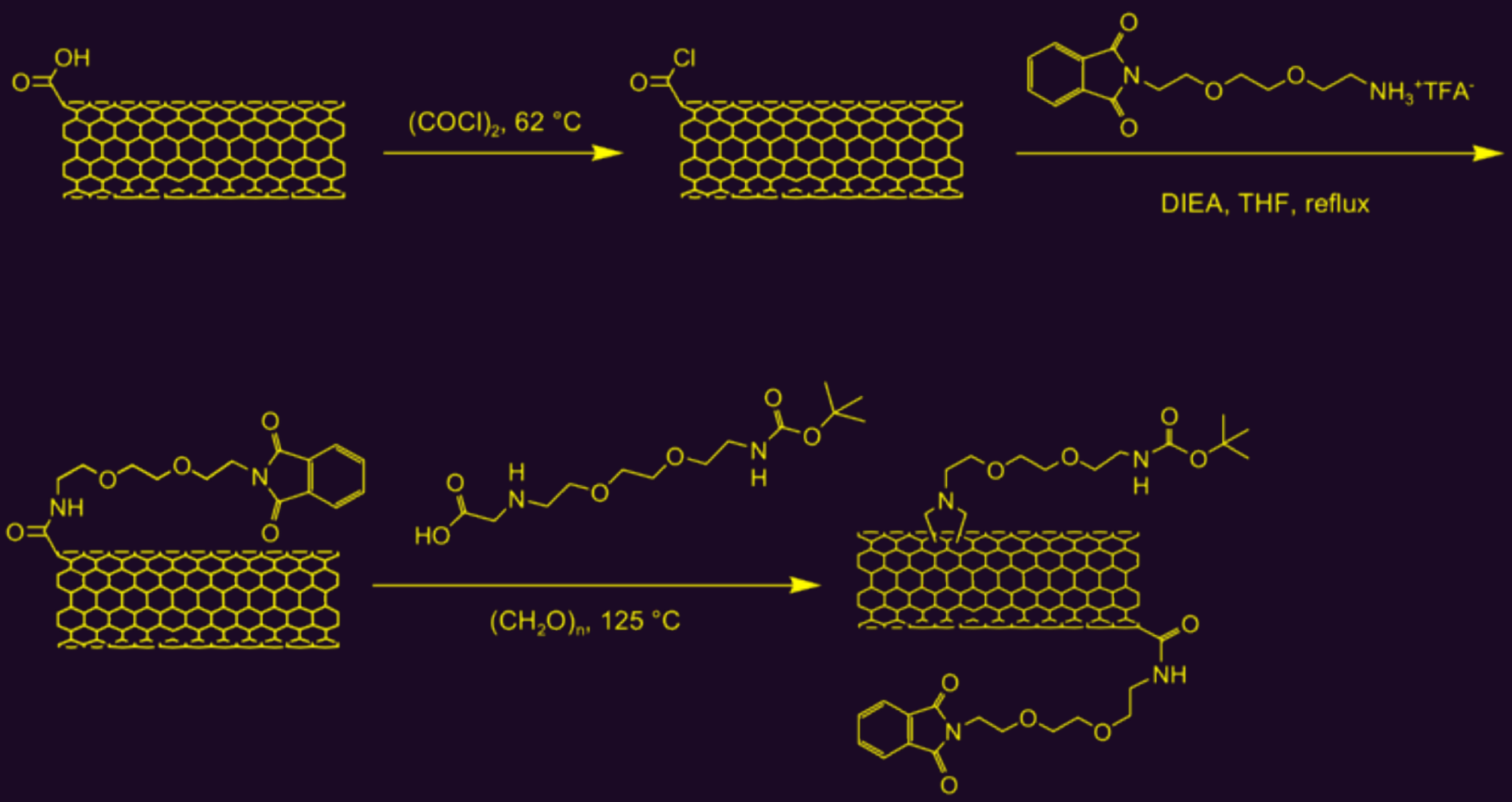
Antifungal activity of CNT–AmB conjugates

Fungal strain	MWNT-AmB	AmB
C. albicans ATCC 90029	10	> 80
C. albicans L21	10	> 80
C. parapsilosis ATCC 90118	2.5	5
C. parapsilosis L51	2.5	5
C. dubliniensis L70	2.5	1.25
C. tropicalis L42	1.25	2.5
C. lusitaniae 1557VC2	2.5	2.5
C.guillermondii EMAT S	2.5	2.5
C. famata M100	2.5	10
C. famata SA550	20	> 80

ACS Nano, 2010, with M. Benincasa and R. Gennaro

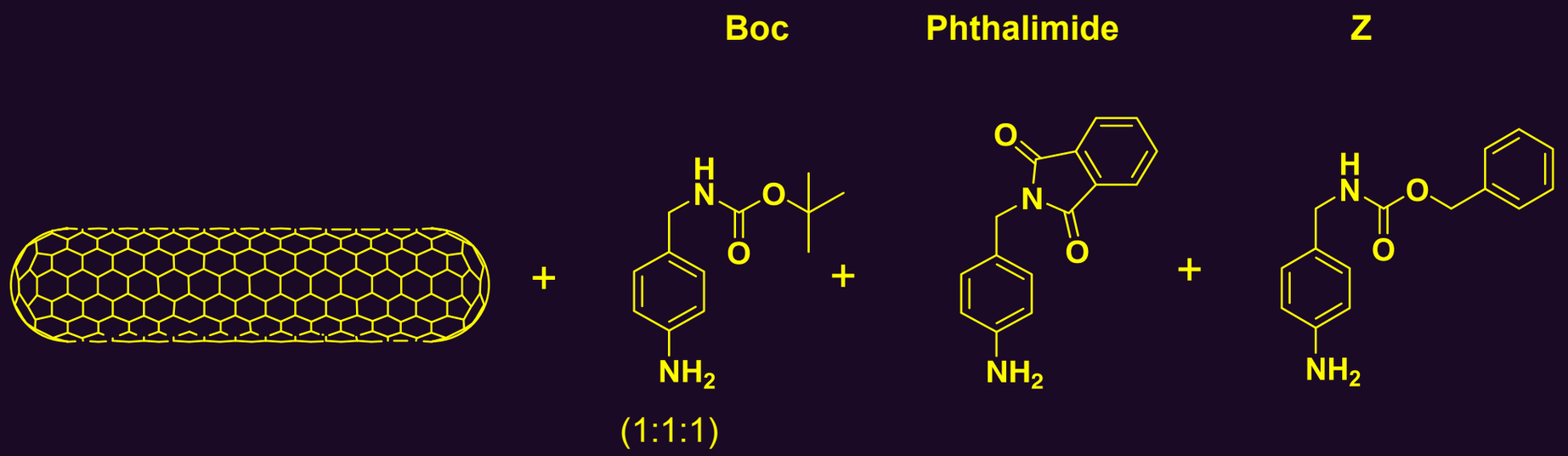
Double Functionalization of Carbon Nanotubes





Wu W et al. Angew. Chem. Int. Ed. 2005, 44, 6258

One-pot triple functionalization of carbon nanotubes



Arylation

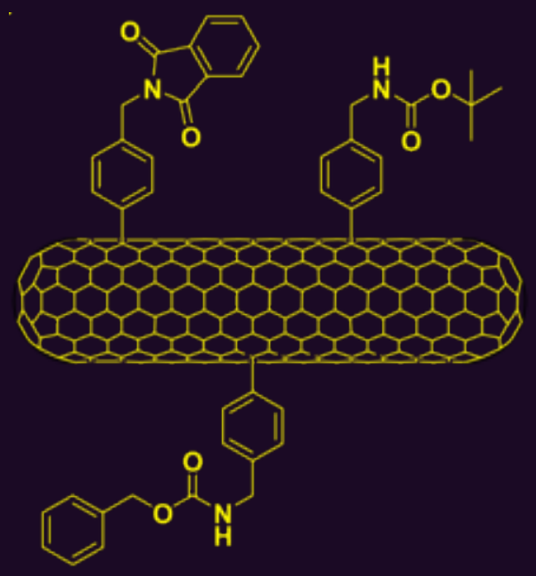
Isoamyl nitrite

o-Dichlorobenzene (ODCB)

Acetonitrile

60 °C, 24 h

In situ generation of diazonium salts

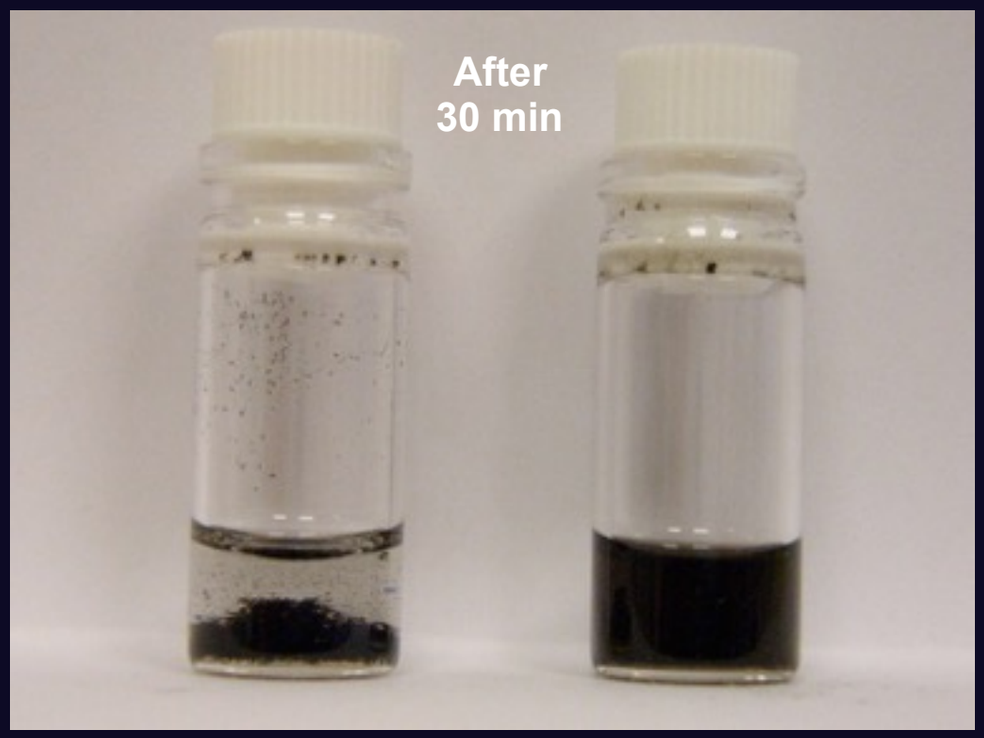


Ménard-Moyon C et al. Chem. Eur. J. 2011, 17, 3222

Characterization of trifunctionalized SWNTs

Solubility

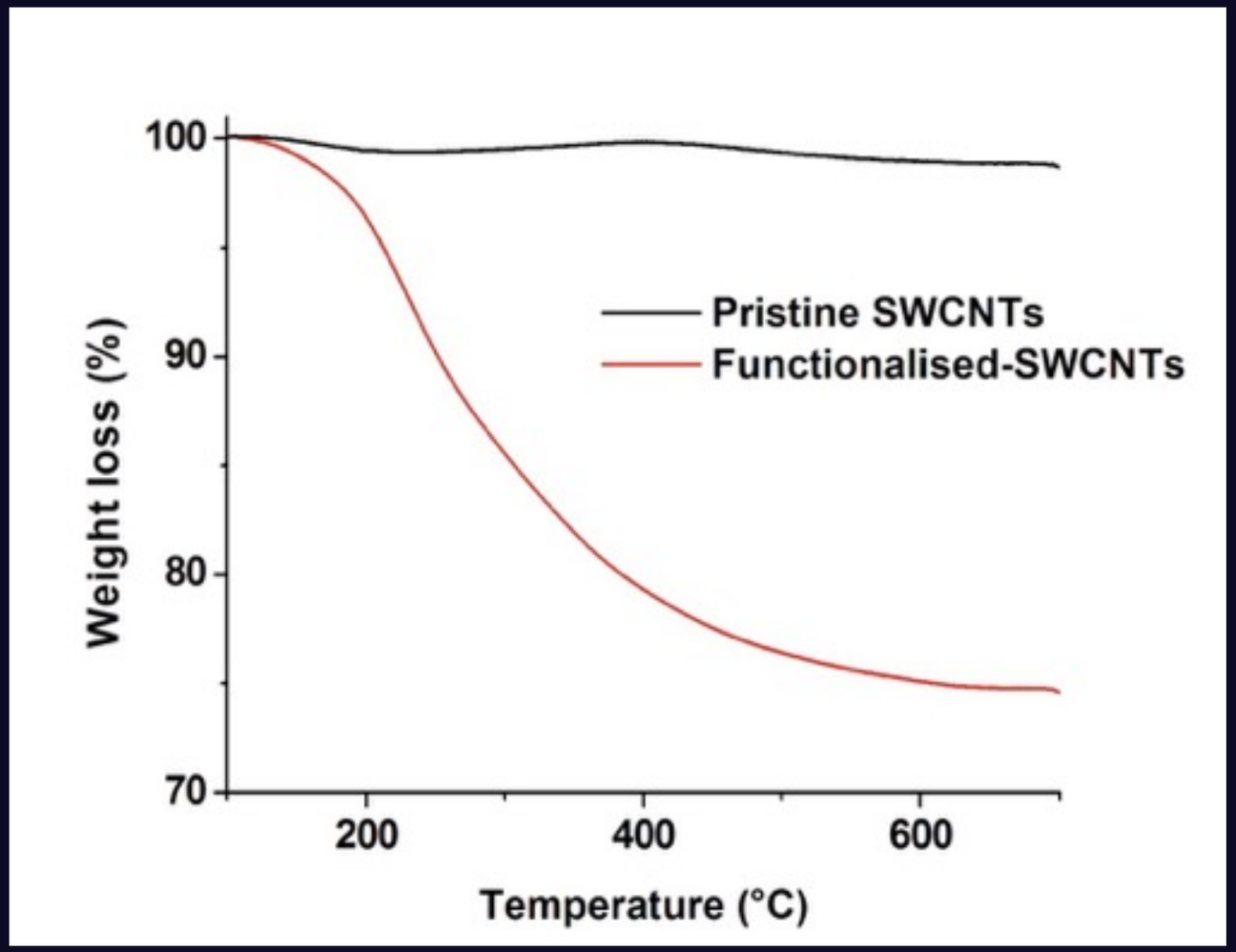
Sonication of CNTs in DMF (10 mg/mL)
for 1 min in a water bath



Pristine SWCNTs

Trifunctionalized SWCNTs

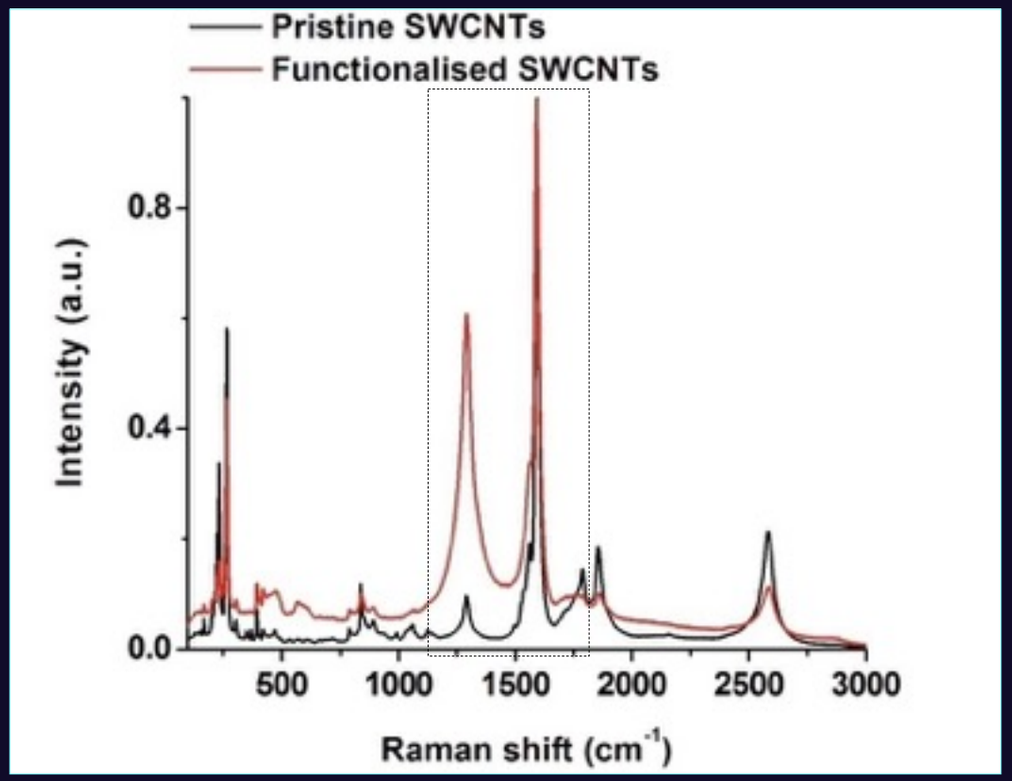
Thermogravimetric analysis (TGA)



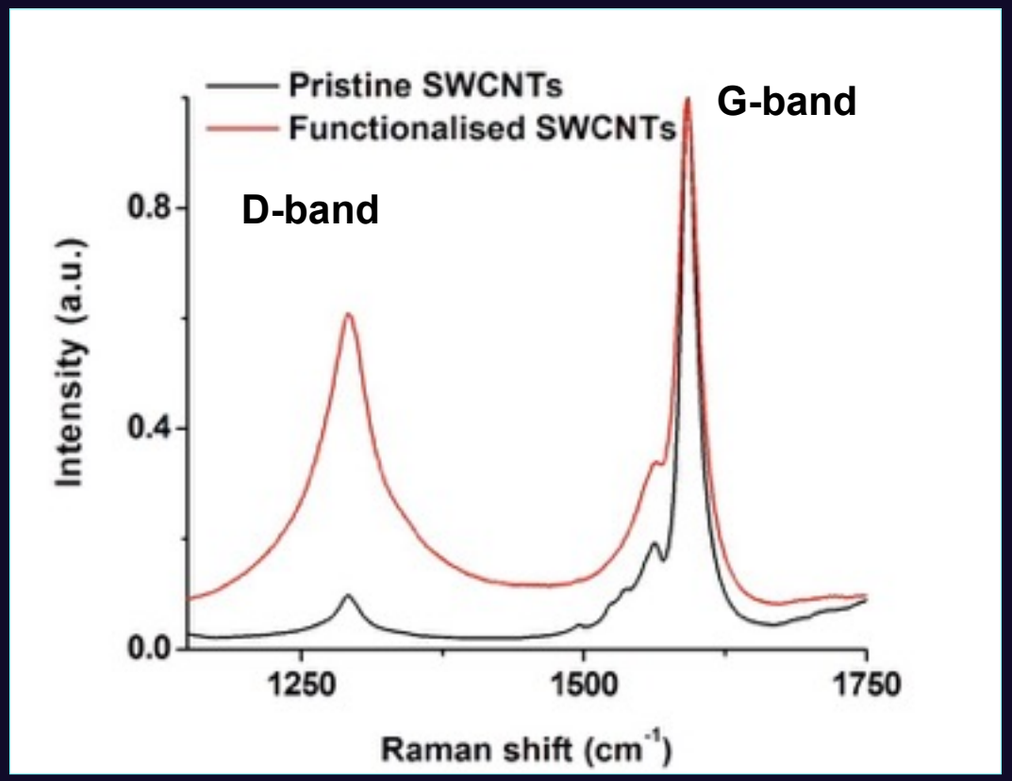
Ménard-Moyon C et al. Chem. Eur. J. 2011, 17, 3222

Characterization of trifunctionalized SWNTs
Raman spectroscopy: D-band

785 nm



785 nm

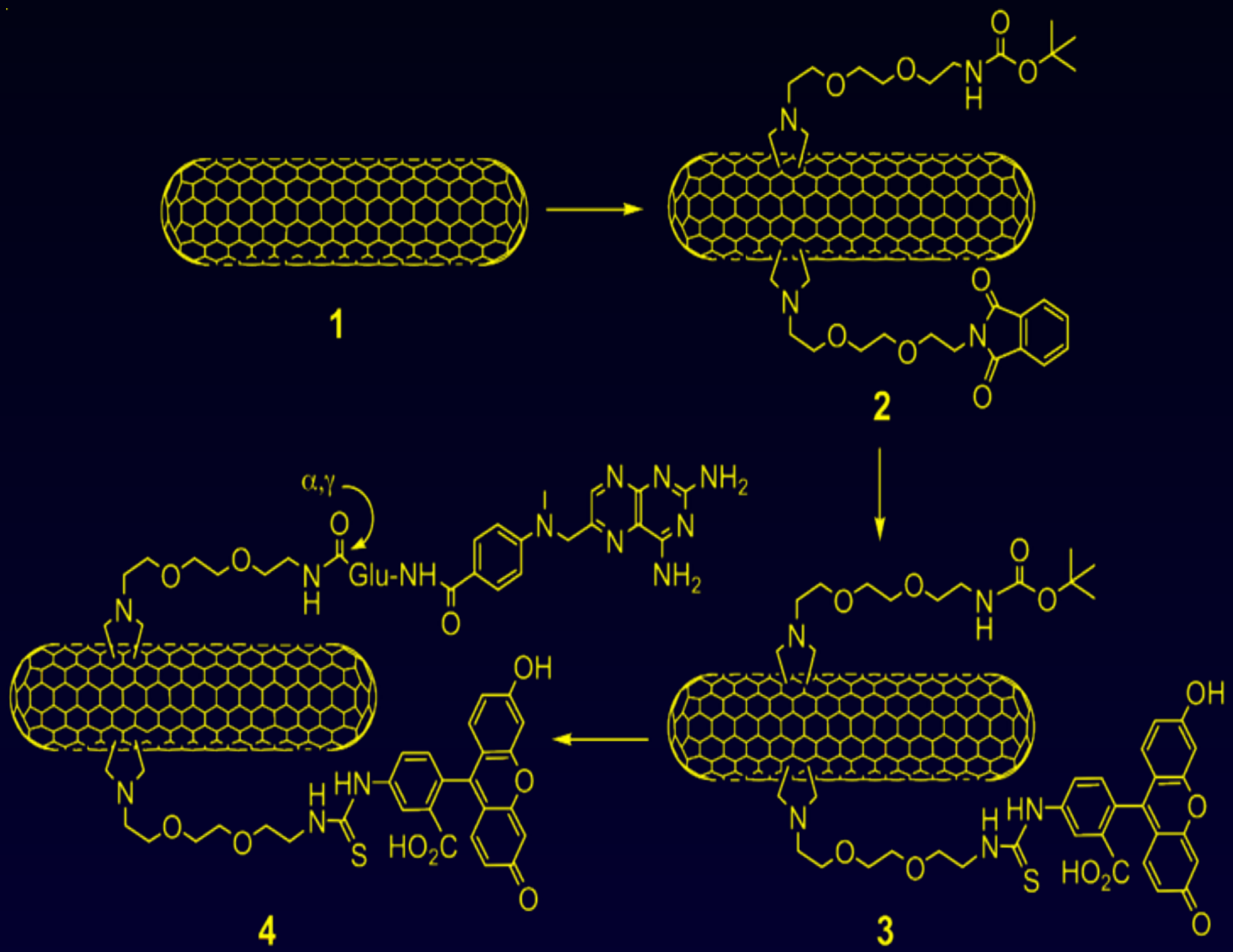


Increase of the relative intensity of the D-band

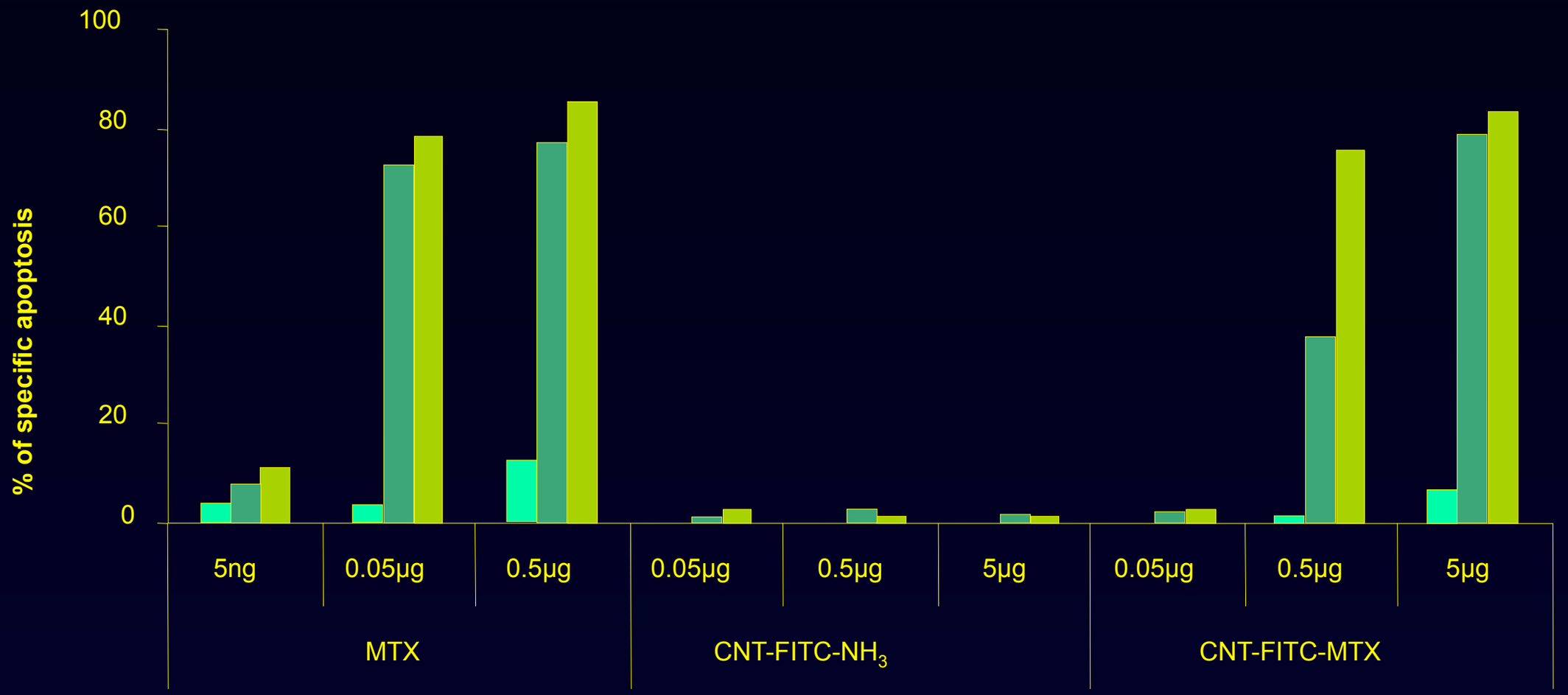
Functionalization is covalent

(Rehybridation of sp^2 to sp^3 carbon atoms)

Functionalization of Carbon Nanotubes with Anticancer Molecules: Methotrexate



Apoptotic Activity of CNT Functionalized with Methotrexate (human breast carcinoma, MCF-7)

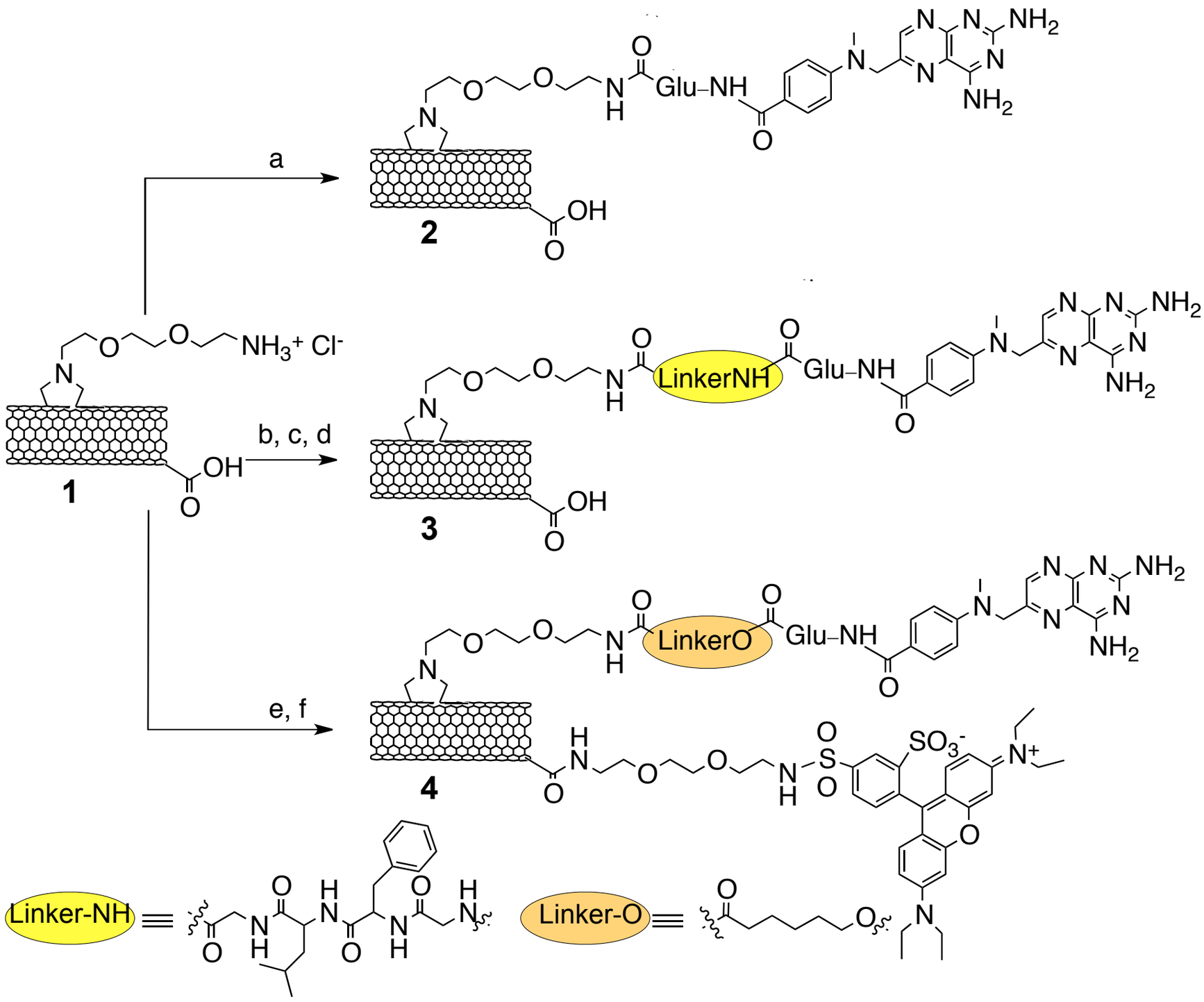


Apoptosis induced after 24 h

Apoptosis induced after 48 h

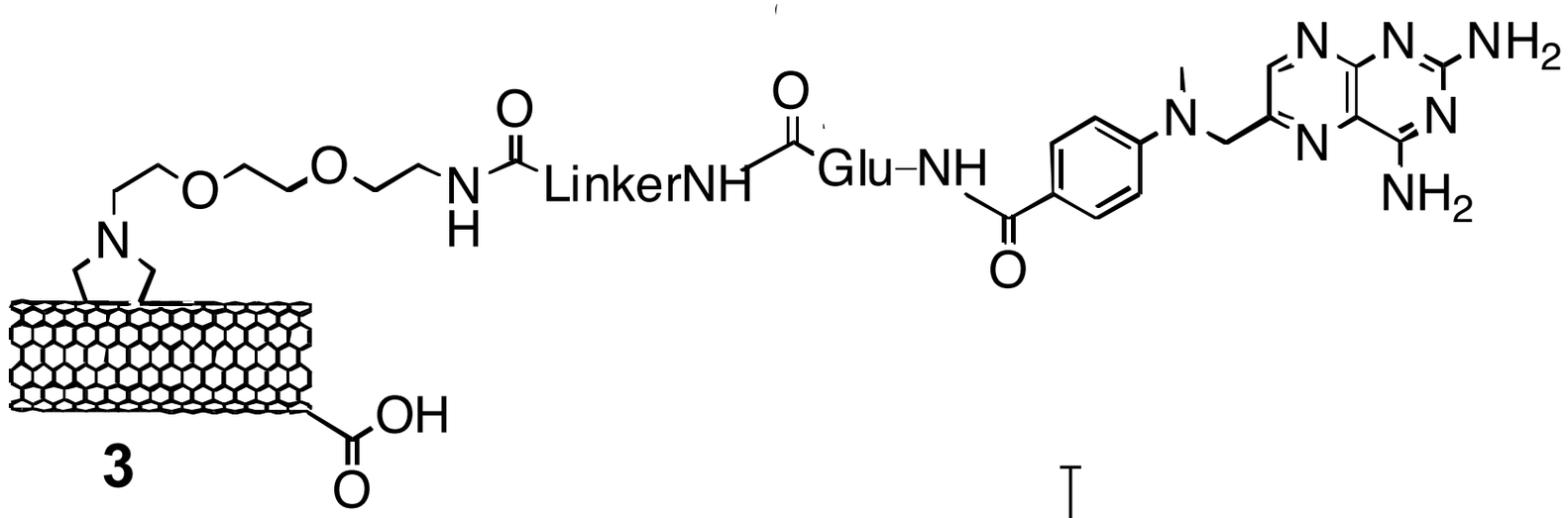
Apoptosis induced after 72 h

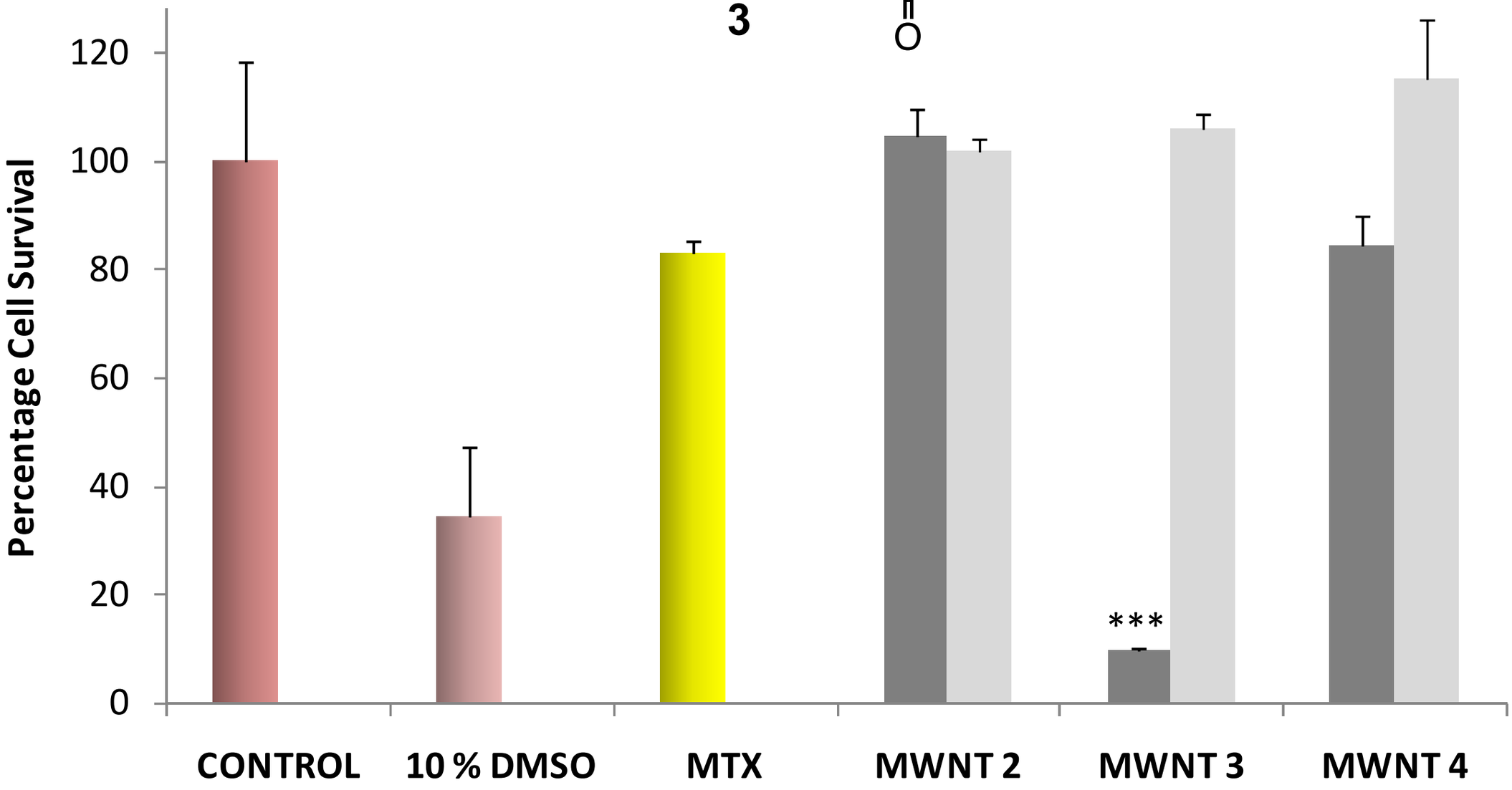
Synthesis of multi-walled carbon nanotube-methotrexate conjugates using cleavable linkers



This peptide linker is selectively cleaved by proteases over-expressed in tumor cells.

6-hydroxyhexanoic ester is an esterase–sensitive, hydrophobic spacer that has been widely used in prodrug conjugate synthesis.





Cell survival of MCF-7 cells after treatment with MWNT conjugates **2-4** for 24 h (dark grey bars). MTX concentration was kept constant at 10 μM with and without MWNTs. Light grey bars correspond to the cytotoxicity effects of MWNT **1** devoid of the drug used as control at the same dose of the related MWNT-MTX conjugate. 10 % DMSO was used as a positive control for cytotoxicity. *** indicate statistical significance ($p<0.005$) between MWNT **3** and MTX alone