Supplementary Information

Derivation of Eqn (3)

If the total amount of DNR in a cell is T, then

$$T = c \times V$$

where c and V are the DNR concentration and cell volume, respectively.

Assuming the volume V does not change,

$$\frac{dT}{dt} = V \times \frac{dc}{dt} \qquad (4)$$

Since $\frac{dT}{dt}$ is determined by the uptake rate K_d and the efflux rate K_P of DNR,

$$\frac{dT}{dt} = K_d - K_P \qquad (5)$$

Assuming the drug uptake is a diffusion process and obeys Fick's first law of diffusion,

$$K_d = DA \times \frac{dc}{dx}$$

where D is the diffusion coefficient; A is the cell surface area; dc/dx is the concentration gradient across the cell membrane

$$K_d = DA \times \frac{C_{out} - C_{in}}{x} \qquad (6)$$

where x is the cell membrane thickness; and C_{out} and C_{in} are the extracellular and intracellular DNR concentrations, respectively.

Assuming the drug efflux of DNR involving Pgp is an enzymatic process obeying the Michaelis–Menten equation, the efflux rate F_{out} can be given as follows,

$$K_P = \frac{v_{\max} c_{in}}{K_m + c_{in}} \times A \qquad (7)$$

where $v_{\max}$ and K_m are the maximum rate in Michaelis-Menten equation and the Michaelis-Menten constant for the drug efflux process, respectively.

Substituting eqn (6) and (7) into eqn (4) and (5) and rearranging them, we have

$$\frac{dc}{dt} = \frac{A}{V} \times \left(D \times \frac{c_{out} - c_{in}}{x} - \frac{v_{\max} \times c_{in}}{K_m + c_{in}} \right) \qquad (3)$$

Figure captions

Figure S1 The schematic diagram of the optical setup including the bright-field imaging system and epifluorescence measurement system. DM, dichroic mirror; EX, excitation filter; PMT, photomultiplier tube; CCD, charge-coupled device camera; TV, television monitor; VCR, video cassette recorder.

Figure S2 Optimization of the emission wavelength and the excitation wavelength for DNR measurement. (a) Emission scan of a DNR solution (10 μM) at the excitation wavelength of λ=470 nm, showing an emission maximum at 590 nm. (b) Excitation scan of a DNR solution (10 μM) at the emission wavelength of λ=590 nm, showing an excitation maximum at 470 nm. The dashed lines represent the background without DNR.

Figure S1

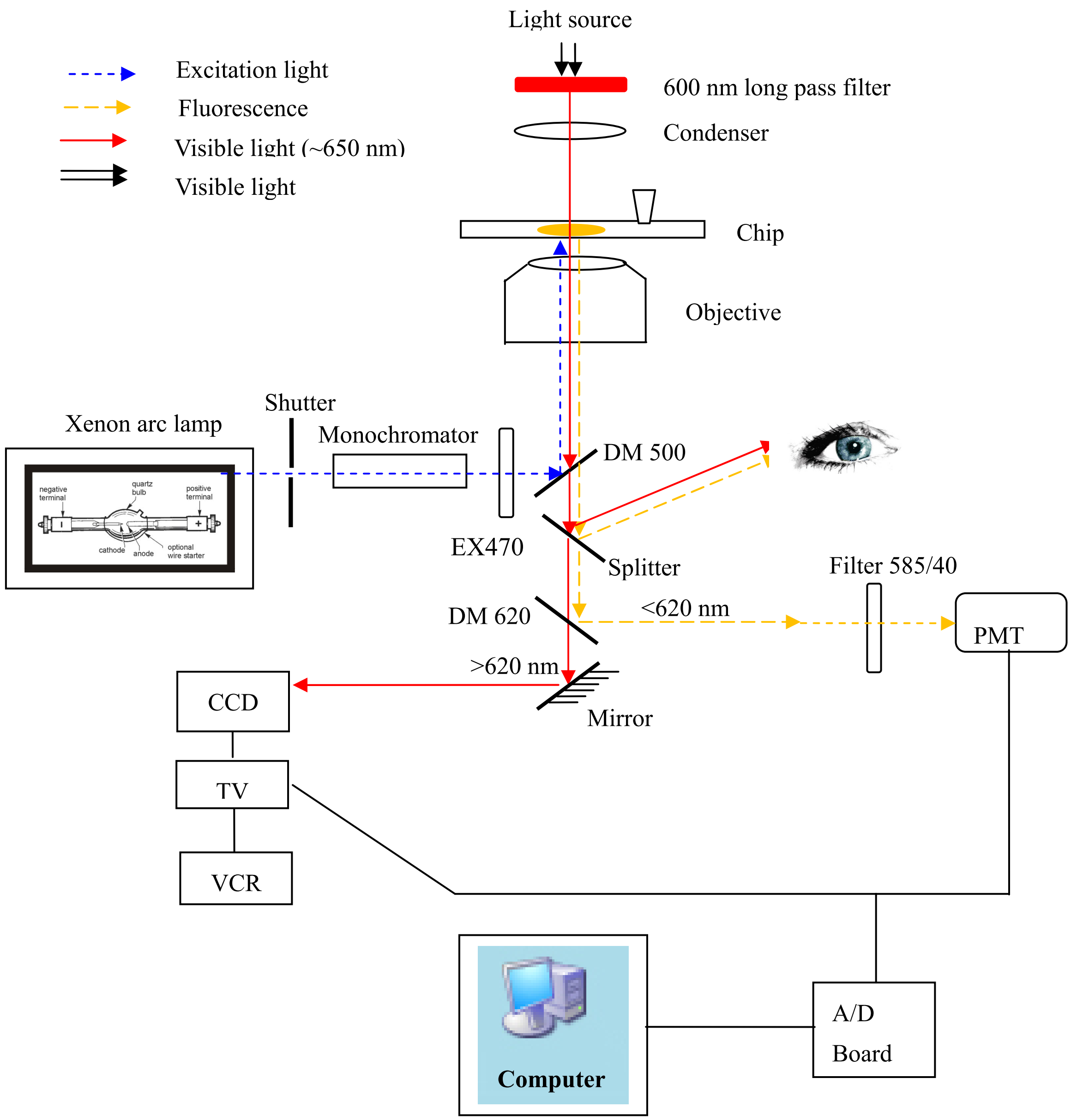
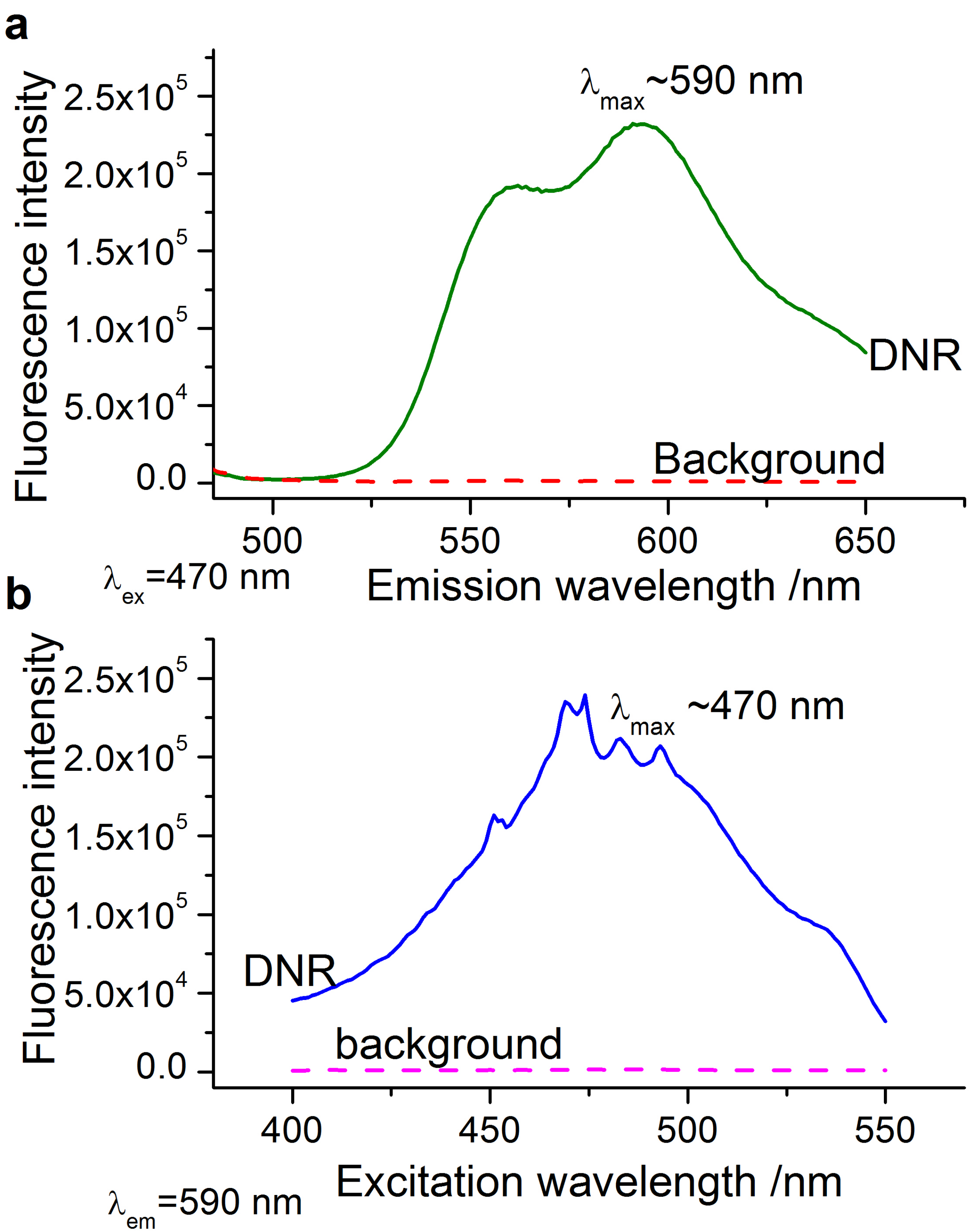

Light source
Excitation light
Fluorescence
Visible light (~650 nm)
Visible light
600 nm long pass filter
Condenser
Chip
Objective
Shutter
Xenon arc lamp
Monochromator
DM 500
EX470
Splitter
Filter 585/40
DM 620
<620 nm
PMT
>620 nm
CCD
Mirror
TV
VCR
A/D
Board
Computer

Figure S2


a
Fluorescence intensity
2.5x10^5
2.0x10^5
1.5x10^5
1.0x10^5
5.0x10^4
0.0
λmax ~590 nm
DNR
Background
500
550
600
650
λex=470 nm
Emission wavelength /nm
b
Fluorescence intensity
2.5x10^5
2.0x10^5
1.5x10^5
1.0x10^5
5.0x10^4
0.0
λmax ~470 nm
DNR
background
400
450
500
550
Excitation wavelength /nm
λem=590 nm