Literature Report IX

nature chemistry

ARTICLES

https://doi.org/10.1038/s41557-020-00554-5

Shortwave infrared polymethine fluorophores matched to excitation lasers enable non-invasive, multicolour in vivo imaging in real time

Emily D. Cosco[1,2], Anthony L. Spearman[1], Shyam Ramakrishnan[2], Jakob G. P. Lingg[2], Mara Saccomano[2], Monica Pengshung[1], Bernardo A. Arús[2], Kelly C. Y. Wong[1], Sarah Glasl[3], Vasilis Ntziachristos[3], Martin Warmer[2], Ryan R. McLaughlin[1], Oliver T. Bruns[2]✉ and Ellen M. Sletten[1]✉

Reporter： Wenchao Jiang

Date： 2020-10-22

CV of Ellen M. Sletten

Ellen M. Sletten

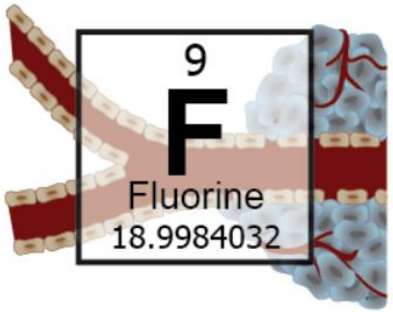
Assistant Professor

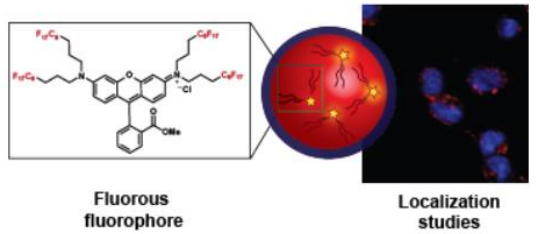
John McTague Career Development Chair

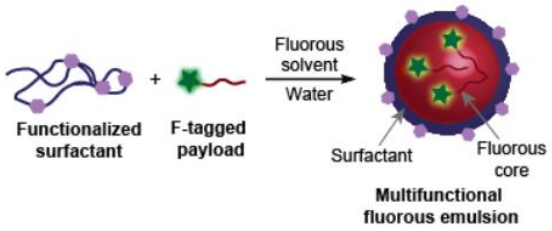
Department of Chemistry and Biochemistry

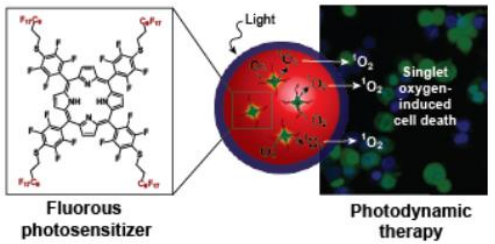
University of California, Los Angeles

FLUOROUS NANOTHERAPEUTICS

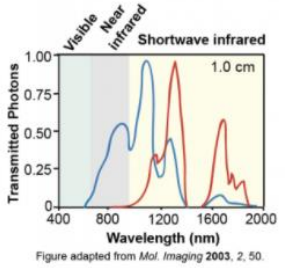


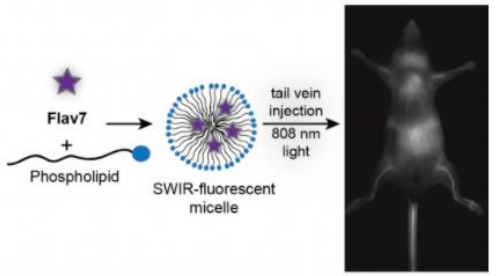






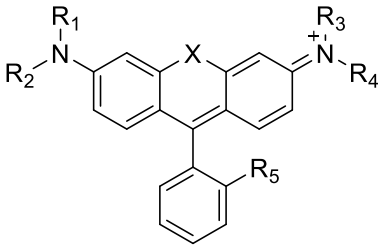
SHORTWAVE INFRARED DIAGNOSTICS

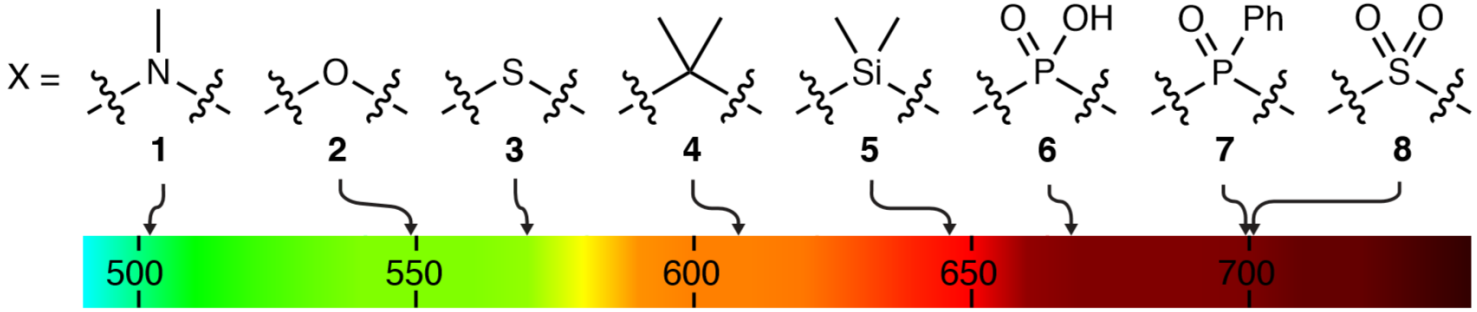




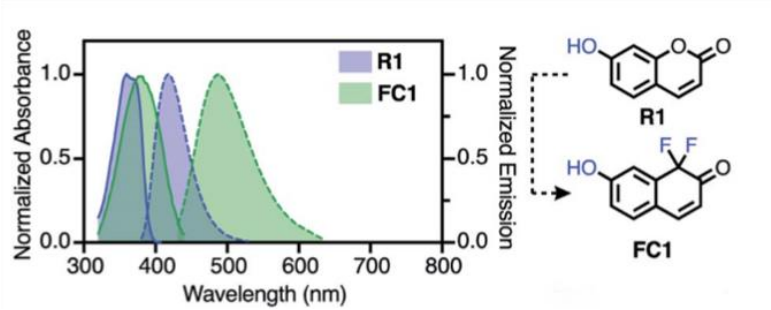
https://slettengroup.chem.ucla.edu/

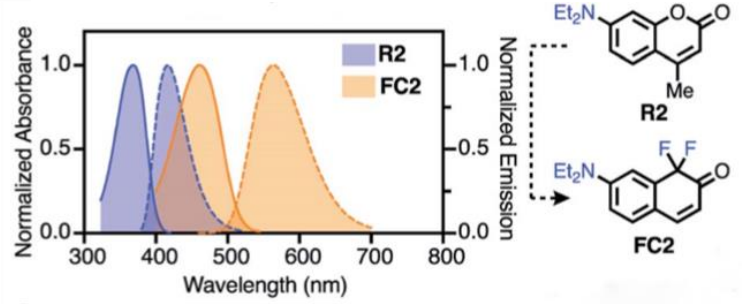
Dyes in Long wavelength region

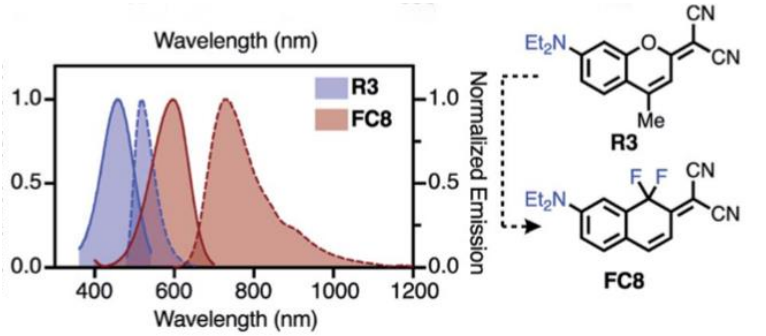




Si-Rho（CN）817/841







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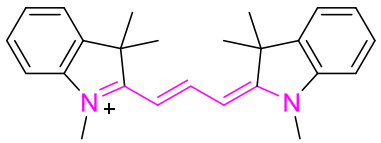
Dyes in Long wavelength region



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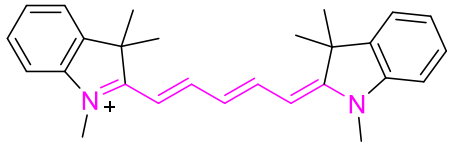

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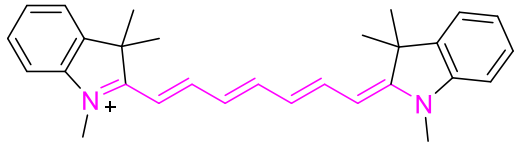

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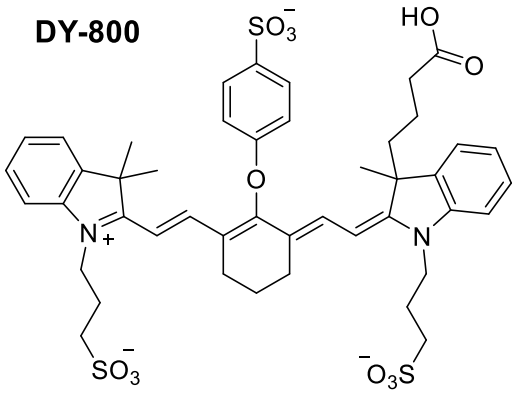

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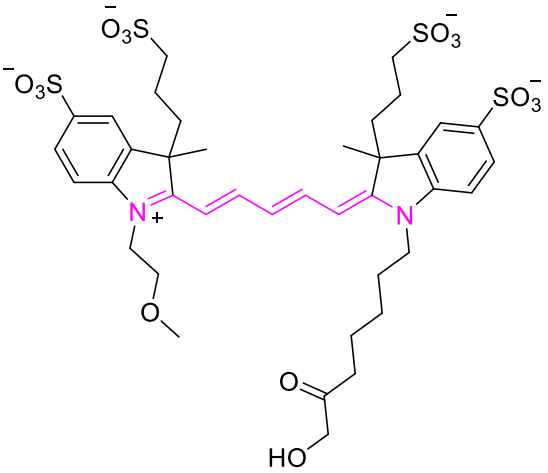

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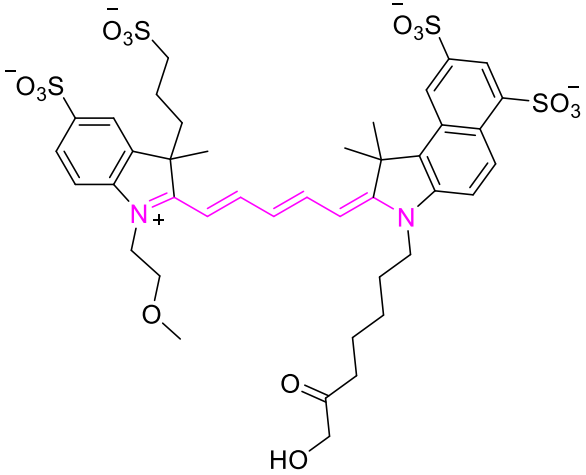

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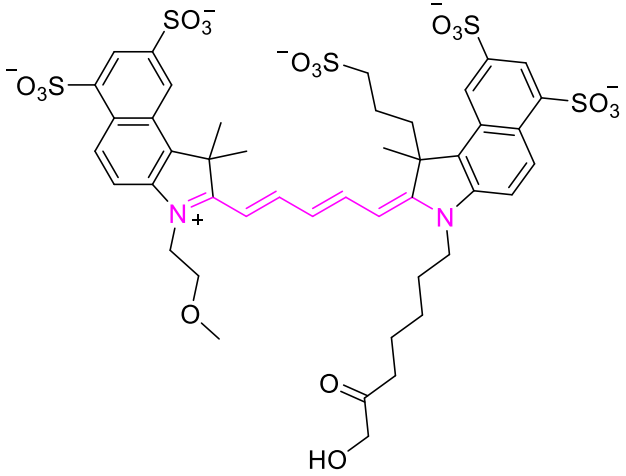

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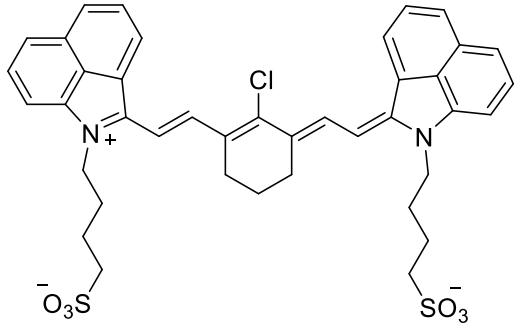

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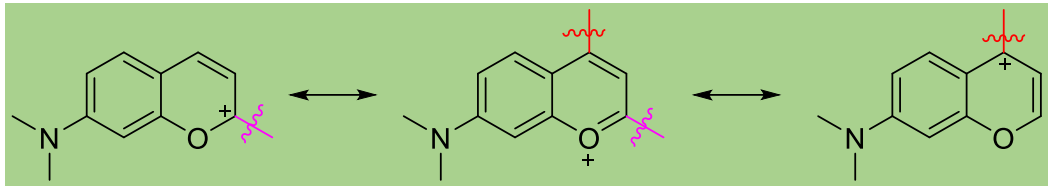
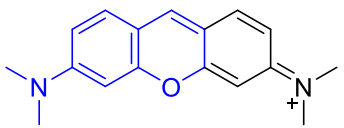
Dyes in Long wavelength region



Pyronin G



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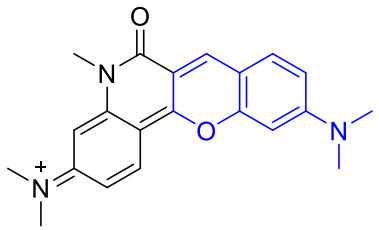

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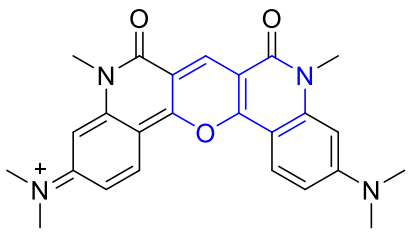
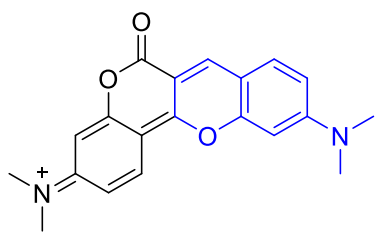
Farbstoff 140



672/710 EtOH

CP1



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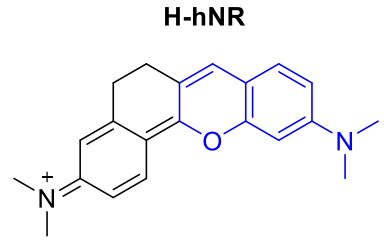
H-hNR



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改变桥连基团?

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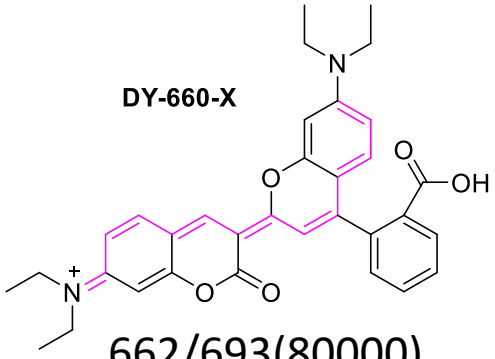

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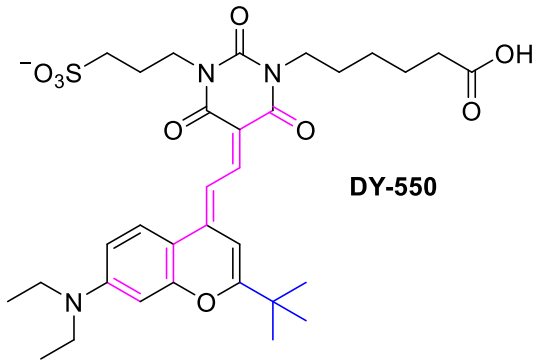

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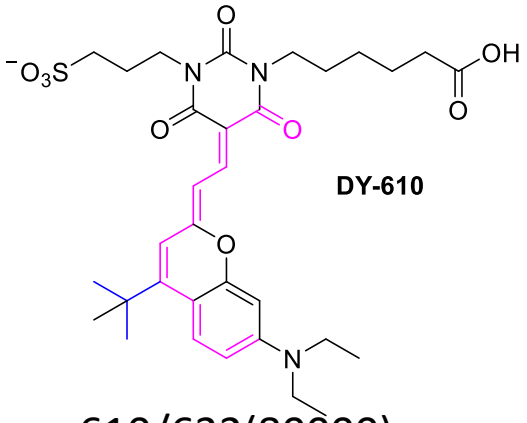

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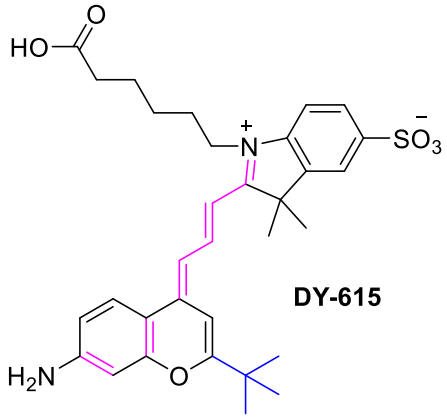
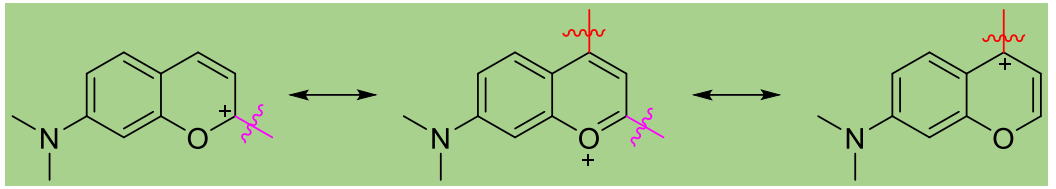
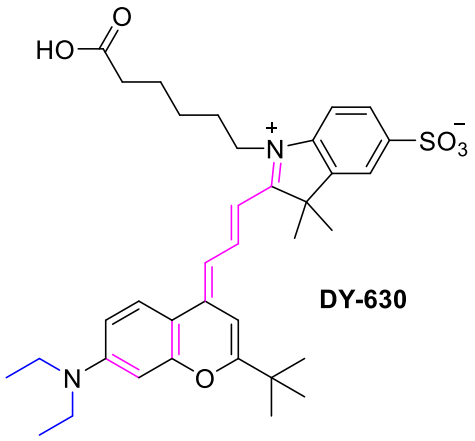


623/643(200000)

烯链构型对吸光度的影响

Dyes in Long wavelength region





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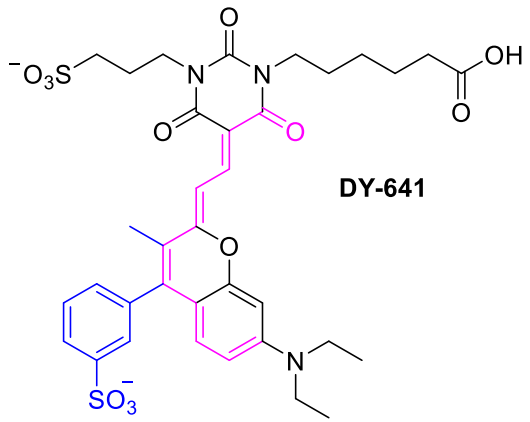

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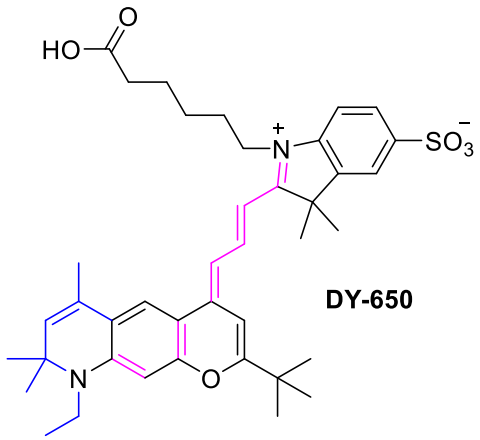

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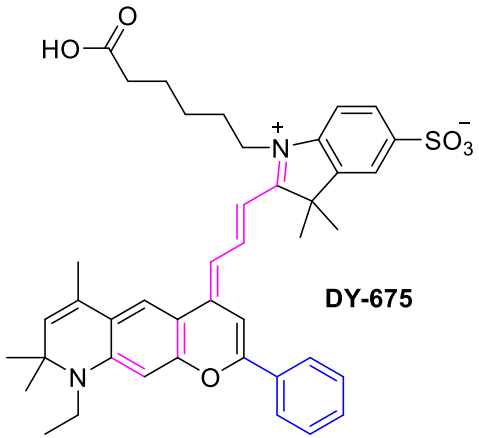

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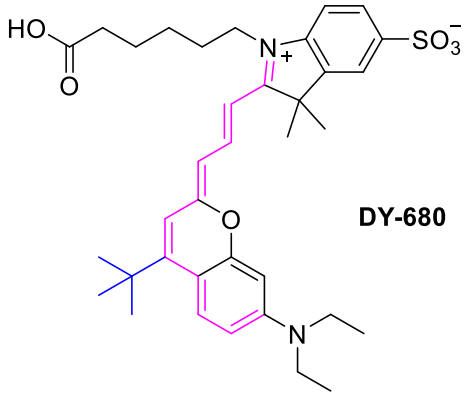

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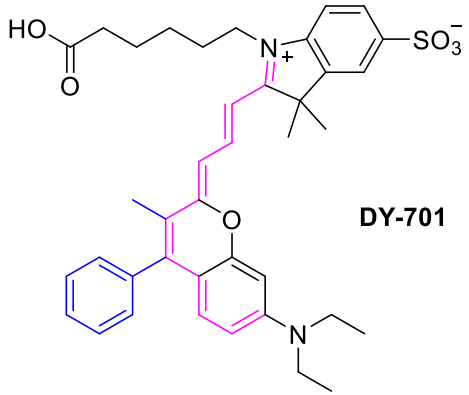

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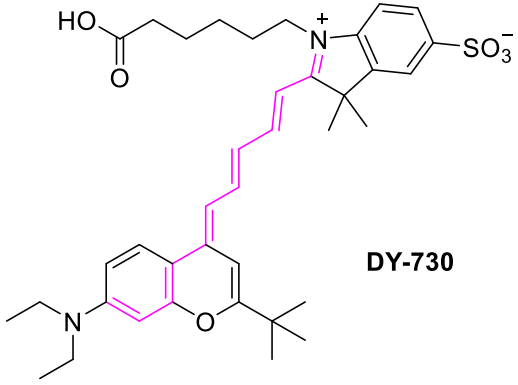

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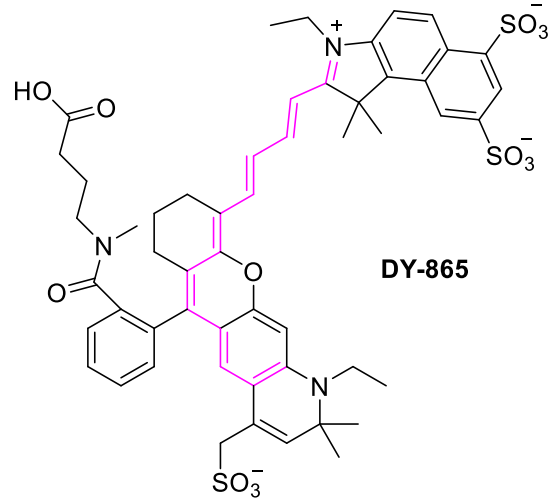

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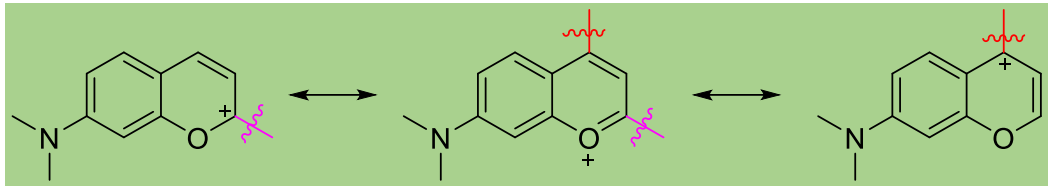
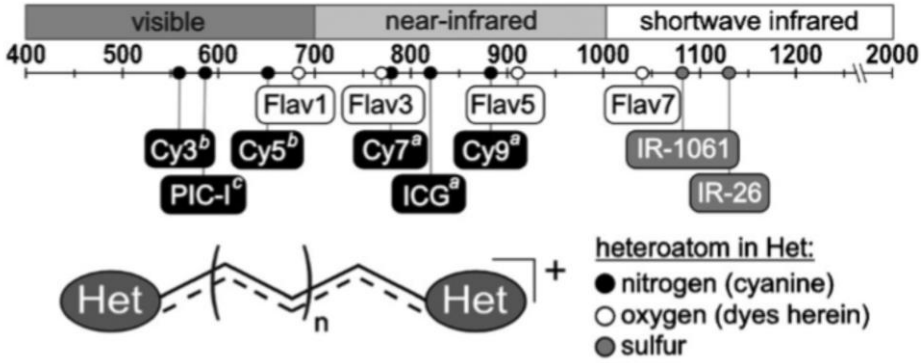
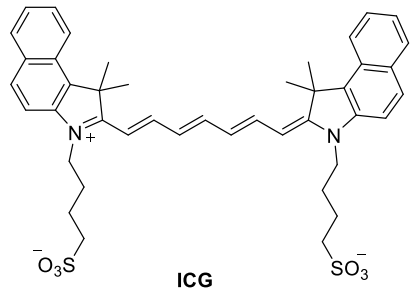
六元环DY-750 751/774（270000）

Dyes in Long wavelength region







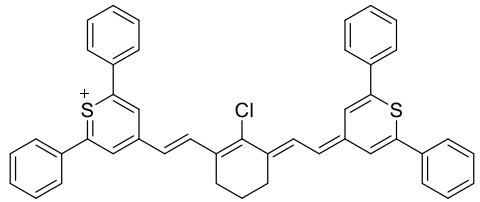
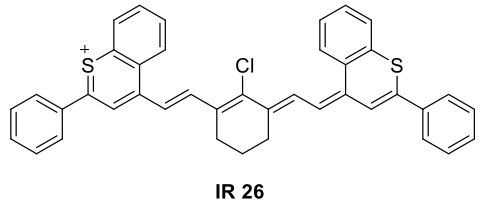
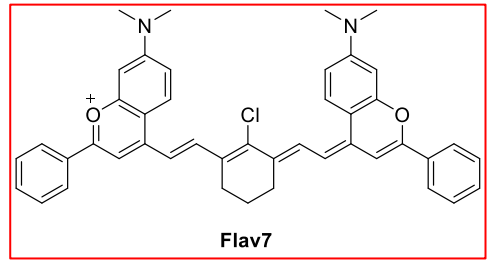
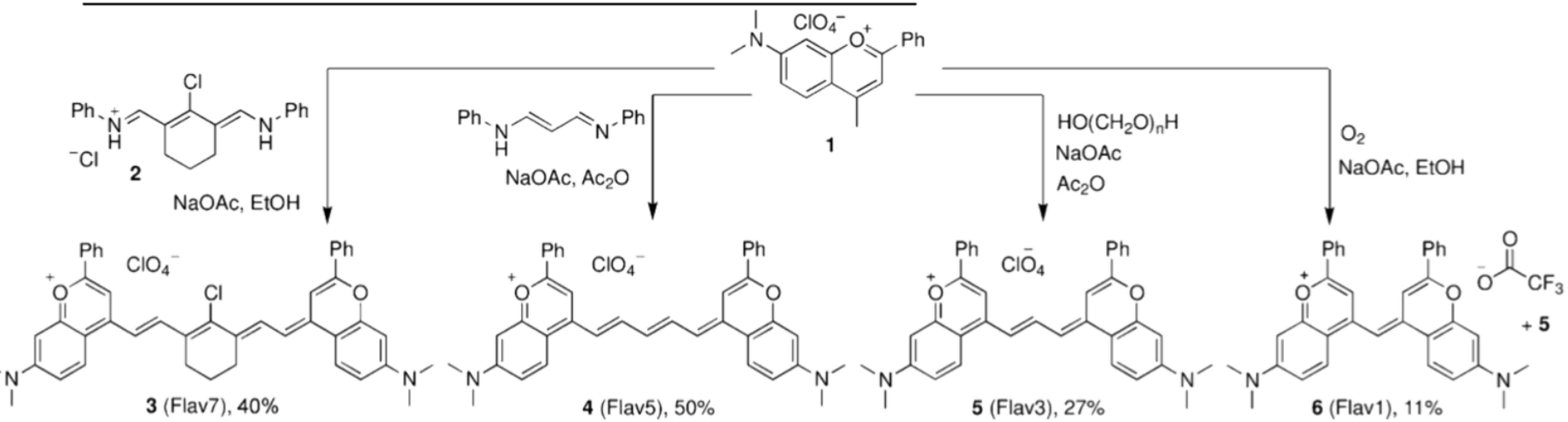


Table 1: Photophysical characterization of **1**, **3**–**6** in dichloromethane.

Compound	$\lambda_{max,abs}$ [nm]	$\varepsilon(\lambda_{max})$ [$M^{-1}cm^{-1}$][a]	$\lambda_{max,em}$ [nm]	Φ_F [%][a]	QE_{max}[6] [$M^{-1}cm^{-1}$]
1	510	17000	587	–	–
6	650	16000	684	0.7	100
5	746	220000	766	2.9	6600
4	862	240000	908	5	10000
3	1026	236000	1045	0.53	1200

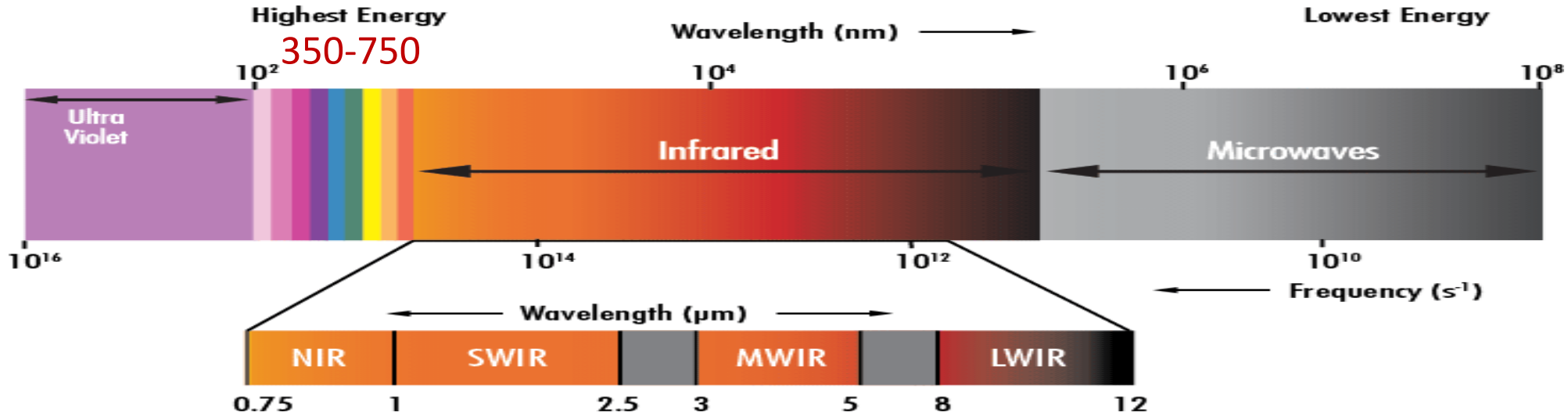






Angew.Chem. Int. Ed. 2017, 56,13126–13129

Introduction



https://www.edmundoptics.com/knowledge-center/application-notes/imaging/what-is-swir/

- Low photon penetration
- High background autofluorescence
- Light scattering
- Limited wavelength range(multiplexed experiments)

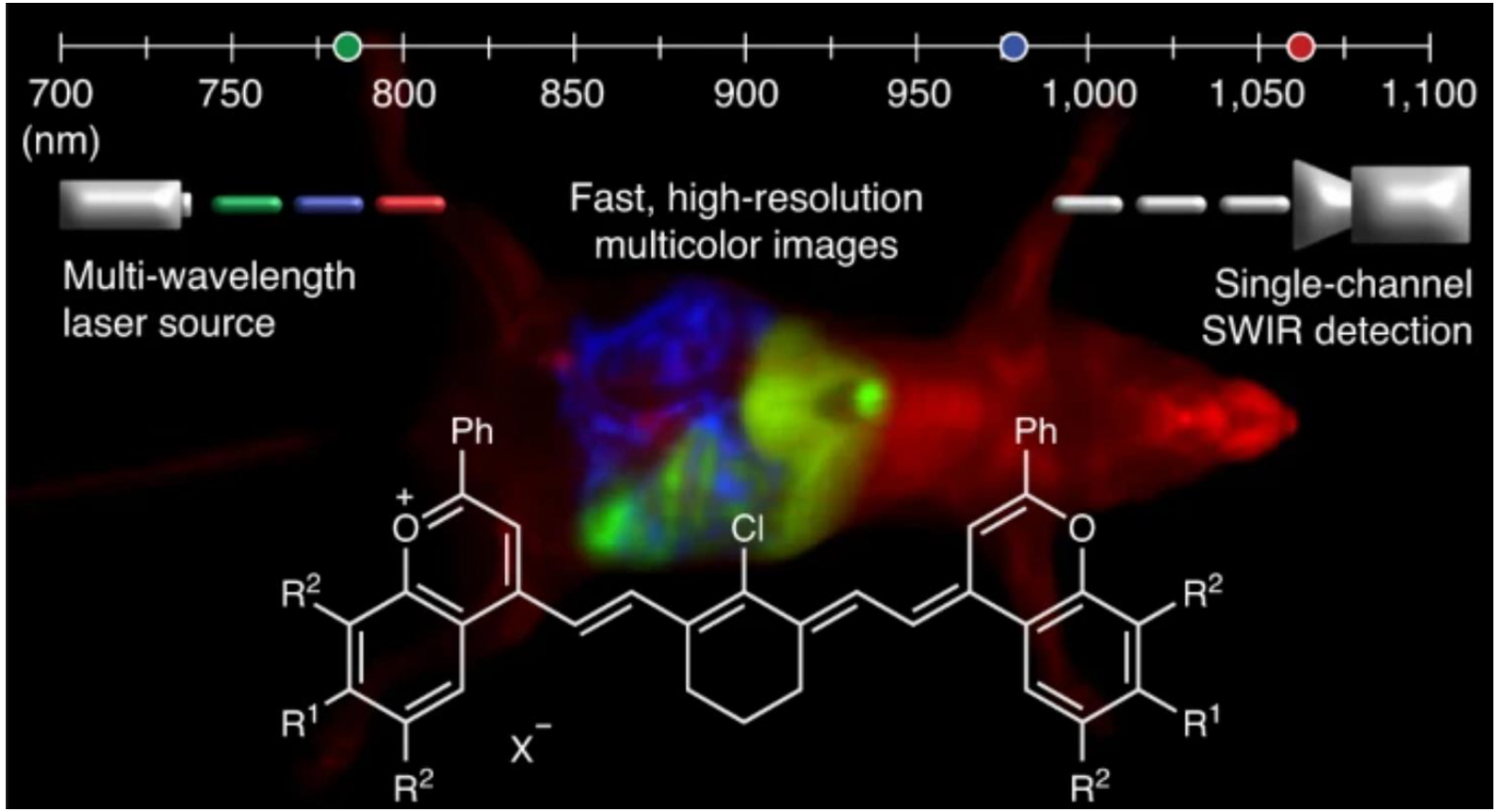
Spatial and temporal resolution

↓ Higher

Bright fluorophores & Rapid detection

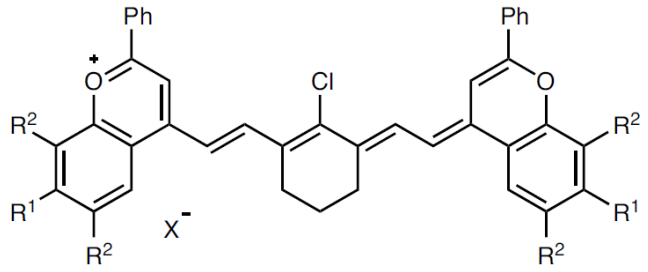
Introduction

Excitation multiplexing and ‘colour-blind’ single-channel detection of



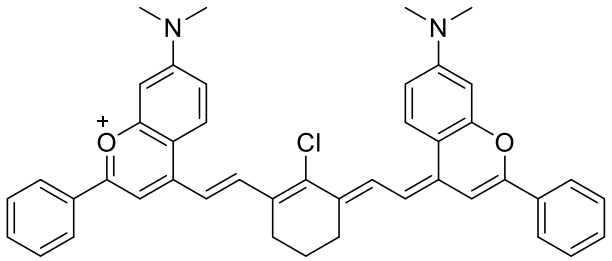
Bright, ‘excitation-matched’ polymethine fluorophores

Flavylium heptamethine dyes

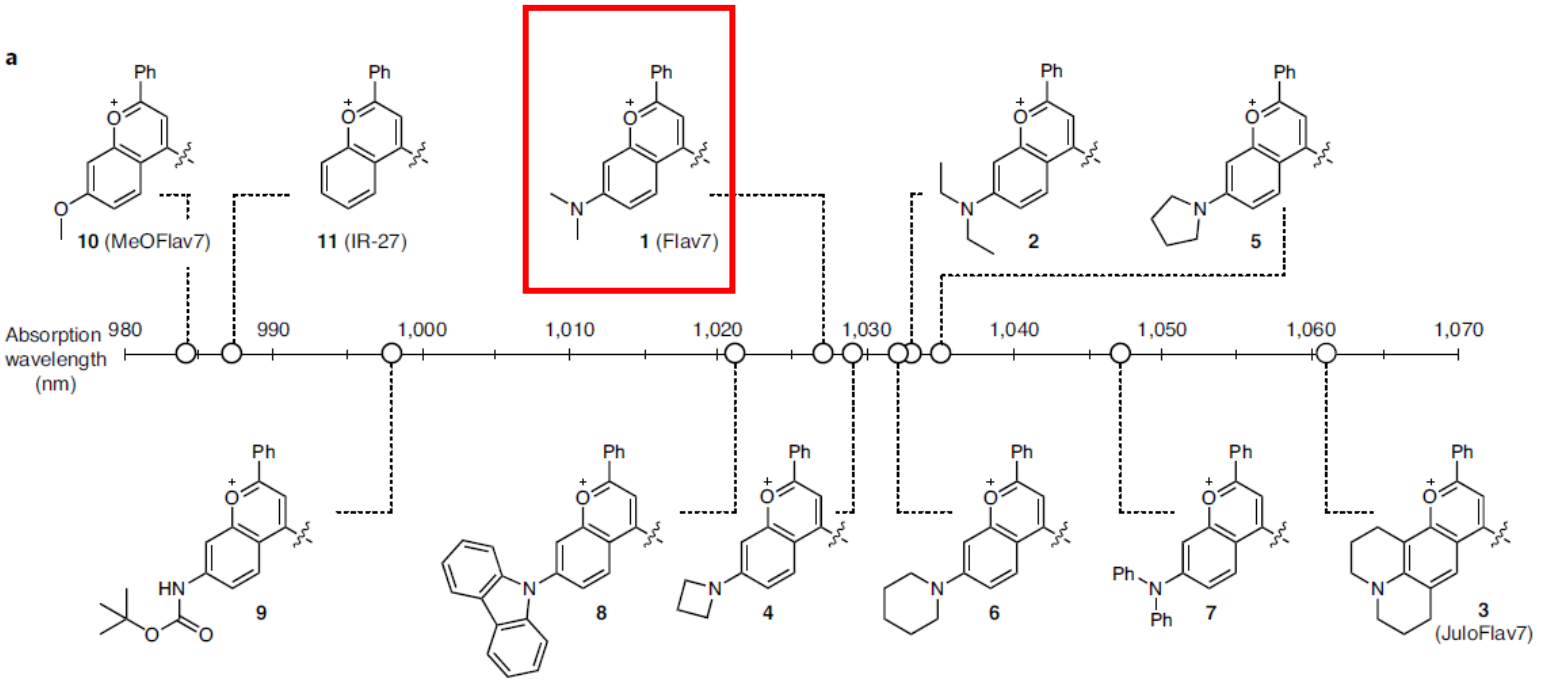


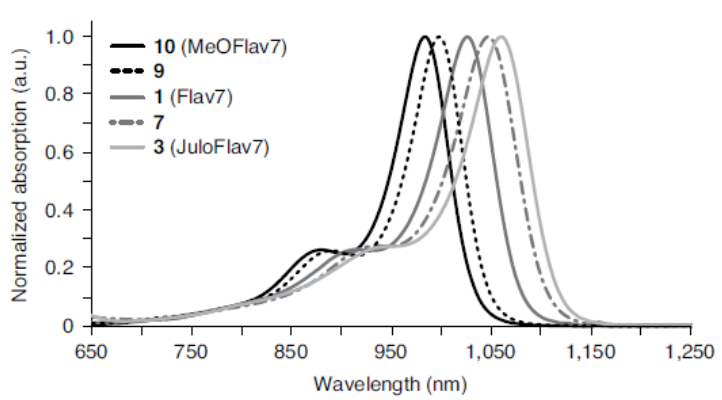
Flav7 (**1**): R_1 = $N(Me)_2$; R_2 = H; prior work

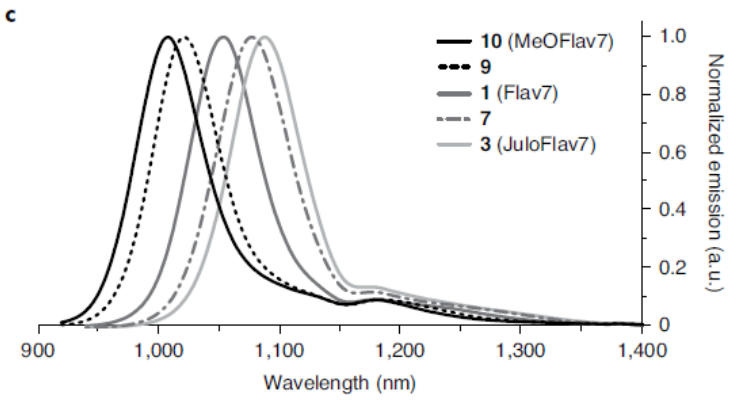
2–**11**: R_1 = alkyl and aromatic amines, methoxy, H; R_2 = H, alkyl; this work



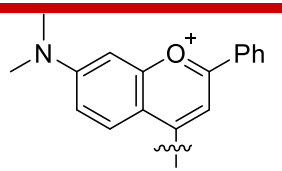
Flav7



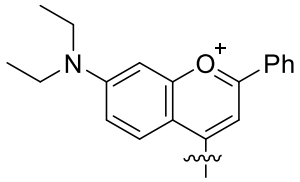




Flavylium heptamethine dyes



1 (Flav7)



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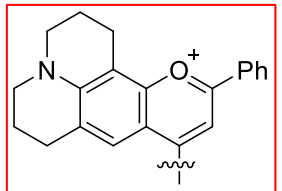
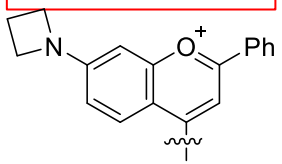


3 (JuloFlav7)



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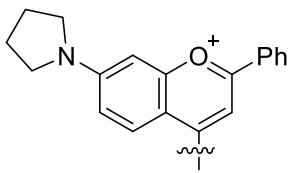

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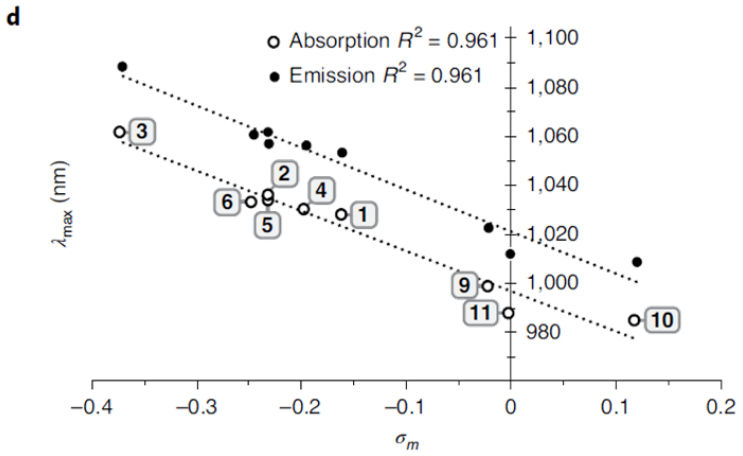
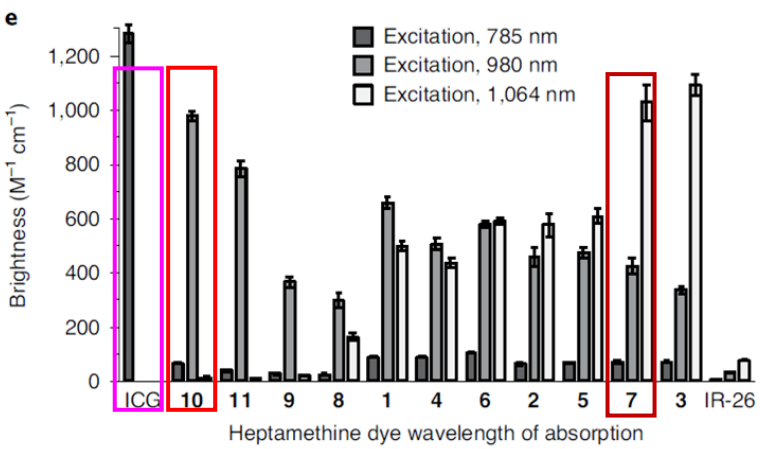
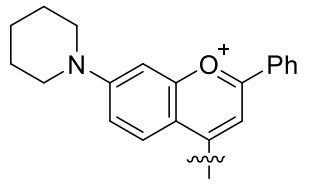




Dye	$\lambda_{max,abs}$ (nm)	ε_{max} ($M^{-1}cm^{-1}$)[a]	$\lambda_{max,em}$ (nm)	Φ_F (%)[a]	Brightness(ε_{max}) ($M^{-1}cm^{-1}$)[a]
1 (Flav7)	1,027	241,000	1,053	0.61	1,470
2	1,033	190,000	1,057	0.62	1,180
3 (JuloFlav7)	1,061	238,000	1,088	0.46	1,090
4	1,029	207,000	1,056	0.51	1,060
5	1,034	247,000	1,061	0.48	1,190
6	1,032	110,000	1,060	0.54	590
7	1,047	210,000	1,078	0.58	1,220
8	1,021	140,000	1,048	0.45	630
9	998	108,000	1,022	0.42	450
10 (MeOFlav7)	984	190,000	1,008	0.52	990
11 (IR-27)	987	231,000	1,011	0.35	810
ICG	787[b]	194,000[b]	818[b]	0.66[b,c]	1,200[c]
IR-26	1,080	171,000	1,114	0.05[d]	86

[a]See Supplementary Table 5 for errors in ε_{max}, Φ_F, and brightness(ε_{max}). [b]Data taken from the literature[36] (ethanol (EtOH)). [c]Value includes the percent emission between 1,000 and 1,300 nm (5%)[37]. [d]Value from the literature[51] (1,2-dichloroethane); treated as a constant for relative Φ_F measurements.



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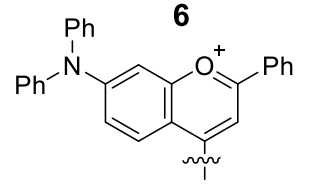

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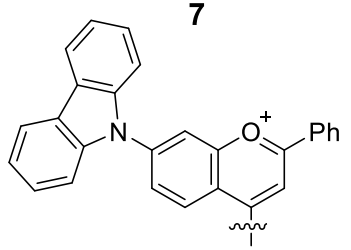
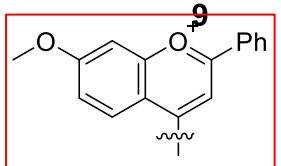
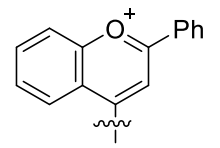


8



9

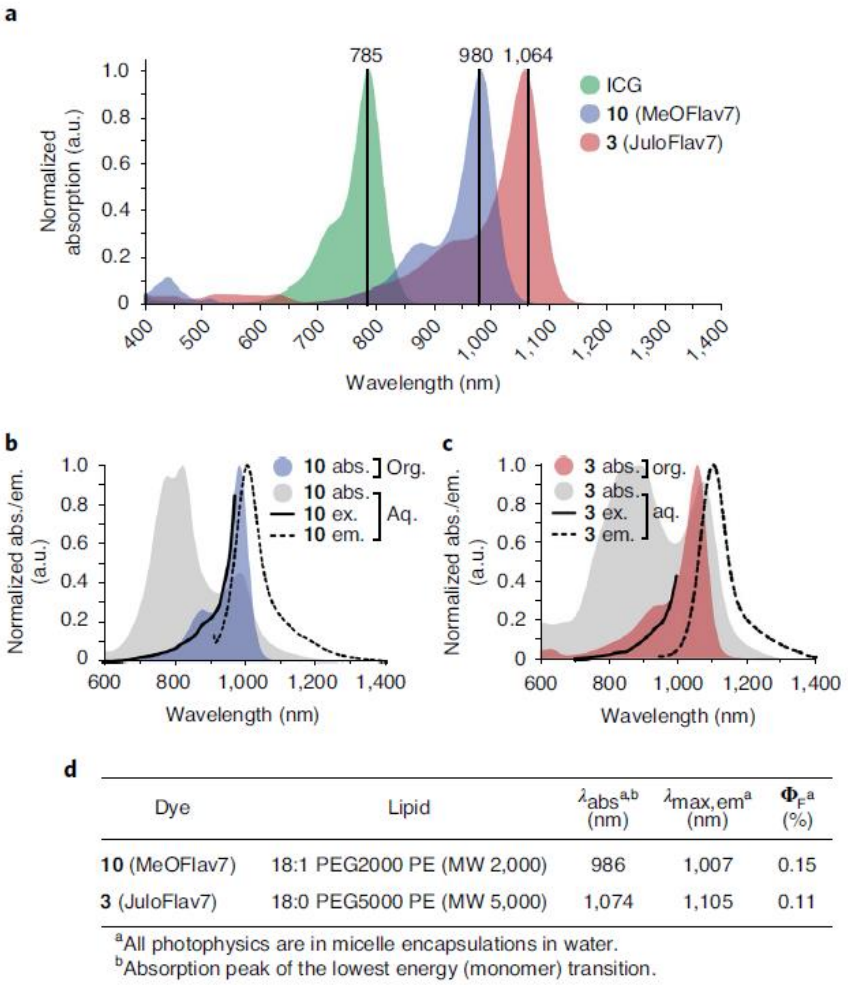
10 (MeOFlav7)



11 (IR-27)

Spectroscopy and imaging

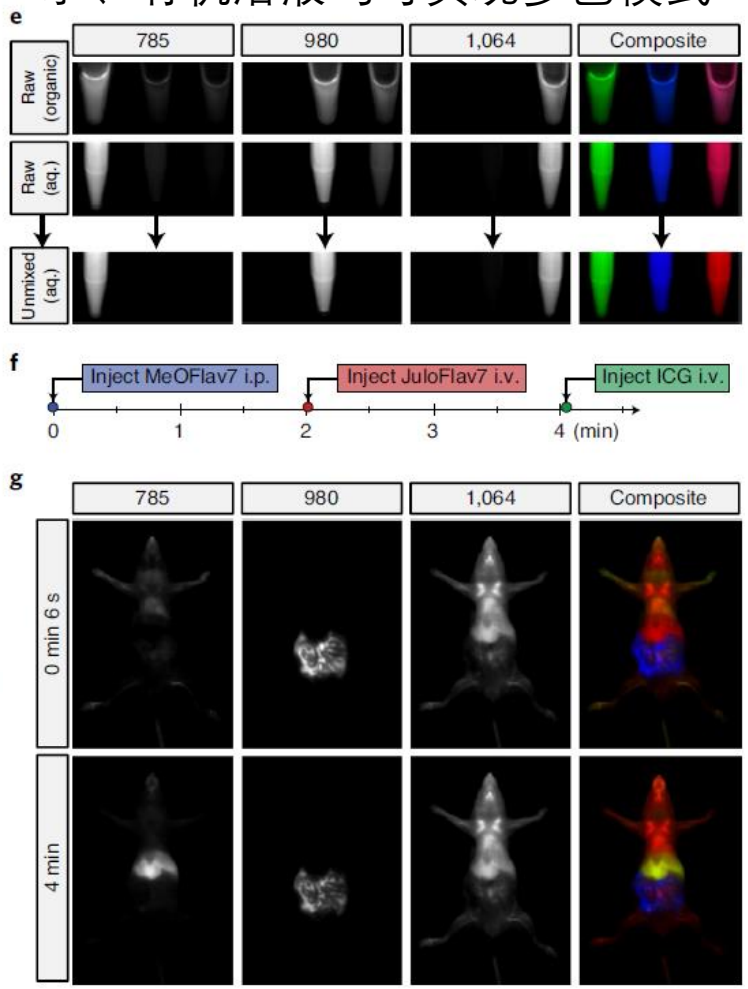
水、有机溶液均可实现多色模式

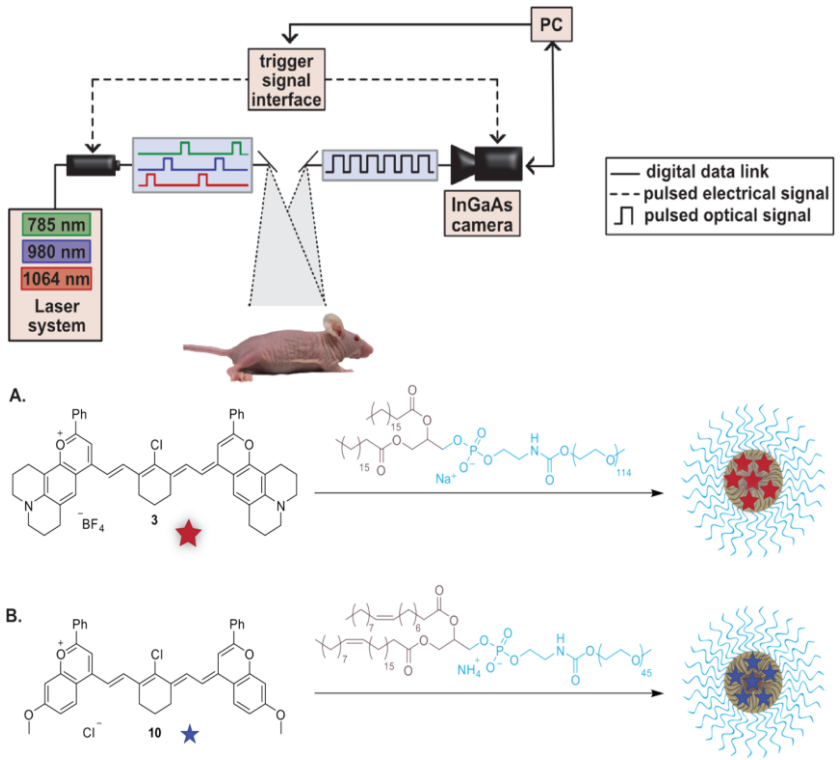


d

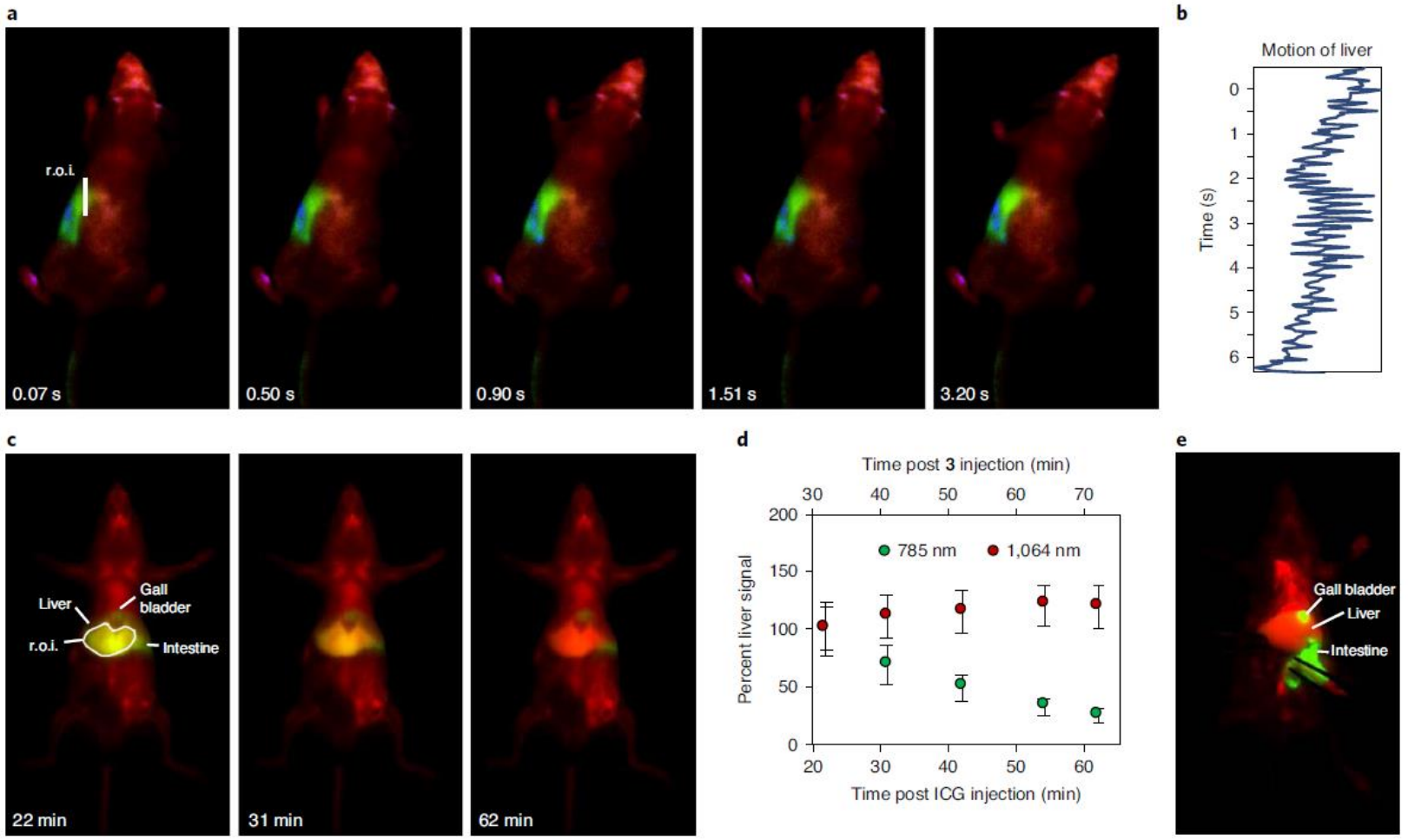
Dye	Lipid	λ_{abs}[a,b] (nm)	$\lambda_{max,em}$[a] (nm)	Φ_F[a] (%)
10 (MeOFlav7)	18:1 PEG2000 PE (MW 2,000)	986	1,007	0.15
3 (JuloFlav7)	18:0 PEG5000 PE (MW 5,000)	1,074	1,105	0.11

[a]All photophysics are in micelle encapsulations in water.
[b]Absorption peak of the lowest energy (monomer) transition.



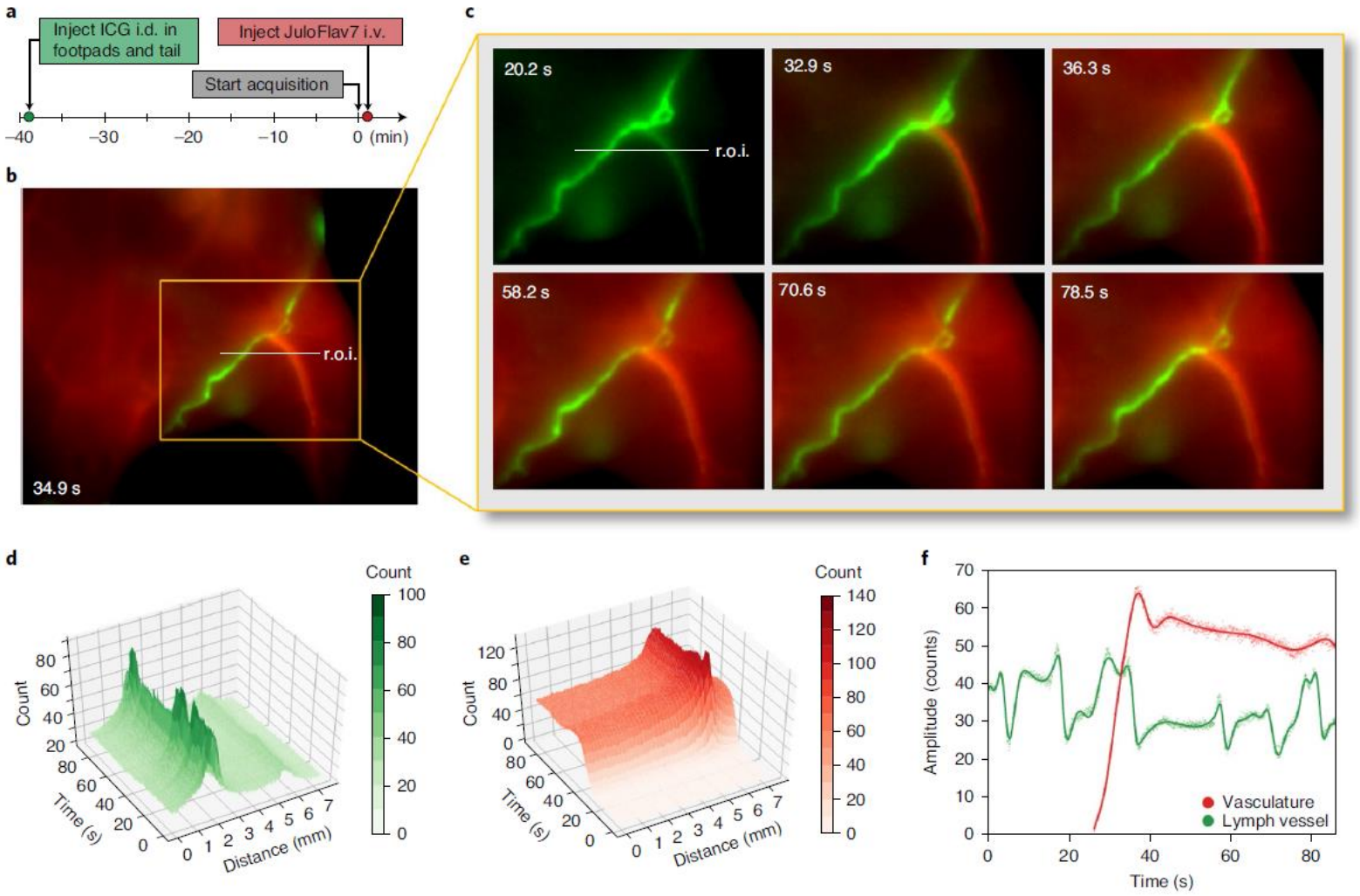


Spectroscopy and imaging



Applications enhanced by SWIR multiplexed imaging. **a**, Multiplexed imaging of an awake mouse showing one continuous movement of the head with 785, 980 and 1,064 nm excitation wavelengths (average power density = 78 mW cm^{-2}) and 1,150–1,700 nm collection (10 ms exposure time; 27.8 fps). Displayed images are a single frame. **b**, Awake breathing rate (247 breaths per minute), analysed by quantifying the liver motion (by the centre of mass) over the region of interest (r.o.i.) in **a**. **c**, Imaging of ICG clearance with systemic labelling by JuloFlav7 (3) micelles. Multiplexed in vivo images using 785 and 1,064 nm excitation (100 mW cm^{-2}) and 1,150–1,700 nm collection (5 ms exposure time; 50 fps). Displayed images are averaged over five frames. **d**, Percent signal in the liver of ICG and micelles of JuloFlav7 (3) over one hour. Data are displayed as the mean intensity over the r.o.i. (in **c**) ± standard deviation, *n* = 805 pixels within the r.o.i. **e**, Two-colour necropsy procedure, captured in real time in Supplementary Video 5.
Acquisition settings are as in **c**.

Spectroscopy and imaging



Orthogonal lymphatic and circulatory imaging with high spatiotemporal resolution after intradermal (i.d.) injection of ICG and i.v. injection of JuloFlav7 (3) micelles. **a**, Experimental timeline. **b**, Representative image acquired 30 s after injection of JuloFlav7 (3) micelles. **c**, Time points over the relevant time period analysed in **d**–**f**. **d**,**e**, Three-dimensional plots of the 785 nm channel (**d**) and 1,064 nm channel (**e**) demonstrating simultaneous intensity information in two colours over the r.o.i. indicated in **b** and **c**, and highlighting the spatial and temporal resolution captured. Contour plots are shown in Supplementary Fig. 9. **f**, The signal in each vessel over time can be quantified by plotting the amplitude of the vessel, fit as a Gaussian curve at each frame (points). The data is interpolated using a smoothing spline fit (solid lines). Acquisition, 785 and 1,064 nm excitation wavelengths (96 mW cm^{-2}) and 1,100–1,700 nm collection (20 ms exposure time; 21.7 fps). Displayed images are averaged over five frames.

Summary

- Developing predictably tunable SWIR polymethine fluorophores & triggered multi-excitation SWIR optical configuration
- Demonstrated multicolour whole-animal imaging at video-rate speeds and sub-millimetre resolution
- Opening a new realm in monitoring orthogonal function in mammals, even in awake animals without restraint or implantation