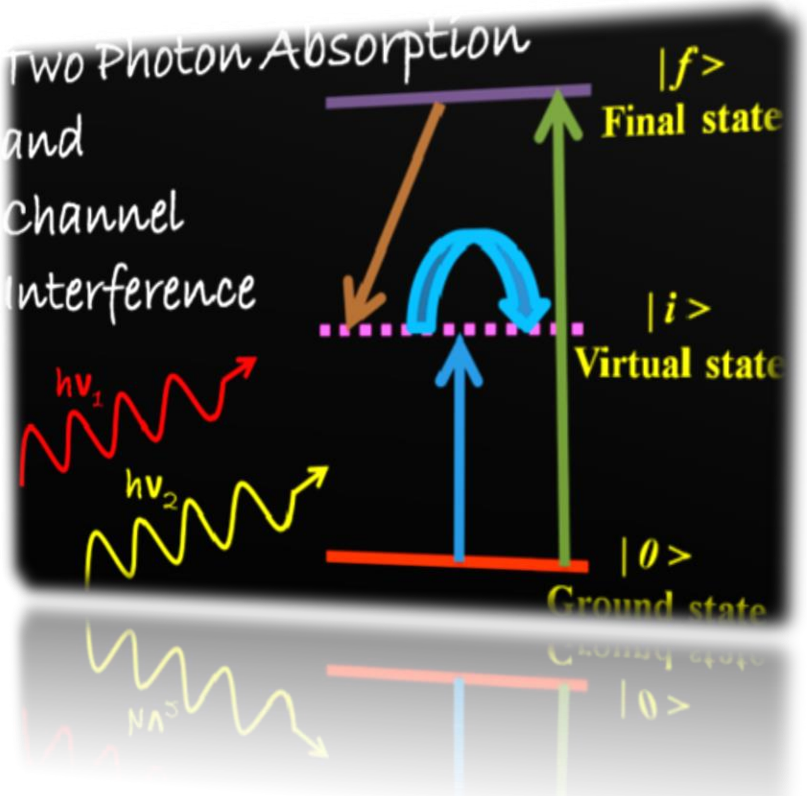
---Literature Reports

Small-Molecule Two-Photon Dyes

1. Two-photon materials： Structure–property relationship

2. Small-Molecule Two-Photon Probes for Bioimaging Applications



Reporter：Qinglong Qiao
Date：2020.07.23

What are two-photon dyes

Nonlinear optics: *induce TP absorption.*

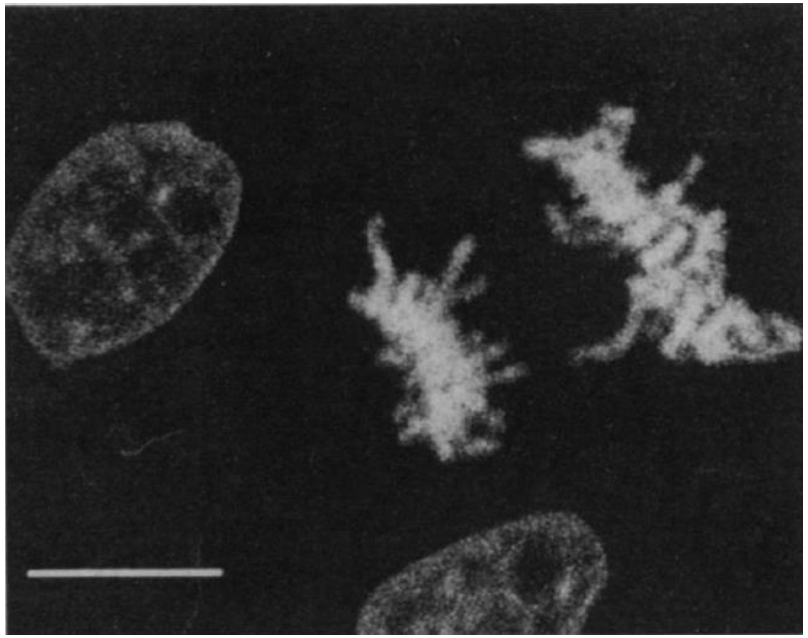
S_1

Two-Photon Laser Scanning Fluorescence Microscopy

WINFRIED DENK,* JAMES H. STRICKLER, WATT W. WEBB

Molecular excitation by the simultaneous absorption of two photons provides intrinsic three-dimensional resolution in laser scanning fluorescence microscopy. The excitation of fluorophores having single-photon absorption in the ultraviolet with a stream of strongly focused subpicosecond pulses of red laser light has made possible fluorescence images of living cells and other microscopic objects. The fluorescence emission increased quadratically with the excitation intensity so that fluorescence and photobleaching were confined to the vicinity of the focal plane as expected for cooperative two-photon excitation. This technique also provides unprecedented capabilities for three-dimensional, spatially resolved photochemistry, particularly photolytic release of caged effector molecules.

S_0



Application of TPA:

3D optical memory; fluorescence microscopy; nanofabrication ; optical power limiting ; photodynamic therapy...

Different between OPA and TPA *advantages and disadvantages*

1. TPA cross sections

measured by the NLT method varied by orders of magnitude depending on the pulse width

OPA	ε	L mol^{-1} cm^{-1}
TPA	δ	

$$\mathrm{TPA}(N_2) \propto \delta I^2$$

δ TPA in Göppert-Mayer units

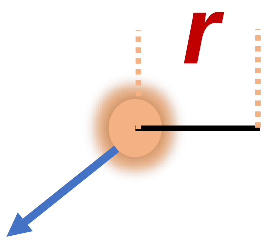
(1 GM = 10^{-50} cm^4 s $photon^{-1}$ $molecule^{-1}$)

Optics Express, 2008,16, 4029

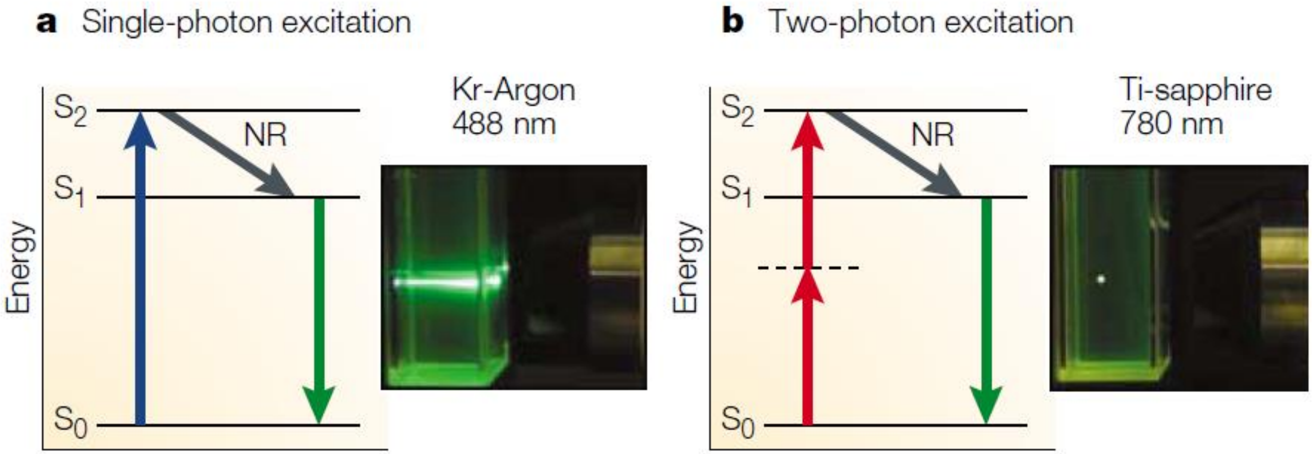
2. Spatial resolution

OPA efficiency → $1/r^2$

TPA efficiency → $1/r^4$

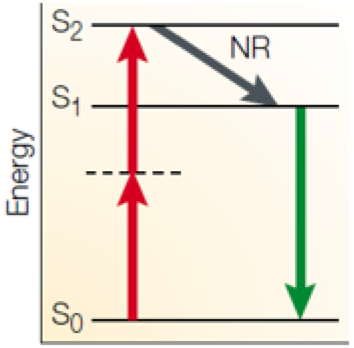


Focal point



Different between OPA and TPA *advantages and disadvantages*

3. Laser (Excitation)



Transmit deepness $\propto \lambda^4$

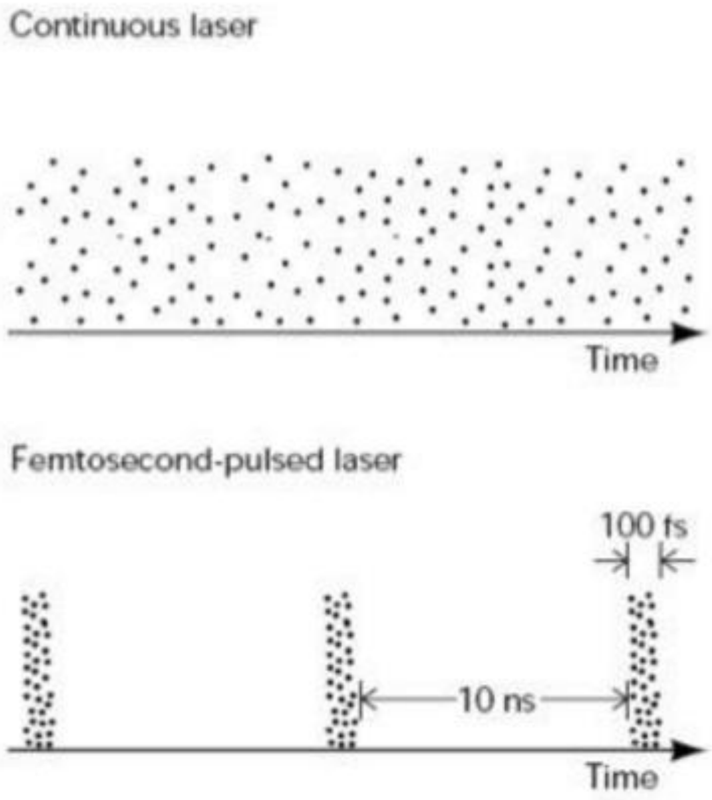
500 nm *vs* 800 nm **1:6.6**

•Suitable for tissue imaging

$$n(1)/n(2) = 2[\varepsilon(\nu)/\delta(\nu)](h\nu/I),$$

ε $\sigma=(\nu) = 10^4\ M^{-1}cm^{-1}$,
$\delta(\nu)$ = 100 GM, and I = 10 GW/cm^2, indicating that a maximum laser excitation greater than

10 GW/cm2



W/cm^2

M-GW/cm^2

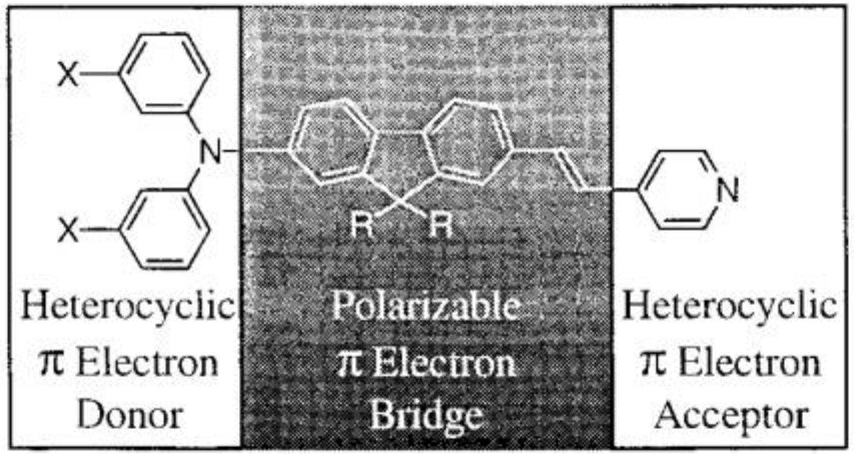
Ideal TP Dyes

donor–bridge–acceptor (D–π–A) dipoles

donor–bridge–acceptor (D–π–A) dipoles
donor–bridge–donor (D–π–D) and donor–acceptor–donor (D–A–D) quadrupoles, Octupoles

triphenylamine, paracyclophanes, multi-annulenes, and porphyrins

Chem. Commun., 2009, 153–164 review



Chem. Mater., 1998, 10, 1863–1874

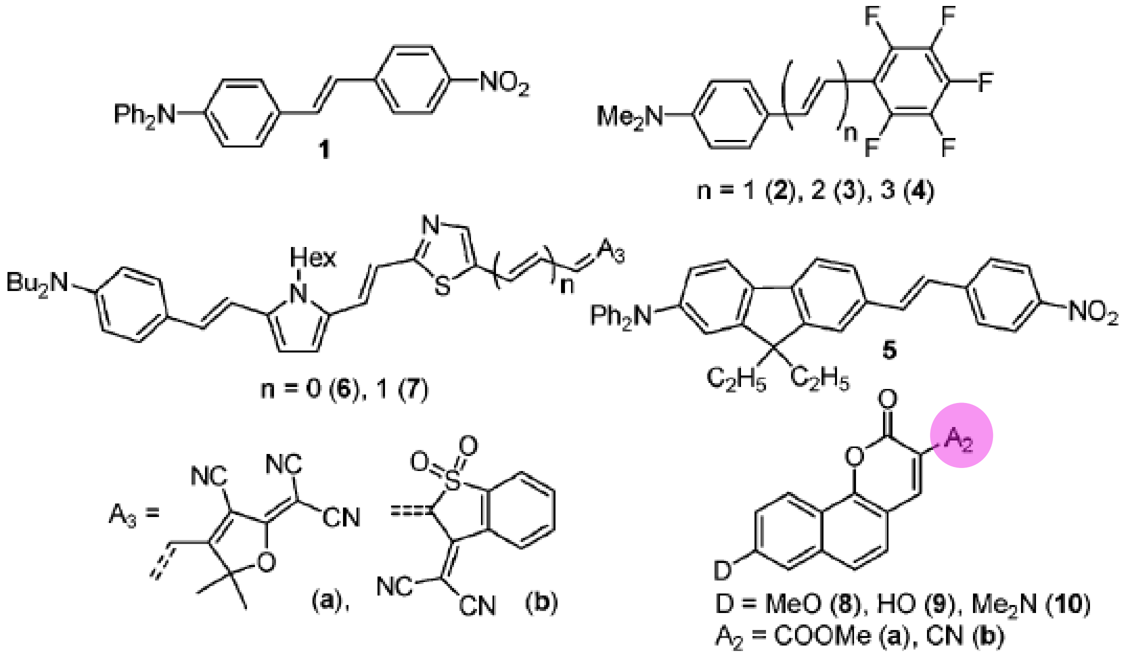


Table 1 Photophysical data for **1–10**[a]

Cpd	Solvent	$\lambda_{max}^{(1)}$ [b]	λ_{max}^{fl} [c]	Φ [d]	$\lambda_{max}^{(2)}$ [e]	δ_{max} [f]
1	THF	431	583		840[h]	125
2	Toluene	370	439	0.022	750	120
3	Toluene	396	479	0.025	825	300
4	Toluene	412	525	0.026	850	500
5	MeCN	410			670[i]	1300
6a	THF	718				1420
7a	THF	691				1500
7b	CH_2Cl_2	850				1200
8a	H_2O	391	481	0.82	780	140
9a	H_2O	397	482, 551	0.48	780	270
10a	H_2O	453	570	0.19	880	350
10b	H_2O	457	590	0.050	940	470

Ideal TP Dyes

Quadrupolar molecules D–π–D, D–A–D, A–π–A

Stilbene derivatives

Design of Organic Molecules with Large Two-Photon Absorption Cross Sections

Marius Albota, David Beljonne, Jean-Luc Brédas,* Jeffrey E. Ehrlich, Jia-Ying Fu, Ahmed A. Heikal, Samuel E. Hess, Thierry Kogej, Michael D. Levin, Seth R. Marder,* Dianne McCord-Maughon, Joseph W. Perry,* Harald Röckel, Mariacristina Rumi, Girija Subramaniam, Watt W. Webb,* Xiang-Li Wu, Chris Xu

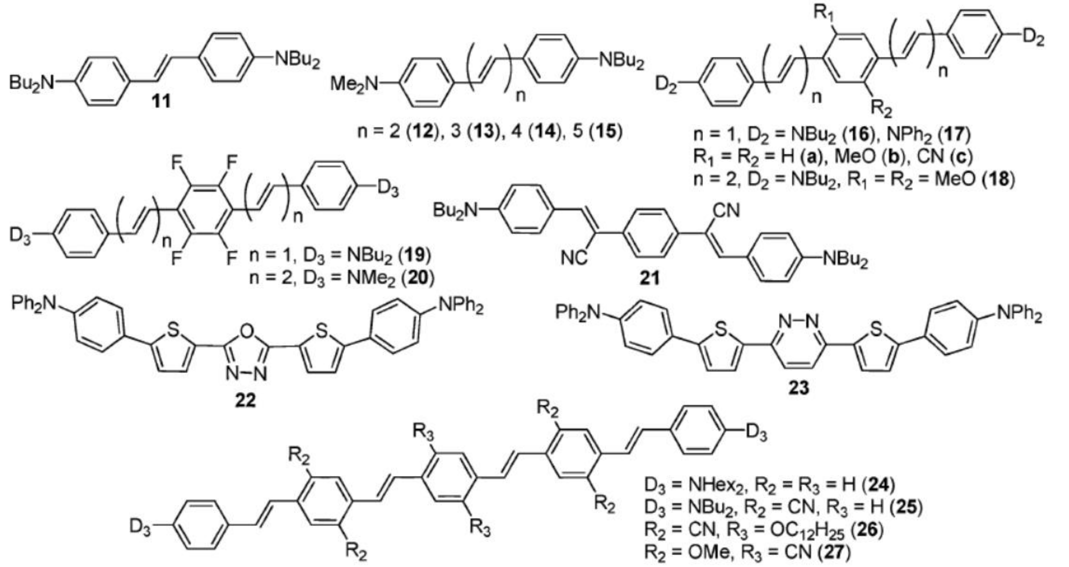
A strategy for the design of molecules with large two-photon absorption cross sections, δ, was developed, on the basis of the concept that symmetric charge transfer, from the ends of a conjugated system to the middle, or vice versa, upon excitation is correlated to enhanced values of δ. Synthesized bis(styryl)benzene derivatives with donor-π-donor, donor-acceptor-donor, and acceptor-donor-acceptor structural motifs exhibit exceptionally large values of δ, up to about 400 times that of *trans*-stilbene. Quantum chemical calculations performed on these molecules indicate that substantial symmetric charge redistribution occurs upon excitation and provide δ values in good agreement with experimental values. The combination of large δ and high fluorescence quantum yield or

Science,1998, 281, 1653–1656.

Structure−Property Relationships for Two-Photon Absorbing Chromophores: Bis-Donor Diphenylpolyene and Bis(styryl)benzene Derivatives

Mariacristina Rumi,[†] Jeffrey E. Ehrlich,[‡] Ahmed A. Heikal,[‡] Joseph W. Perry,[*,†,§] Stephen Barlow,[‡] Zhongying Hu,[‡] Dianne McCord-Maughon,[‡] Timothy C. Parker,[†] Harald Röckel,[‡] Sankaran Thayumanavan,[†,‡] Seth R. Marder,[*,†,§] David Beljonne,[⊥] and Jean-Luc Brédas[†,⊥]

J. Am. Chem. Soc. 2000, 122, 9500-9510



16a	Toluene	408	455	0.88	730[h] (725)	995 (635)
16b	Toluene	428	480	0.88	730[h] (715)	900 (680)
16c	Toluene	490	536	0.69	830[h] (830)	1750

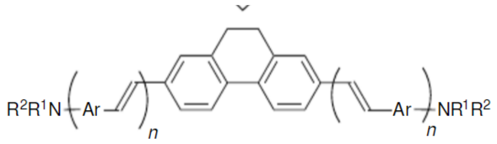
Ideal TP Dyes

Quadrupolar molecules D–π–D, D–A–D, A–π–A

Fluorene and dihydrophenanthrene derivatives

Nanoscale Push–Push Dihydrophenanthrene Derivatives as Novel Fluorophores for Two-Photon-Excited Fluorescence**

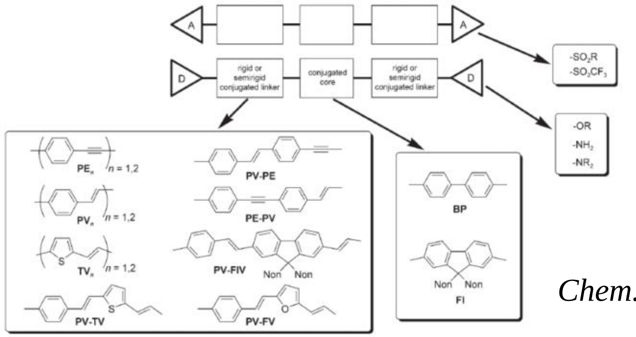
Lionel Ventelon, Sandrine Charier, Laurent Moreaux, Jerome Mertz, and Mireille Blanchard-Desce*



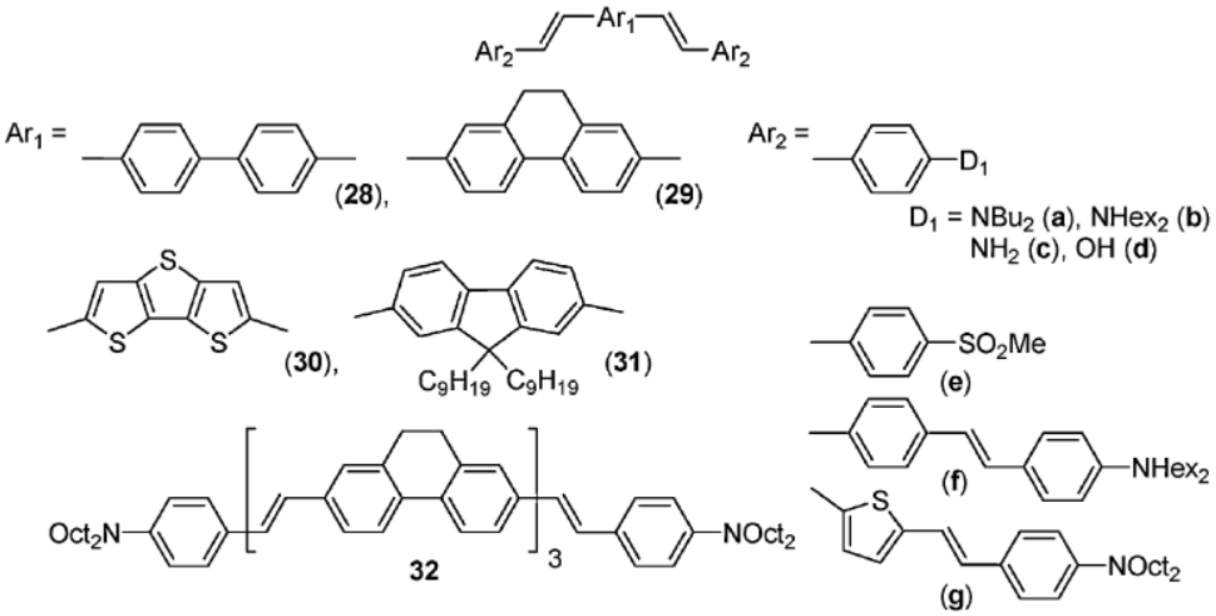
Angew. Chem., Int. Ed., 2001, 40, 2098–2101

Synthesis, Fluorescence, and Two-Photon Absorption of a Series of Elongated Rodlike and Banana-Shaped Quadrupolar Fluorophores: A Comprehensive Study of Structure–Property Relationships

Olivier Mongin,* Laurent Porrès, Marina Charlot, Claudine Katan, and Mireille Blanchard-Desce*[a]



Chem.Eur. J., 2007, 13, 1481–1498

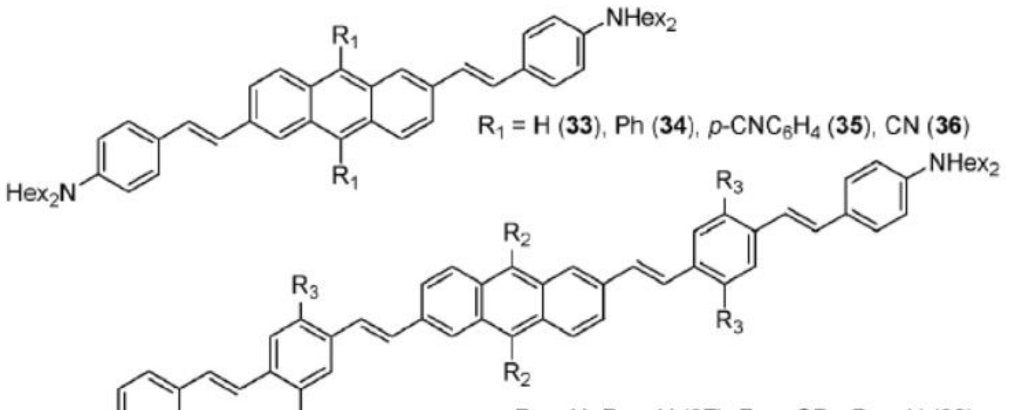


Cpd	Solvent	$\lambda_{max}^{(1)\ b}$	$\lambda_{max}^{fl\ c}$	Φ^d	$\lambda_{max}^{(2)\ e}$	$\delta_{max}^{\ f}$
28b	Toluene	401	456	0.84	730	1040
29a	DMSO	421	540	0.77	765	1200
29e	DMSO	384		0.92	740	150
29f	Toluene	428	477	0.82	740	2270
29g	Toluene	465	521	0.52	740	2560
30a	DMSO	465	582	0.63	795	530
31a	Toluene	415	457	0.79	740	1260
31f	Toluene	431	480	0.85	730	1920
31g	Toluene	470	525	0.47	880	1530

Ideal TP Dyes

Quadrupolar molecules D–π–D, D–A–D, A–π–A

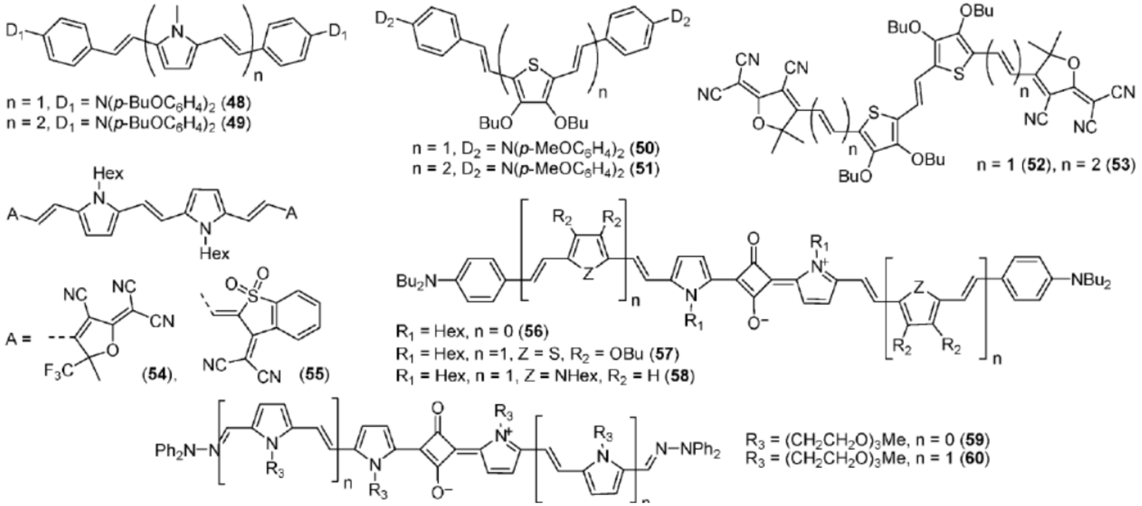
Anthracene Pyrrole, thiophene, and squarainederivatives



R_1 = H (**33**), Ph (**34**), *p*-CNC$_6$H$_4$ (**35**), CN (**36**)

R_2 = H, R_3 = H (**37**), R_2 = OPr, R_3 = H (**38**)
R_2 = H, R_3 = OMe (**39**), R_2 = CN, R_3 = H (**40**)
R_2 = CN, R_3 = OMe (**41**)

Cpd	δ_{max} [f]
33	1100
34	770
35	1570
36	2290
37	1140
38	1810, 1900
39	2580, 2490
40	5530
41	3650



n = 1, D$_1$ = N(*p*-BuOC$_6$H$_4$)$_2$ (**48**)
n = 2, D$_1$ = N(*p*-BuOC$_6$H$_4$)$_2$ (**49**)

n = 1, D$_2$ = N(*p*-MeOC$_6$H$_4$)$_2$ (**50**)
n = 2, D$_2$ = N(*p*-MeOC$_6$H$_4$)$_2$ (**51**)

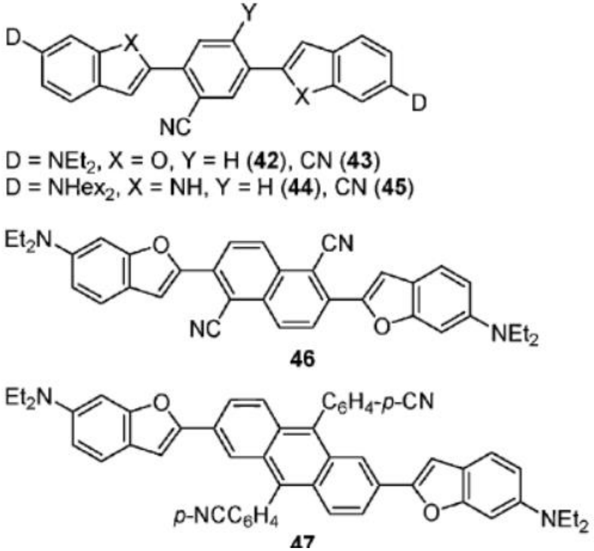
n = 1 (**52**), n = 2 (**53**)

R_1 = Hex, n = 0 (**56**)
R_1 = Hex, n =1, Z = S, R_2 = OBu (**57**)
R_1 = Hex, n = 1, Z = NHex, R_2 = H (**58**)

R_3 = $(CH_2CH_2O)_3Me$, n = 0 (**59**)
R_3 = $(CH_2CH_2O)_3Me$, n = 1 (**60**)

Cpd	δ_{max} [f]
48	800, 520
49	5000, 650
50	2000, 700
51	3800, 800
52	2400
53	4200
54	2900
55	5900
56	27 000
57	18 000
58	33 000
59	9500
60	14 000

Heterocyclic ring as the conjugation bridge



D = NEt$_2$, X = O, Y = H (**42**), CN (**43**)
D = NHex$_2$, X = NH, Y = H (**44**), CN (**45**)

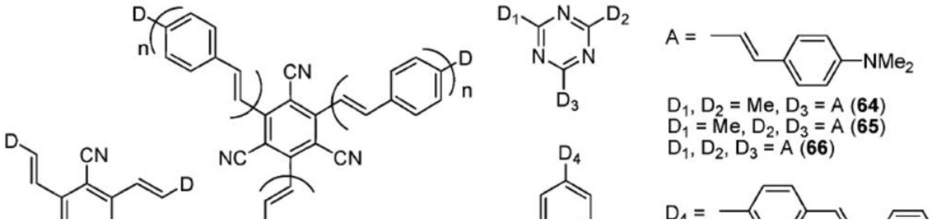
Cpd	Solvent	$\lambda_{max}^{(1)}$ [b]	λ_{max}^{fl} [c]	Φ [d]	$\lambda_{max}^{(2)}$ [e]	δ_{max} [f]
42	Toluene	464	498	0.95	780	700
43	Toluene	527	584	0.41	880	1510
44	Toluene	463	520	0.52	800	690
45	Toluene	538	624	0.07	900	1810
46	Toluene	532	579	0.42	900	1370
47	Toluene	509	581	0.38	880	2150

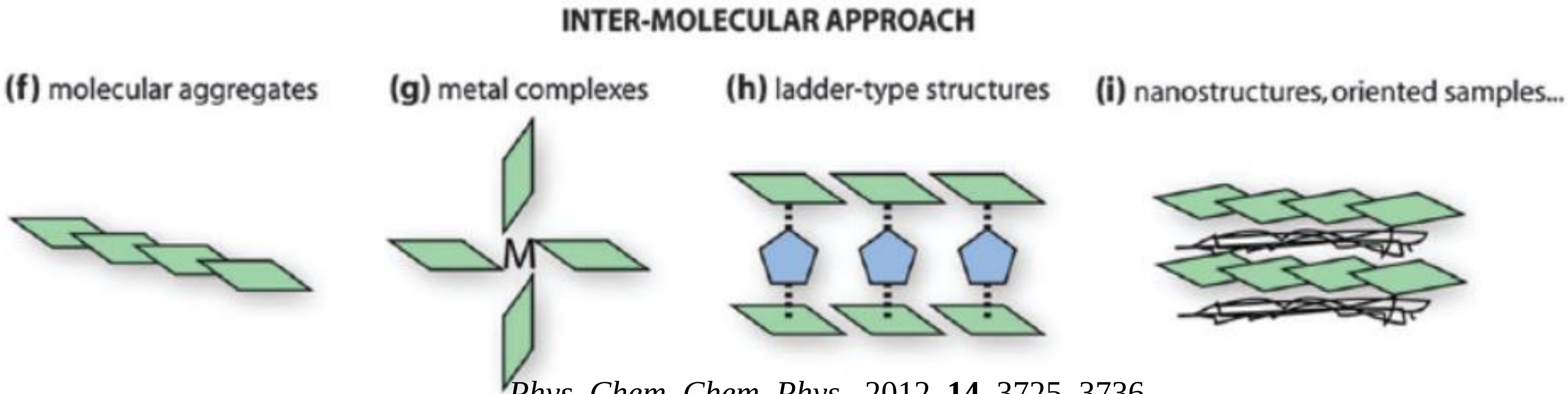
Ideal TP Dyes

Octupolar molecules

Two Photon Absorption Properties of 1,3,5-Tricyano-2,4,6-tris(styryl)benzene Derivatives

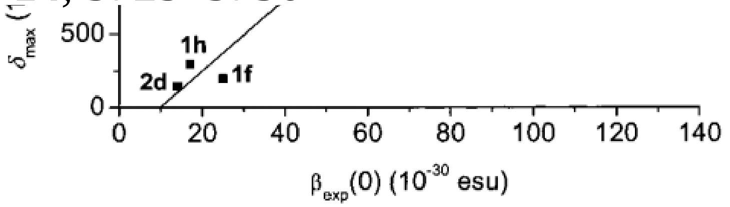
Bong Rae Cho,*,† Kyung Hwa Son,† Sang Hae Lee,† Young-Suk Song,† Yun-Kyoung Lee,†



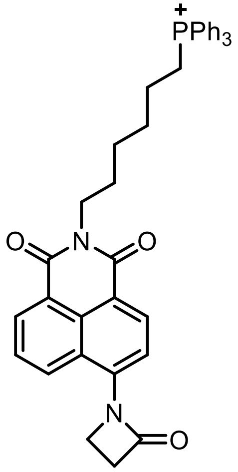


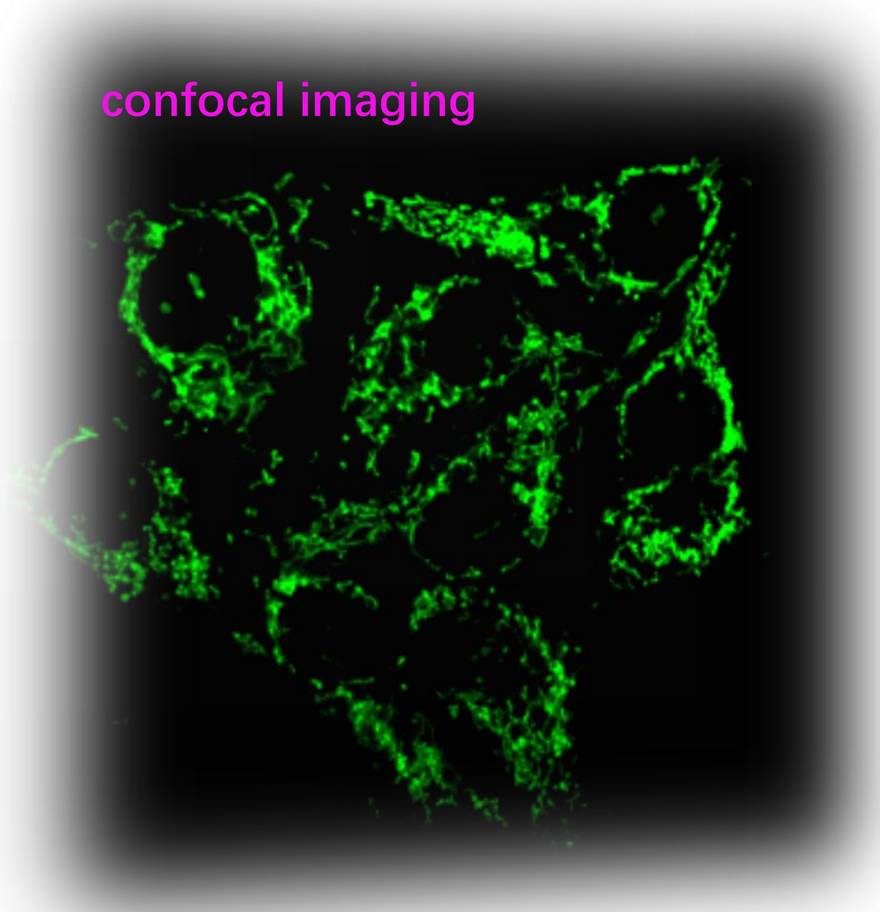
Phys. Chem. Chem. Phys., 2012, **14**, 3725–3736

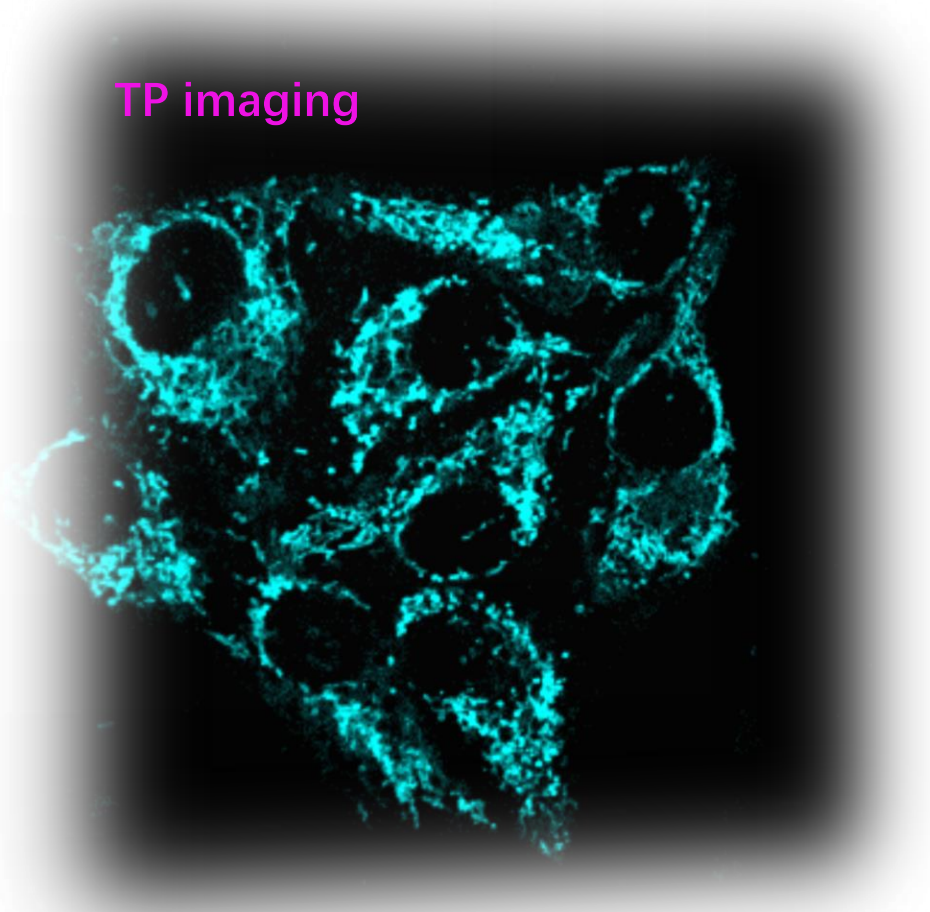
molecules revealed that there is qualitatively a linear relationship between the β and TPA cross section and that both values



2. Small-Molecule Two-Photon Probes for Bioimaging Applications

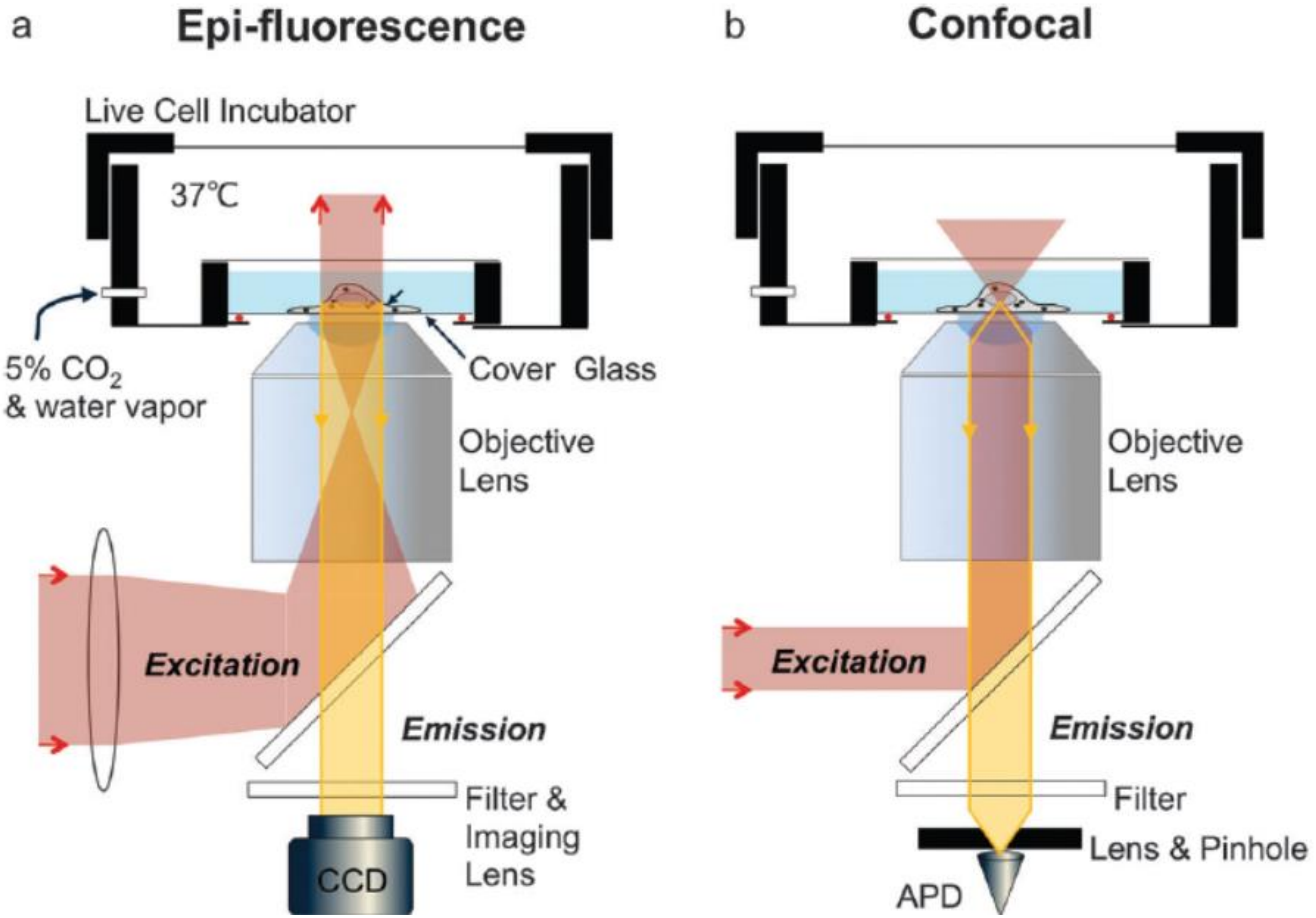






TP imaging system

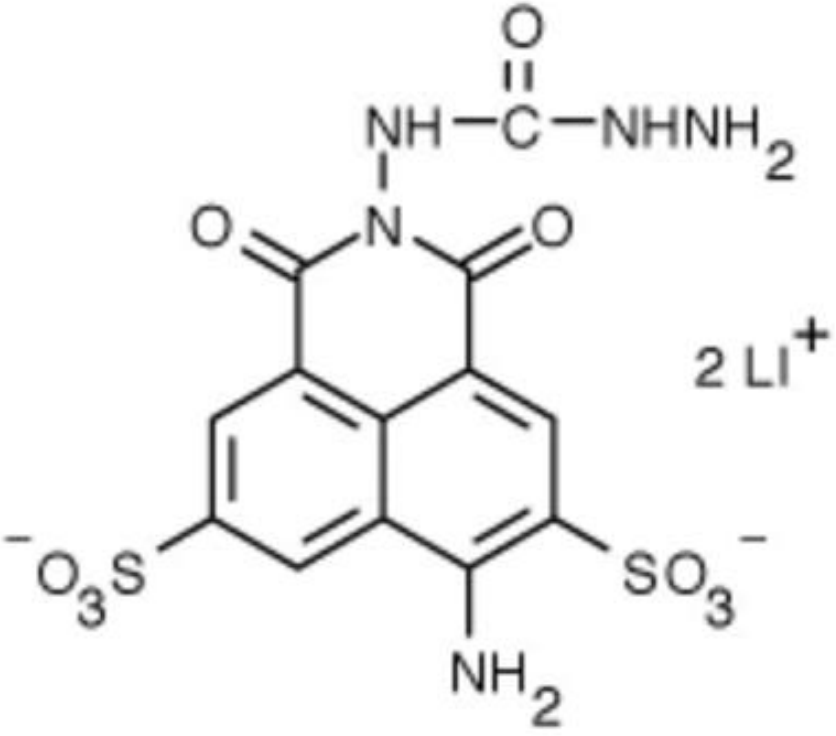
Not based on confocal



Chem. Soc. Rev., 2015, 44, 1302--1317

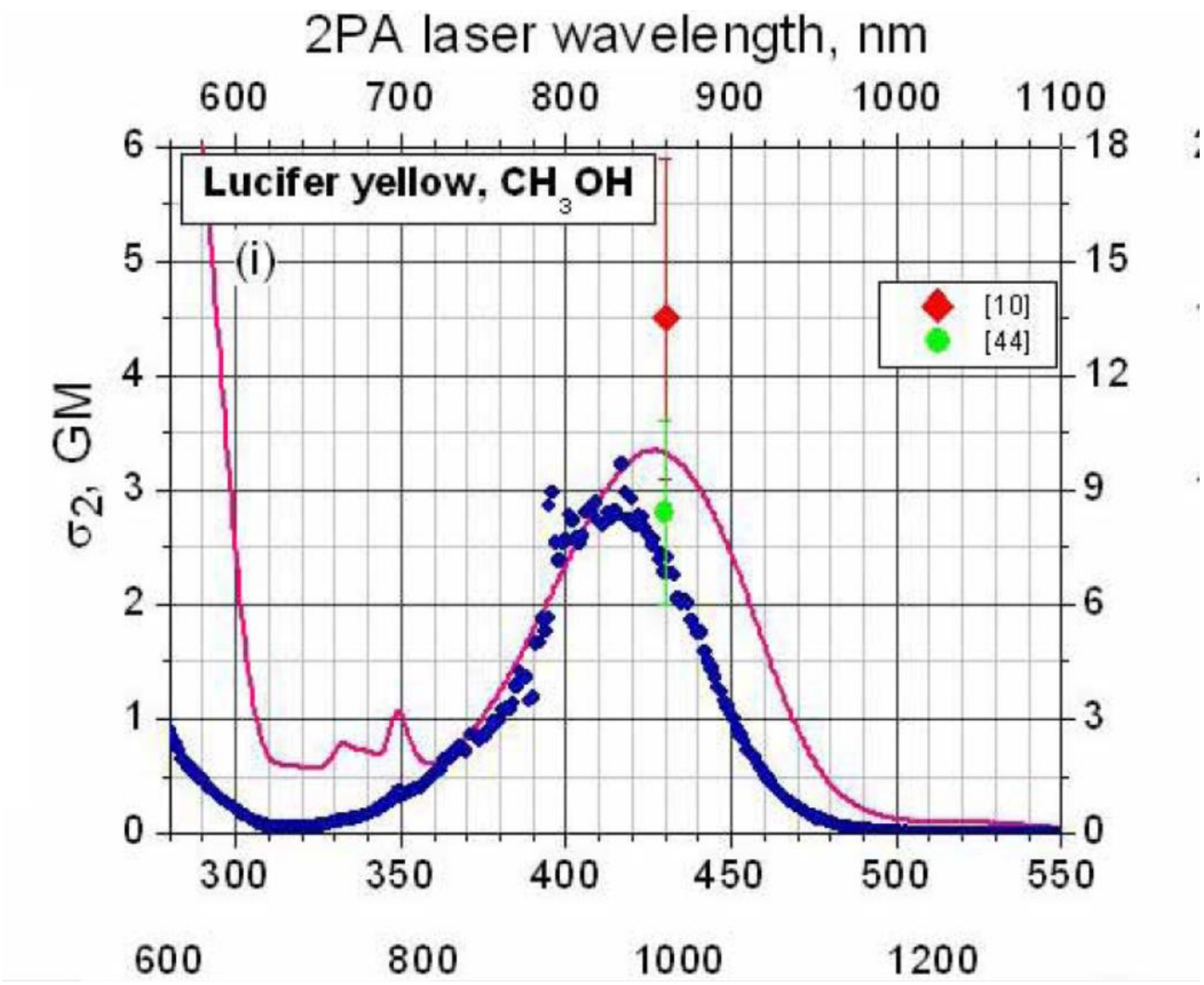
Ideal TP Dyes for imaging

TP absorption cross sections



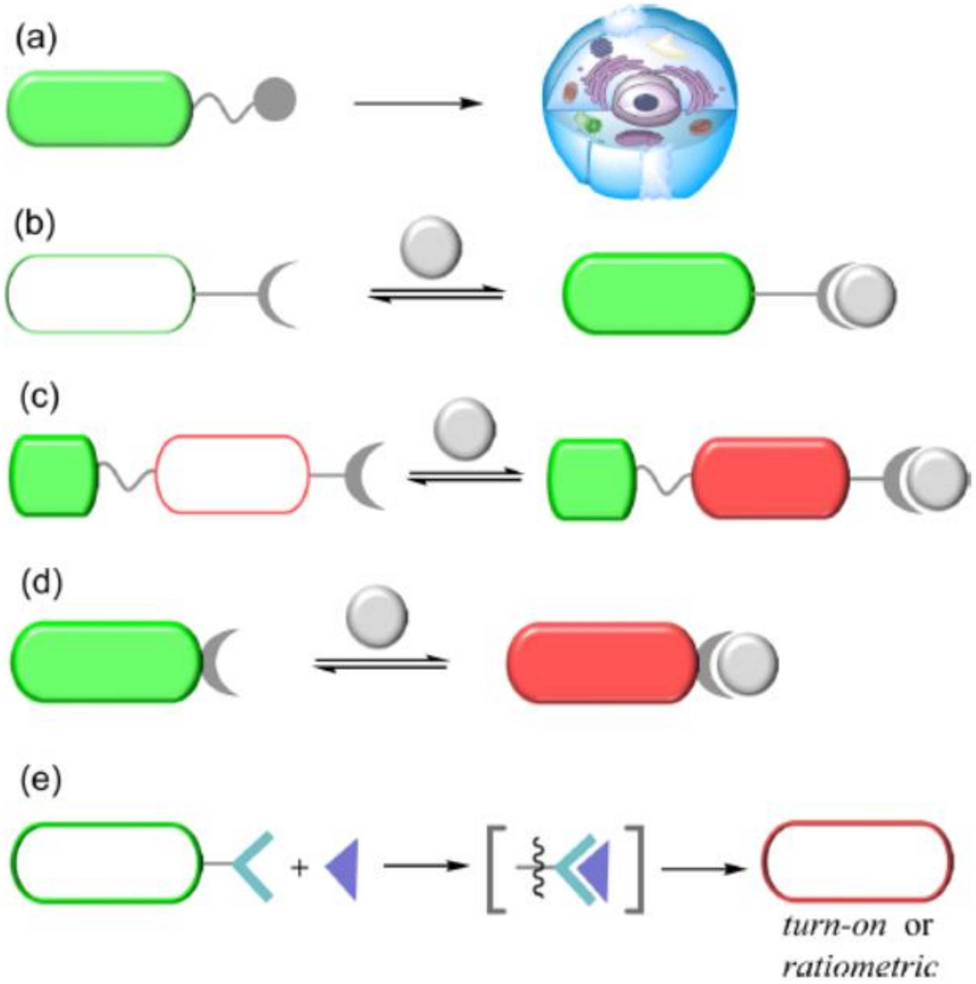
Chem. Rev. 2015, 115, 5014−5055

QE, Stable



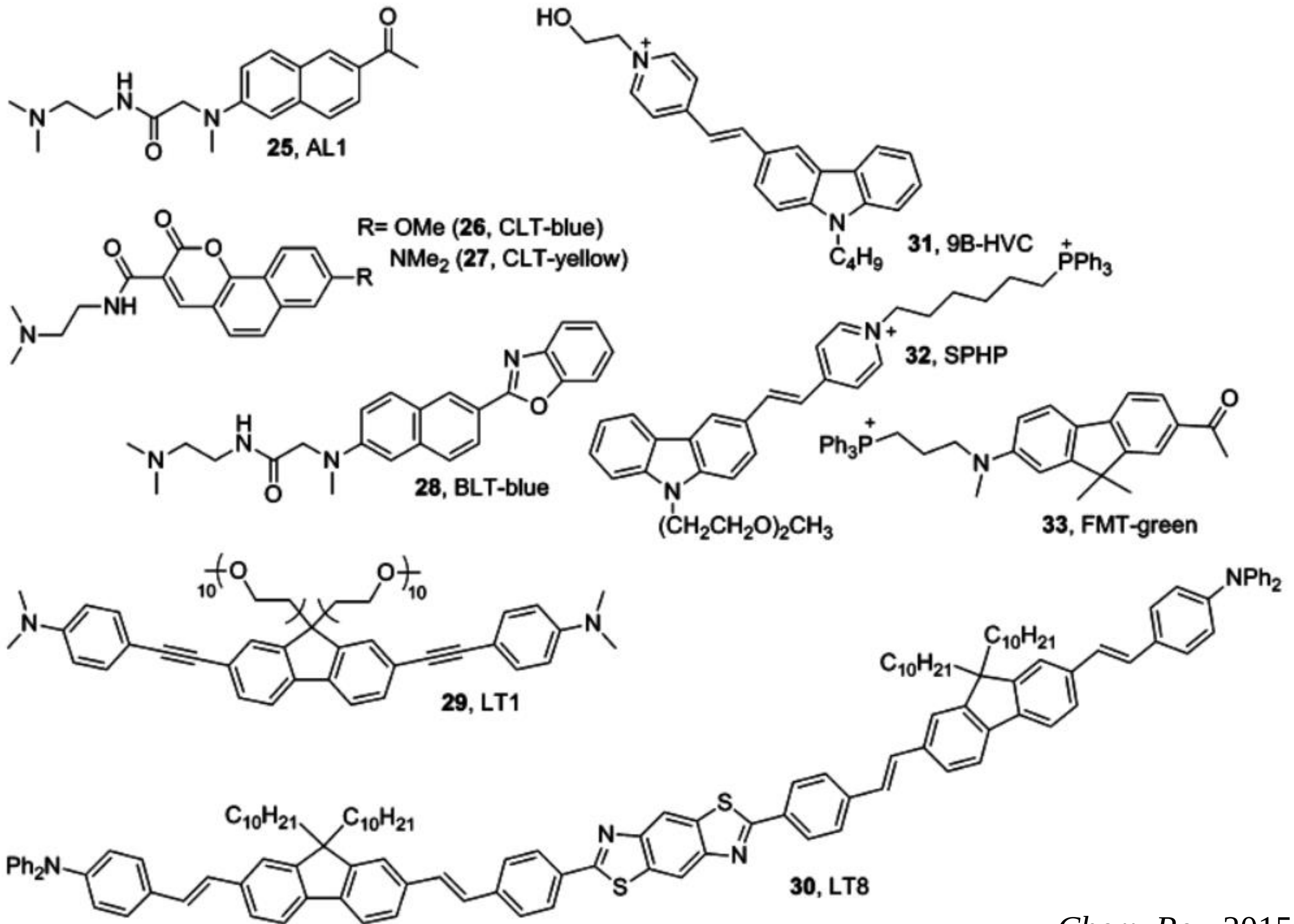
Design of TP probes

Similar with OP probes



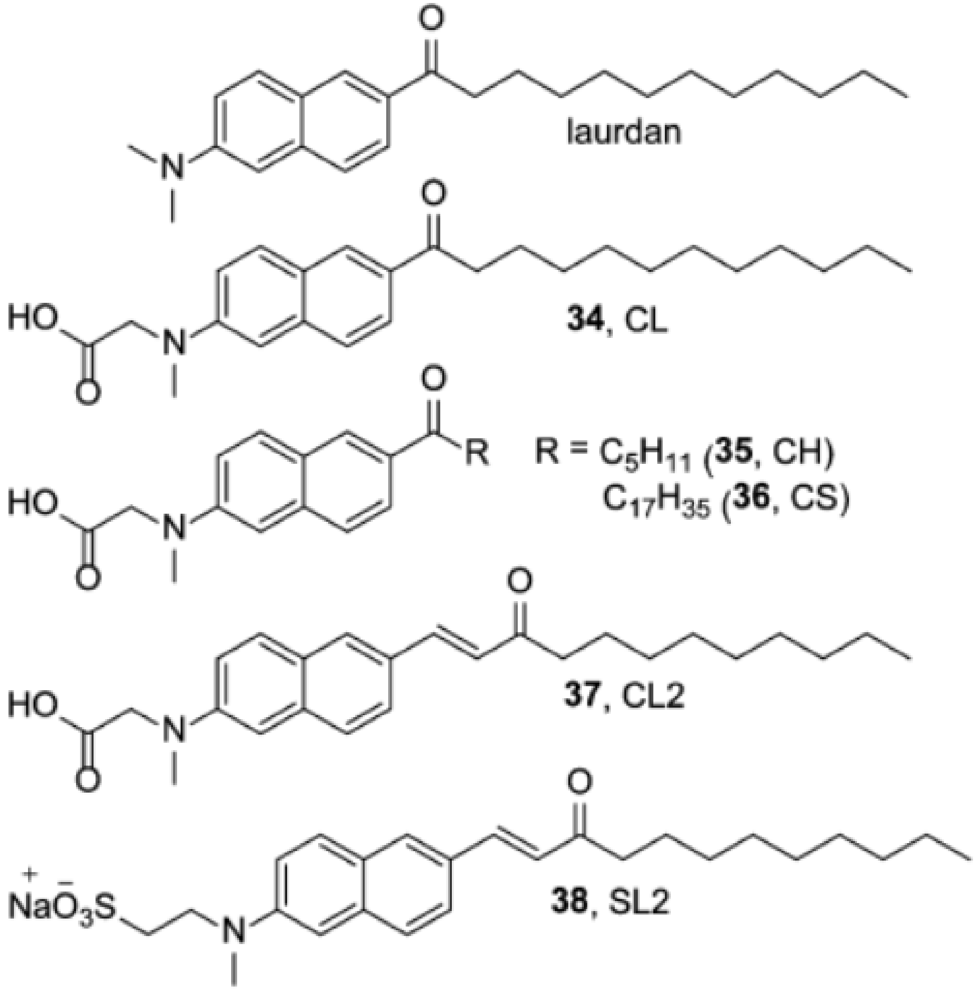
Chem. Rev. 2015, 115, 5014−5055

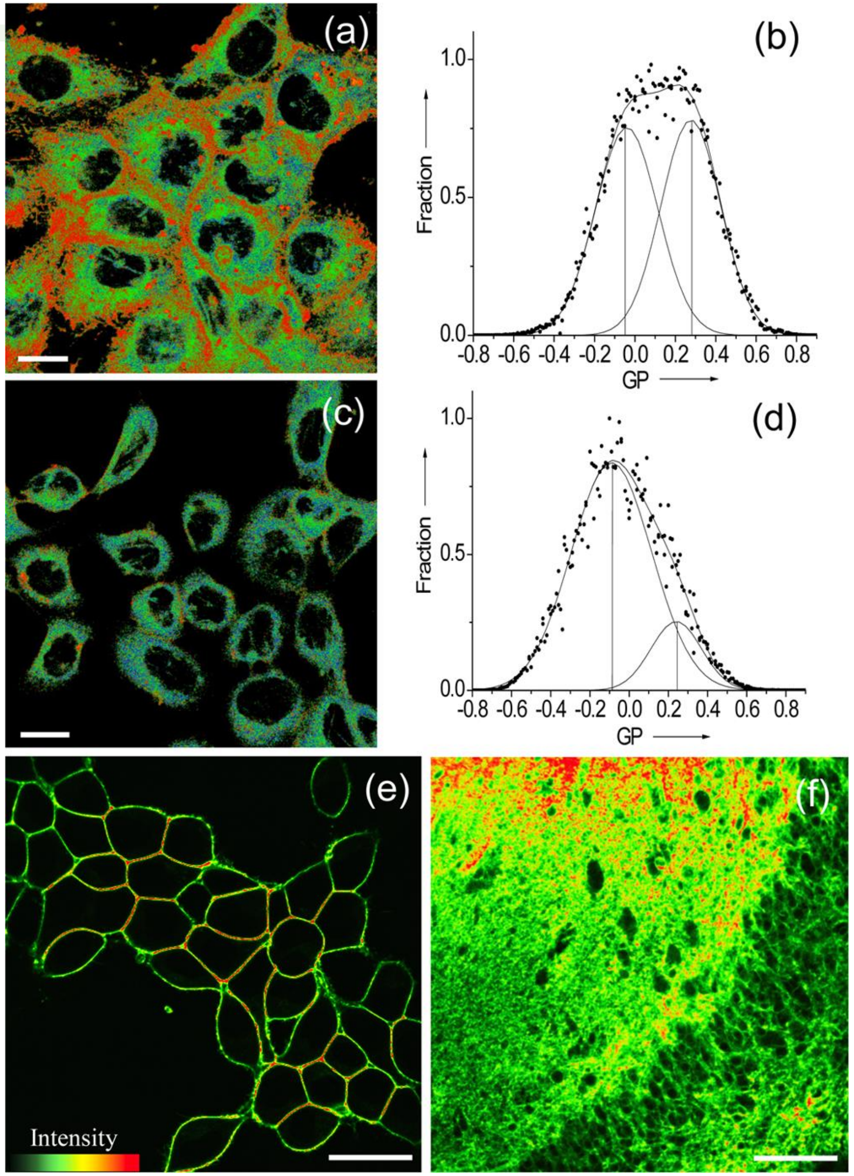
TP probes for organelles



Chem. Rev. 2015, 115, 5014−5055

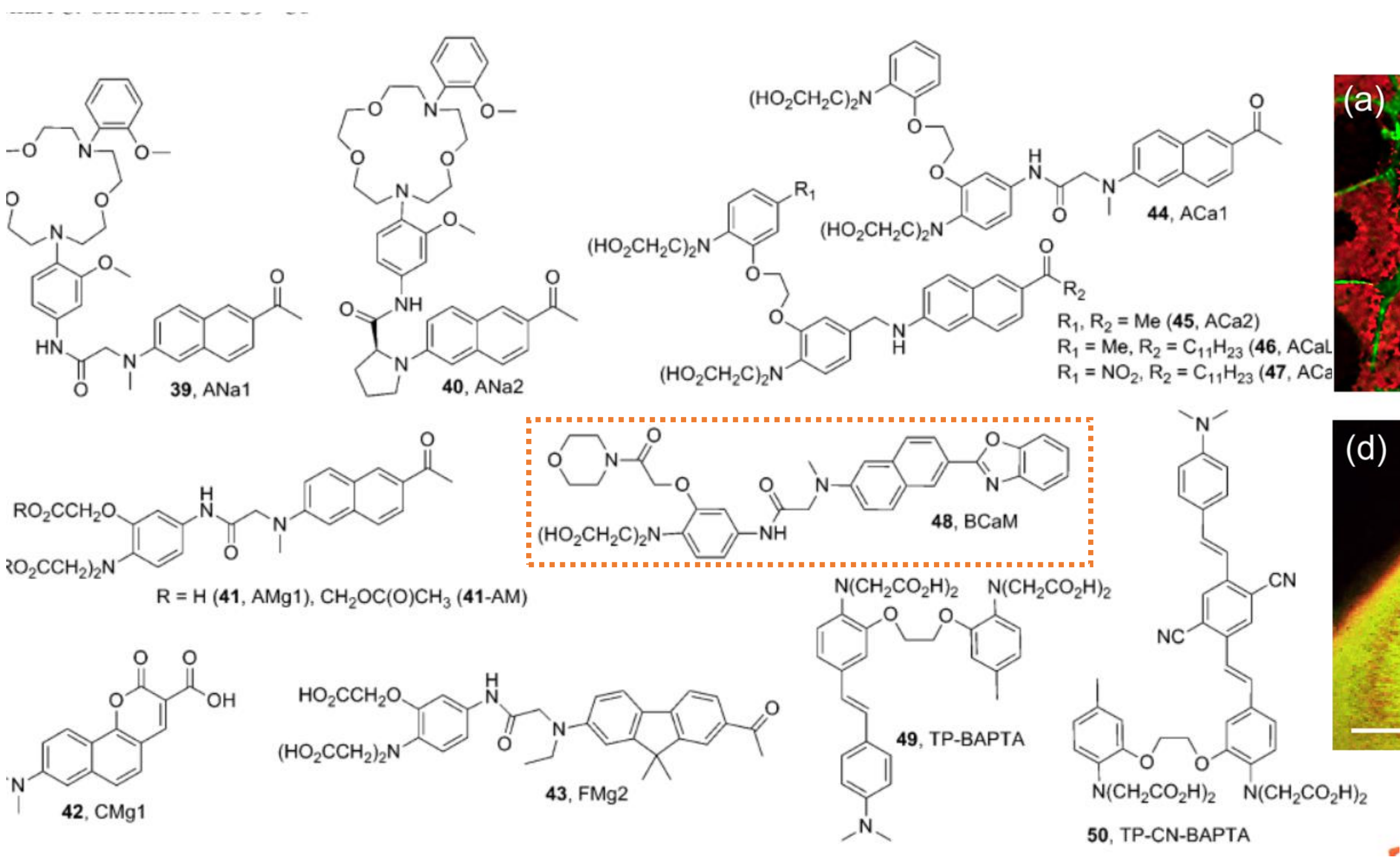
TP probes for organelles

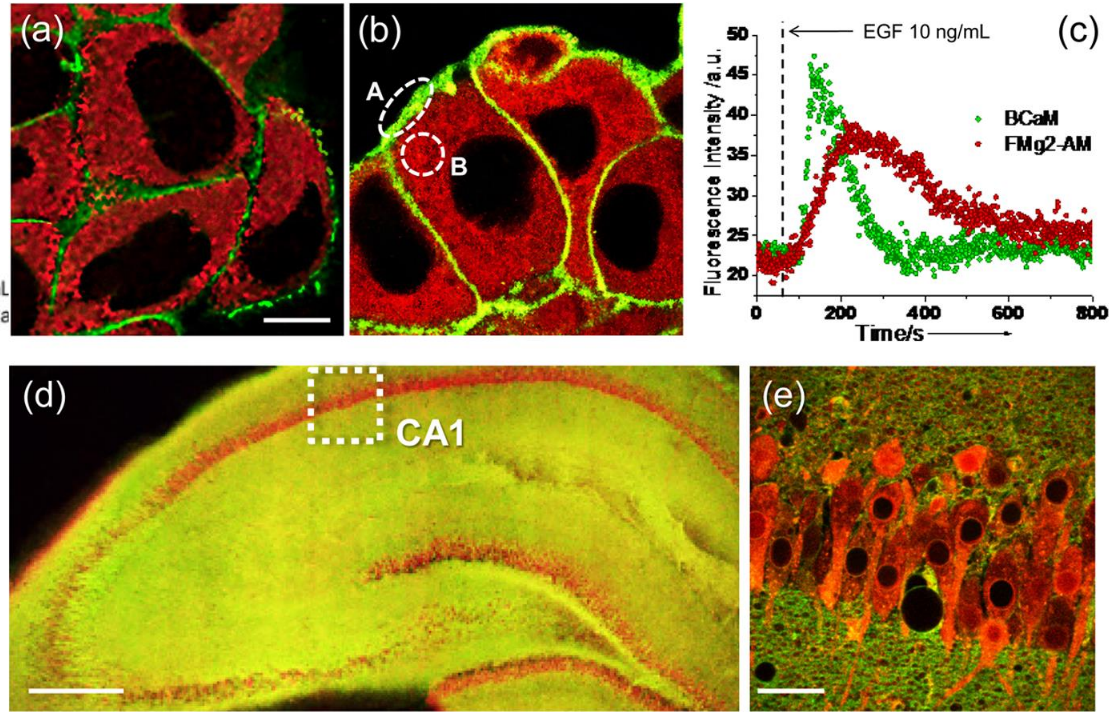




J.Am. Chem. Soc. 2008, 130, 4246.
ChemBioChem 2011, 12, 392.

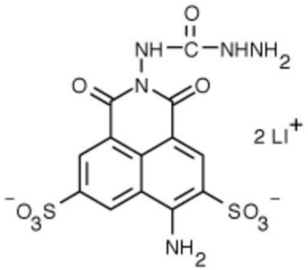
TP probes for metal ions

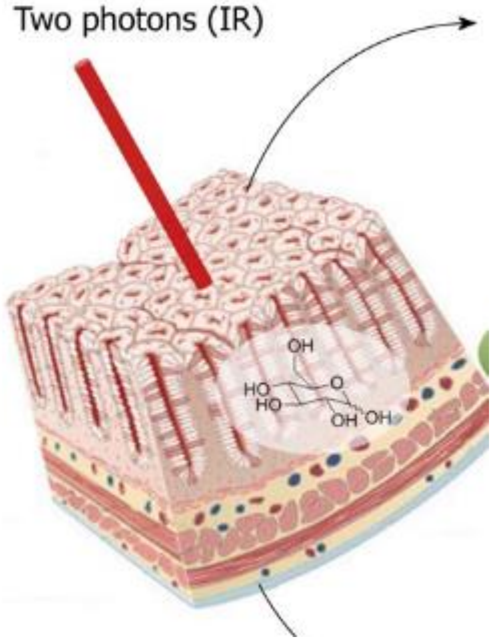




Angew. Chem., Int. Ed. 2010, 49, 6786.

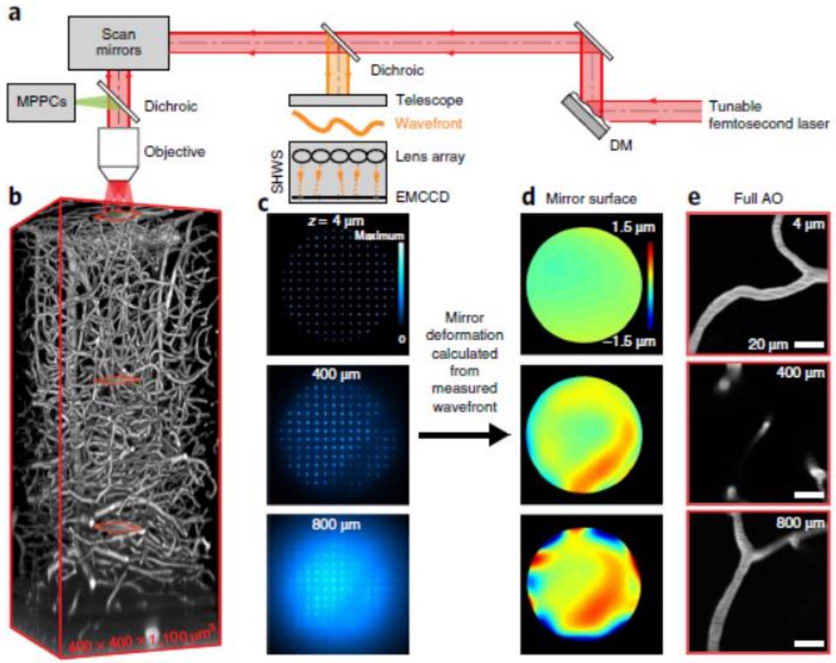
TP probes for new research



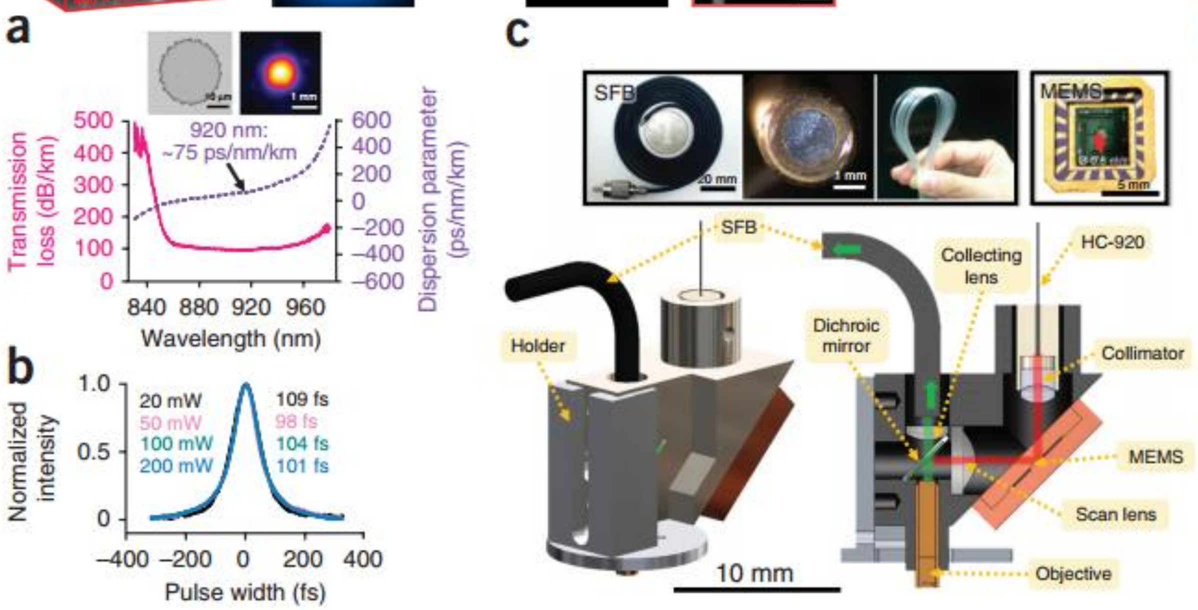


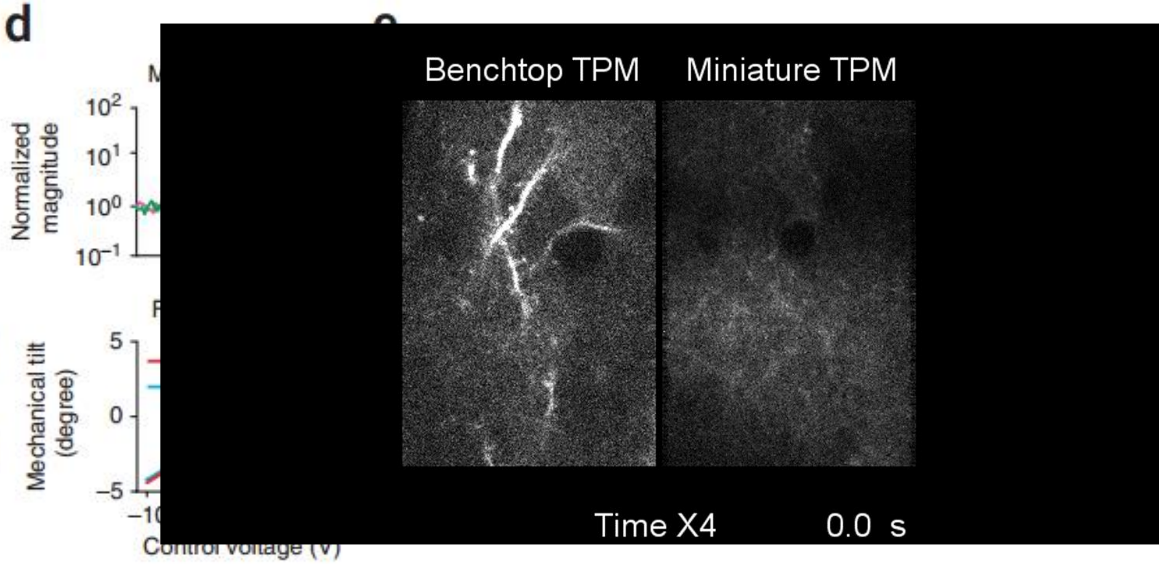
Bong Rae Cho
Daejin University

Large stokes shift; near infrared emission;



We advance two-photon microscopy for near-diffraction-limited imaging up to 850 µm below the pia in awake mice. Our approach combines direct wavefront sensing of light from a guidestar (formed by descanned fluorescence from Cy5.5-conjugated dextran in brain microvessels) with adaptive optics to compensate for tissue-induced aberrations in the wavefront. We achieve high signal-to-noise ratios in recordings of glutamate release from thalamocortical axons and calcium transients in spines of layer 5b basal dendrites during active tactile sensing. *Nature Methods*, 2019, 16, 615-618.





Nature Methods, 2017, 7, 713-719.

Super-resolution imaging through TP microscopy.

3Q

Two-photon absorption standards in the 550-1600 nm excitation wavelength range

17 March 2008 / Vol. 16, No. 6 / OPTICS EXPRESS