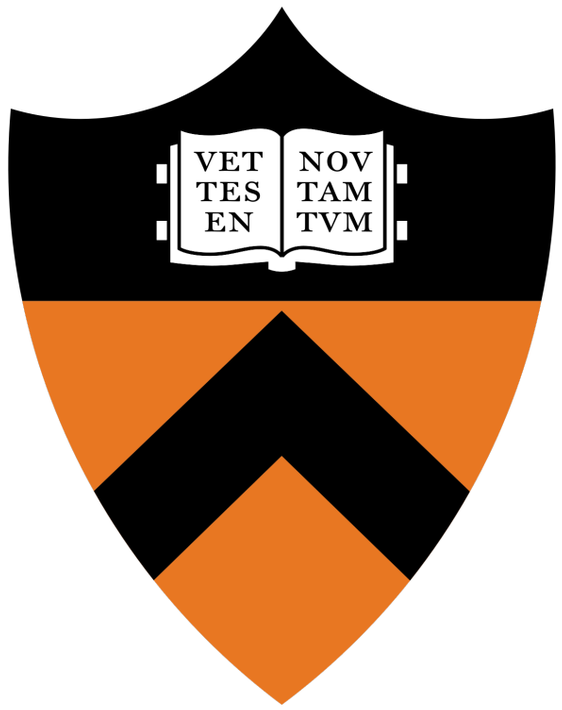
Photon Upconversion



Literature Group Meeting

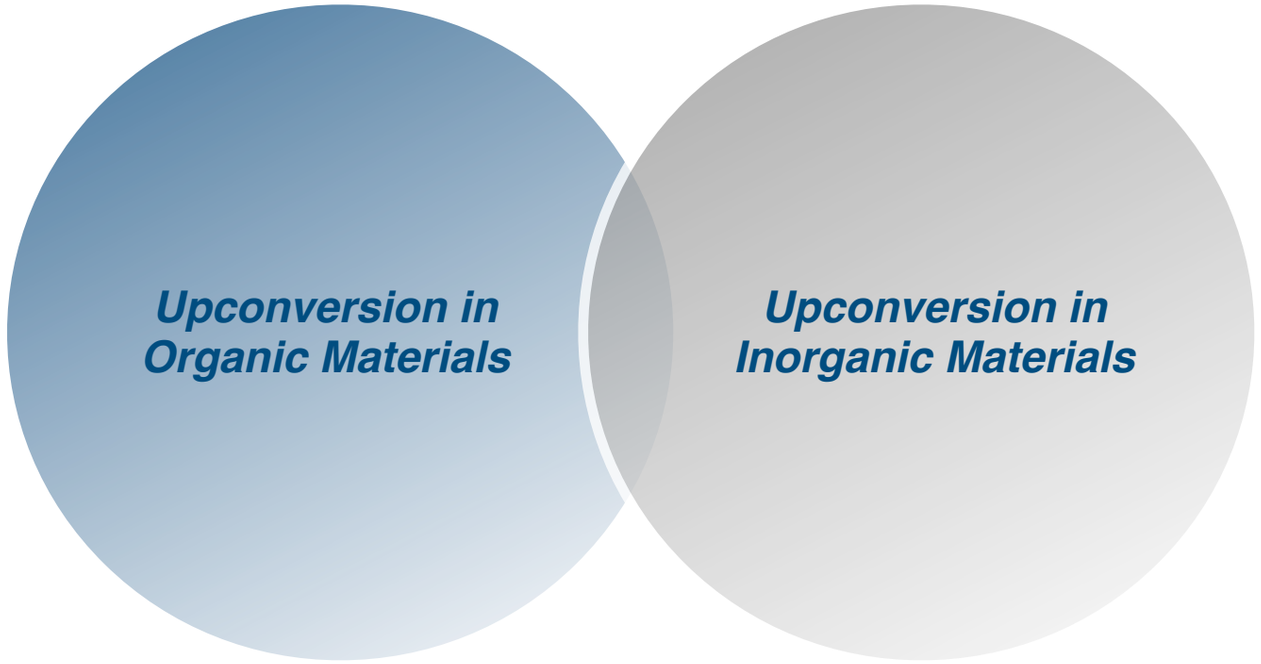
April 16th, 2024

Katherine Burton
MacMillan Group
Princeton University

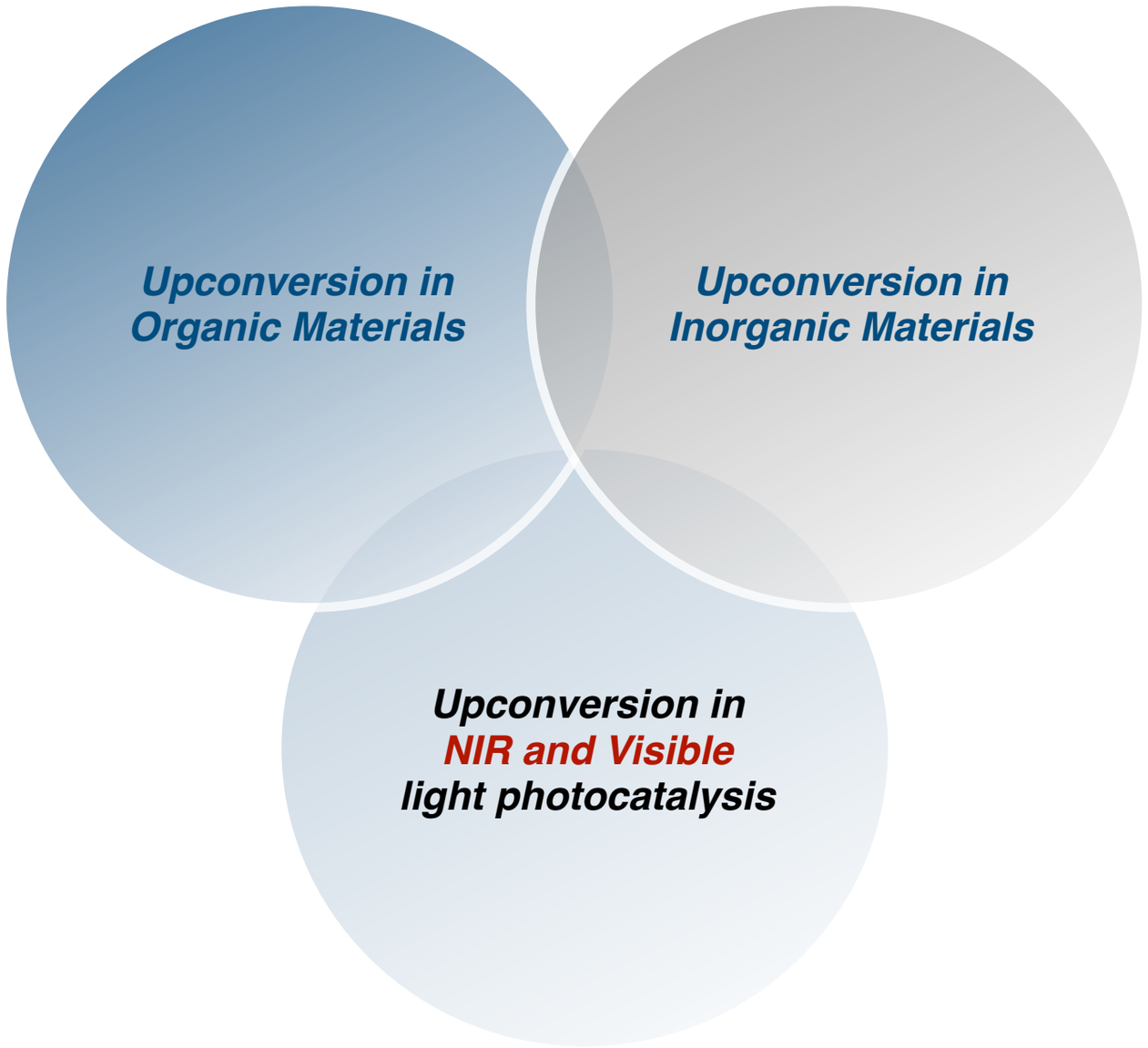
Upconversion Overview

Upconversion in Organic Materials

Upconversion Overview



Upconversion Overview



Understanding the process

The mechanism of photon upconversion

> 7 different mechanisms

Chen, et al. *J. Am. Chem. Soc.* **2023**. *145*, 10061–10070.

Understanding the process

The mechanism of photon upconversion

> 7 different mechanisms

- ***“A photophysical phenomenon that involves changing low-energy photons into high-energy ones”***

Chen, et al. *J. Am. Chem. Soc.* **2023**. *145*, 10061–10070.

Understanding the process

The mechanism of photon upconversion

> 7 different mechanisms

- ***“A photophysical phenomenon that involves changing low-energy photons into high-energy ones”***

anti-Stokes process

Chen, et al. *J. Am. Chem. Soc.* **2023**. *145*, 10061–10070.

Upconversion applied in organic systems

Upconversion in Organic Materials

2 key mechanisms:

- ***Triplet-Triplet Annihilation***
- ***Energy Pooling***

Upconversion applied in organic systems

Upconversion in Organic Materials

2 key mechanisms:

- ***Triplet-Triplet Annihilation***
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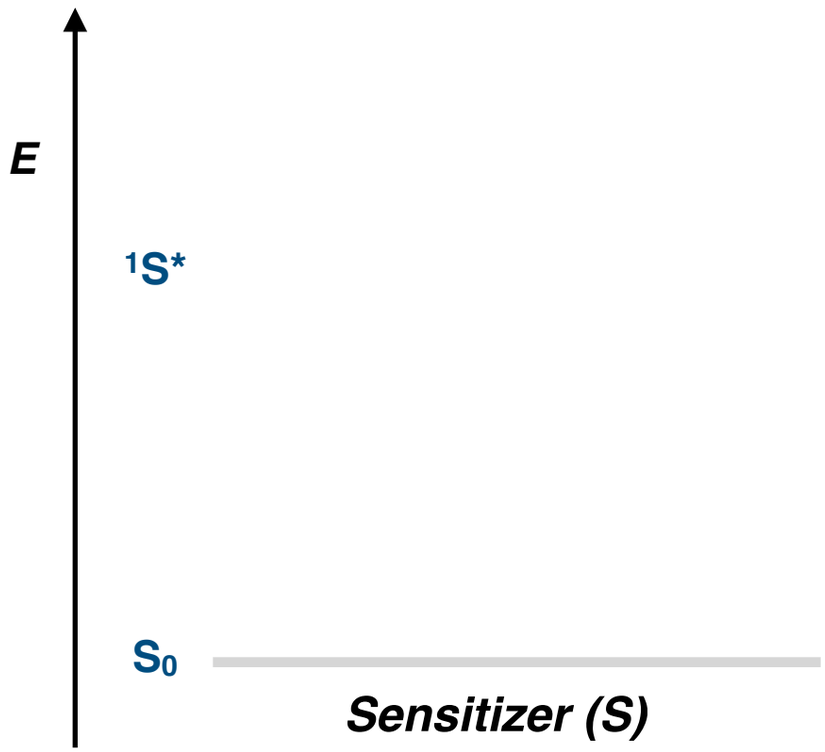
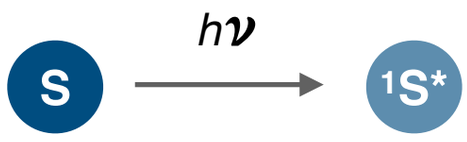
Understanding the process

The mechanism of TTA photon upconversion



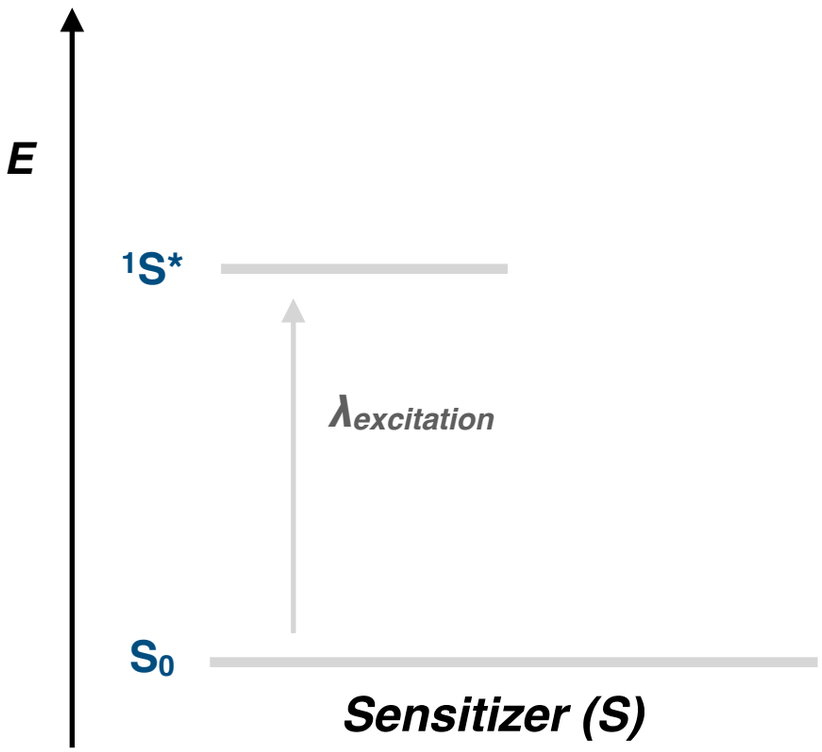
Triplet-Triplet Annihilation (TTA) Upconversion



Singh-Rachford, T. N., Castellano, F. N. *Coord. Chem. Rev.* **2010**. *254*, 2560.

Understanding the process

The mechanism of TTA photon upconversion



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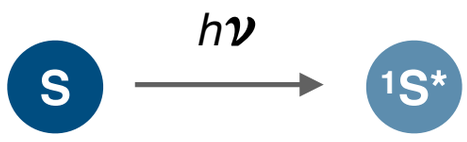

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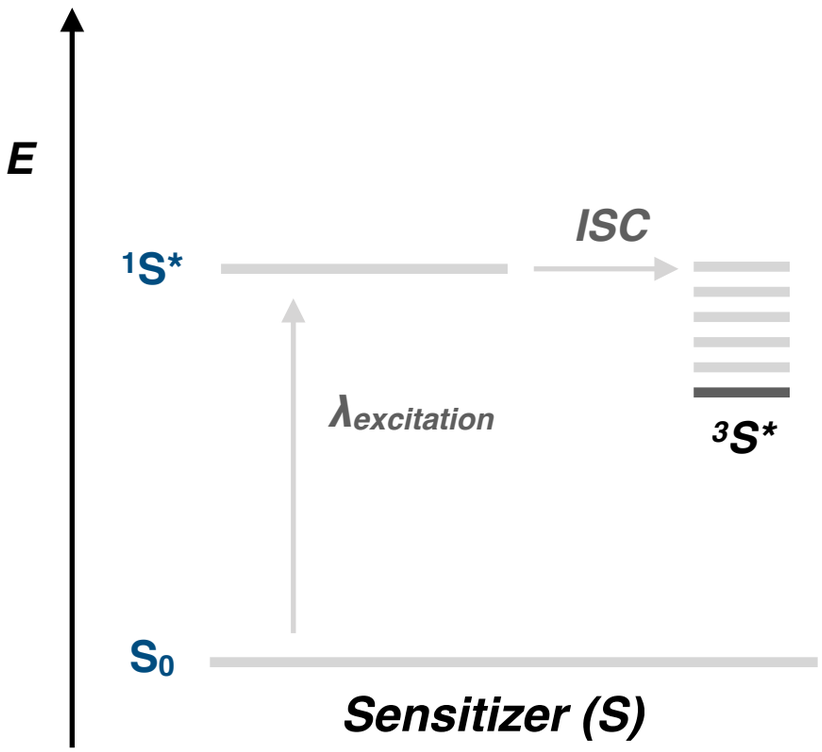
The mechanism of TTA photon upconversion



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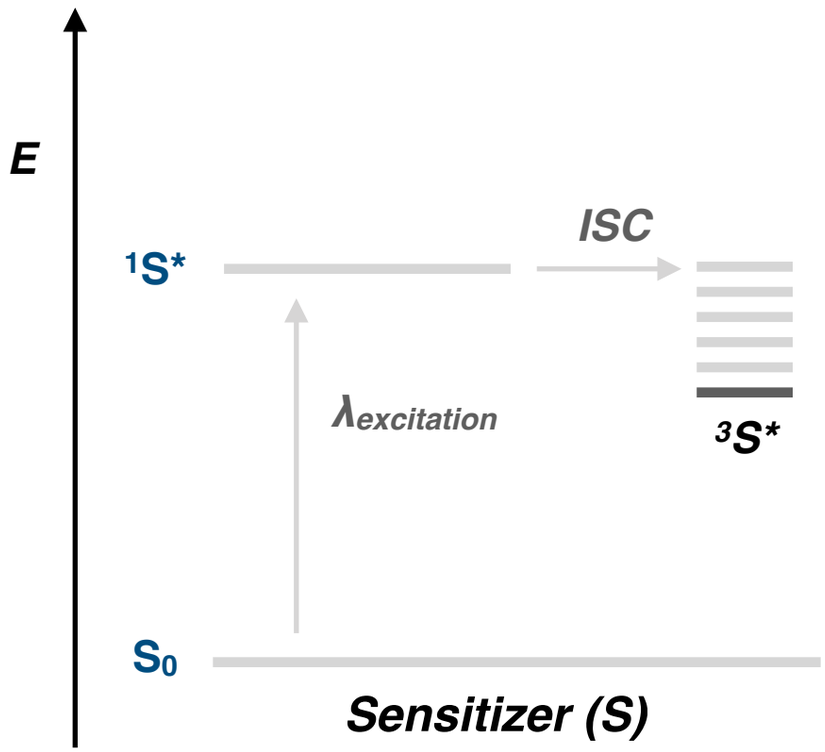


Key point #1

Long-lived triplet excited state

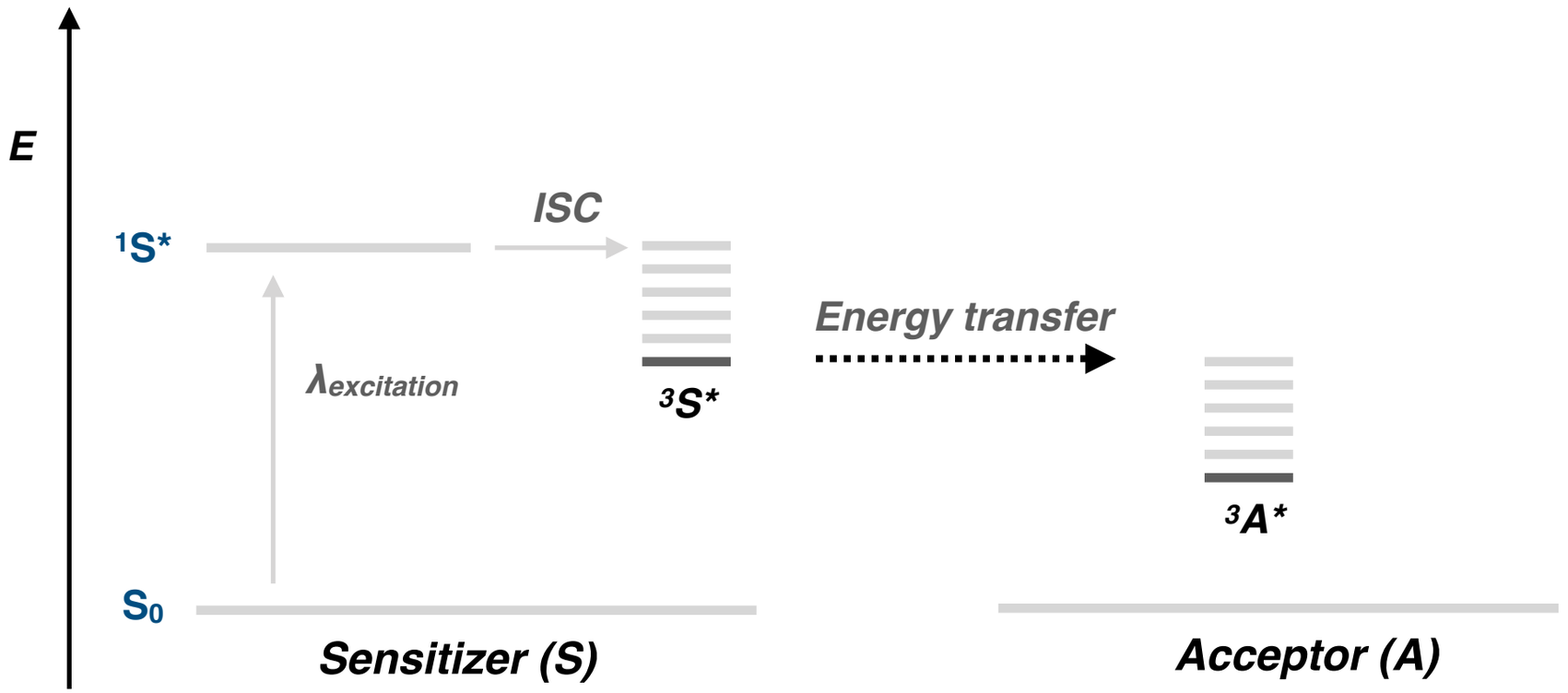
- *Required to populate triplet state of annihilator*

Triplet-Triplet Annihilation (TTA) Upconversion

Singh-Rachford, T. N., Castellano, F. N. *Coord. Chem. Rev.* **2010**. *254*, 2560.

Understanding the process

The mechanism of TTA photon upconversion



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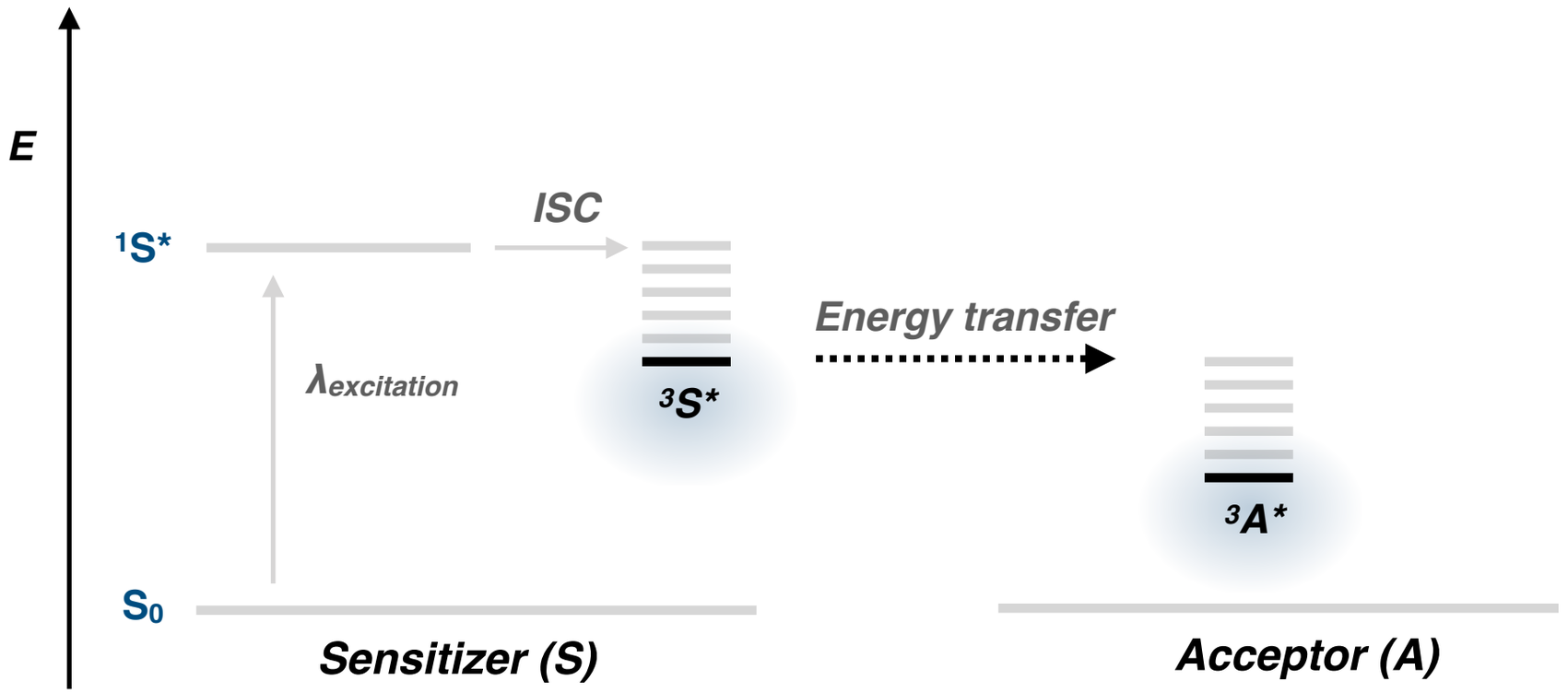
Understanding the process

The mechanism of TTA photon upconversion



Key point #2

For efficient TTA-UC:

Energy $^3S^*$ > $^3A^*$

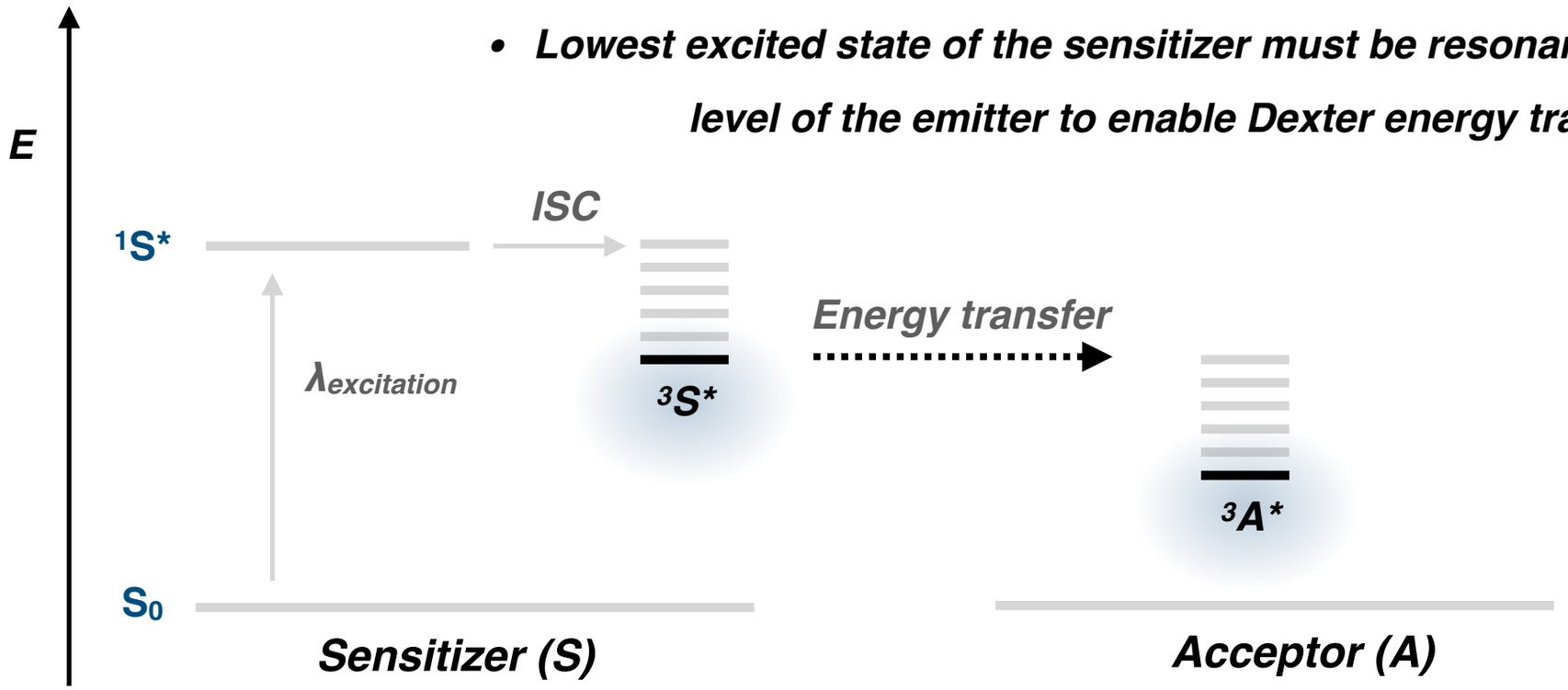
Triplet-Triplet Annihilation (TTA) Upconversion

Singh-Rachford, T. N., Castellano, F. N. *Coord. Chem. Rev.* **2010**. *254*, 2560.

Understanding the process

The mechanism of TTA photon upconversion

- ***Lowest excited state of the sensitizer must be resonant with the $^3A^*$ level of the emitter to enable Dexter energy transfer***



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Triplet-Triplet Annihilation (TTA) Upconversion

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Understanding the process

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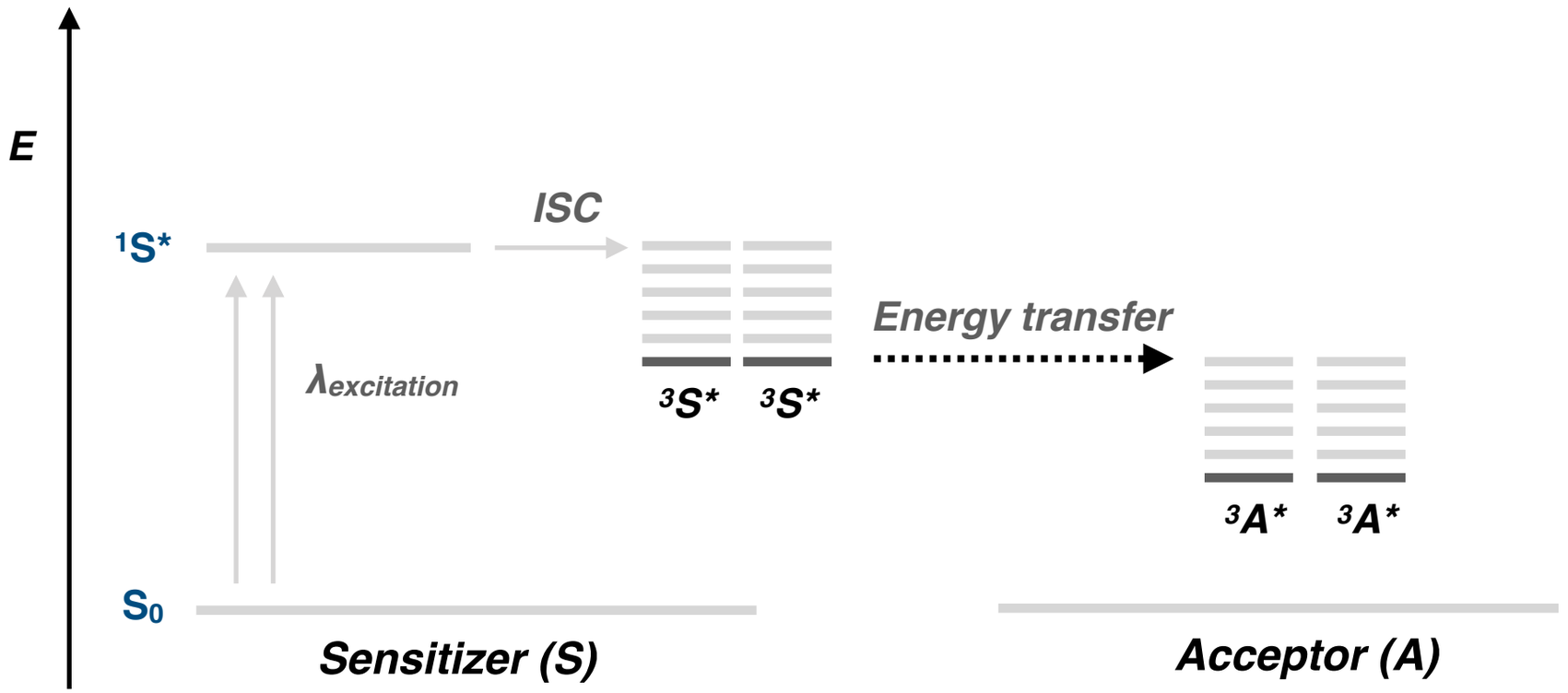

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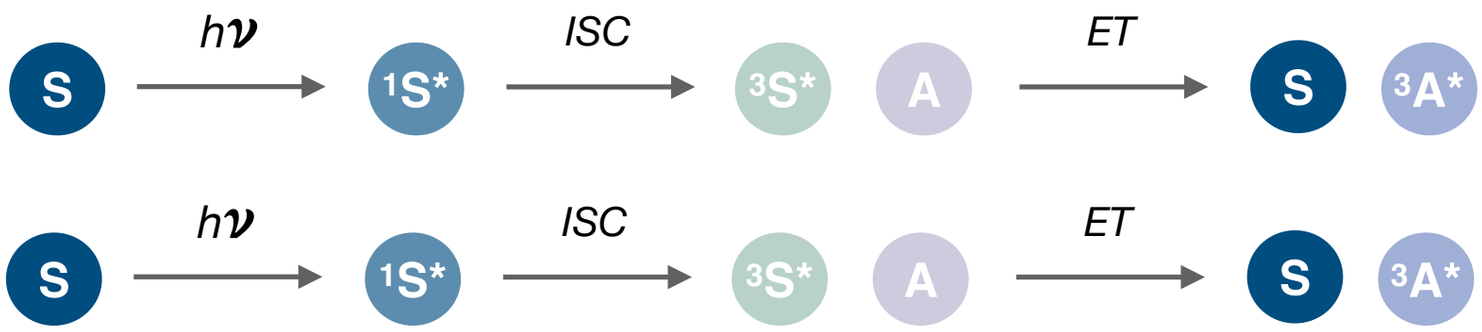

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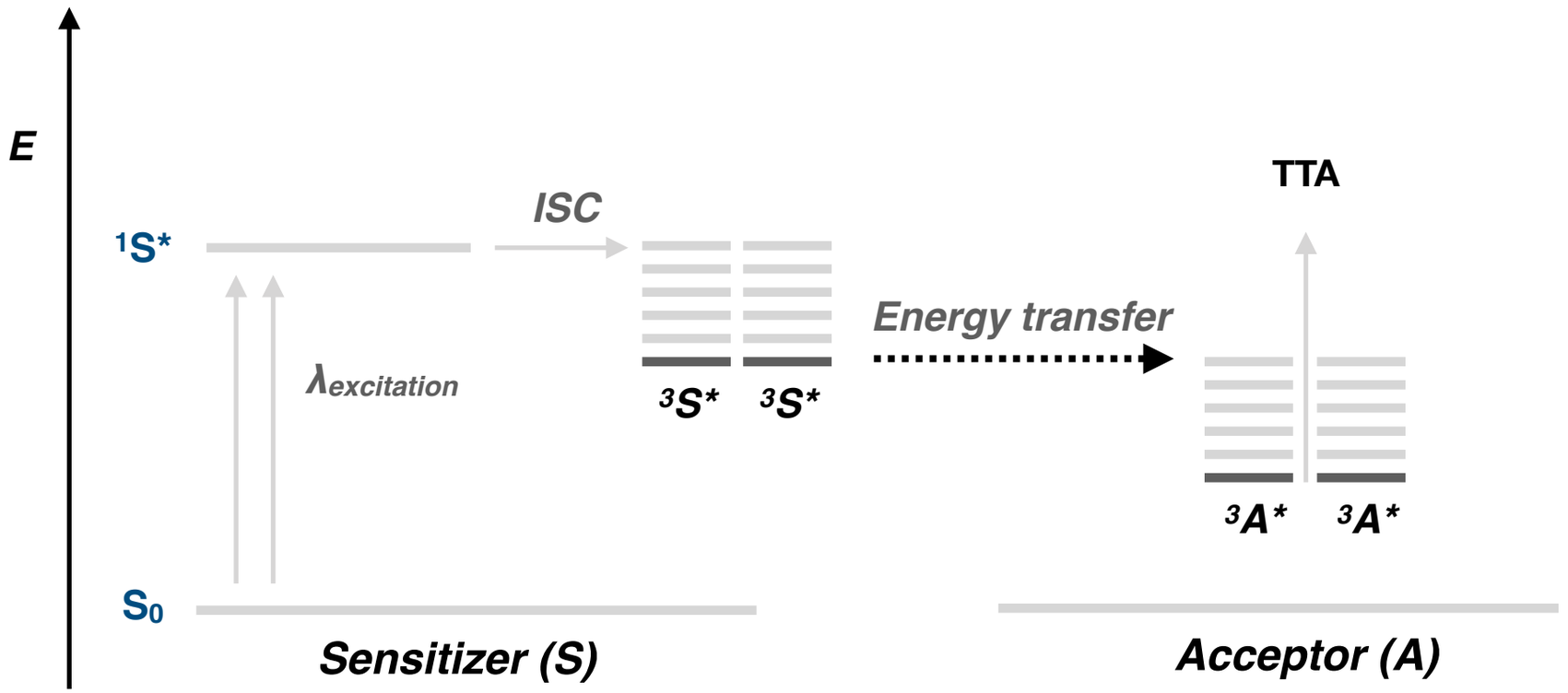
The mechanism of TTA photon upconversion



Triplet-Triplet Annihilation (TTA) Upconversion

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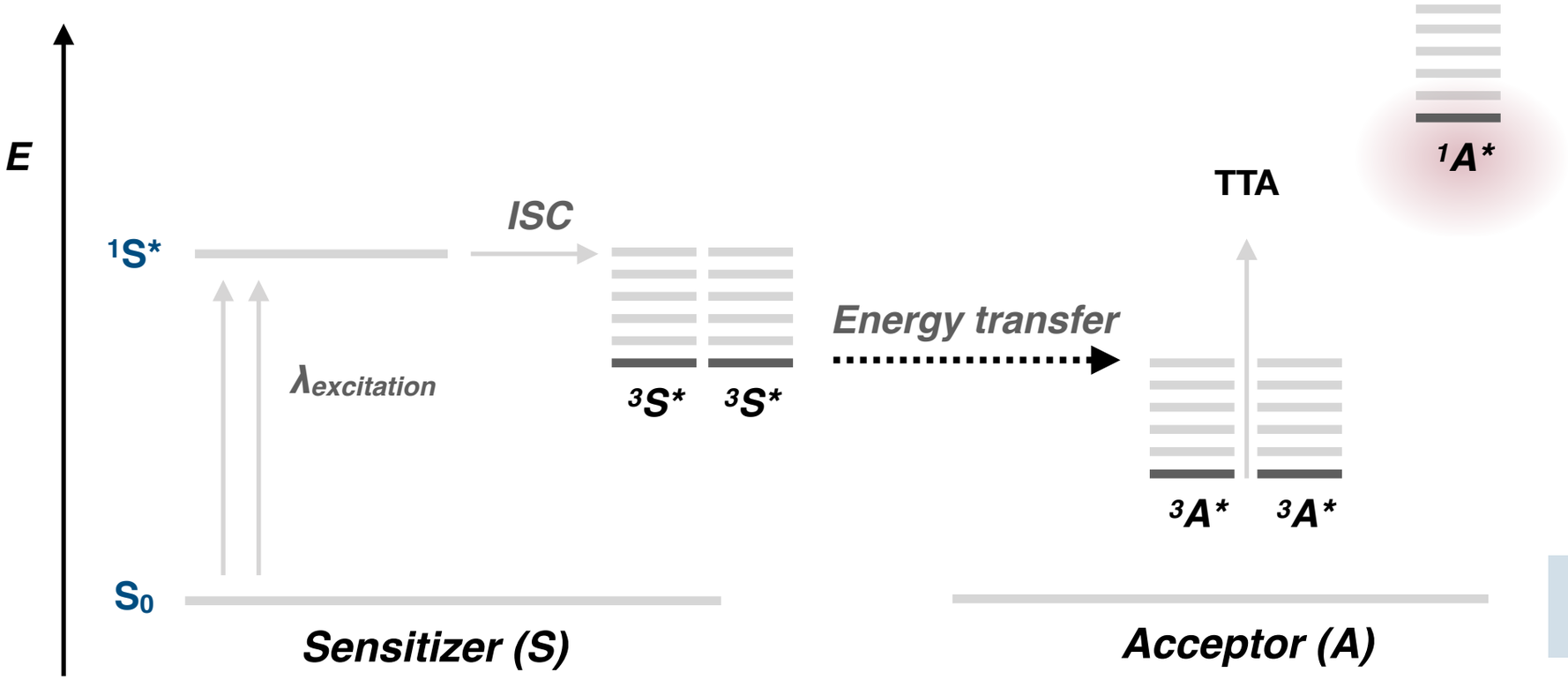


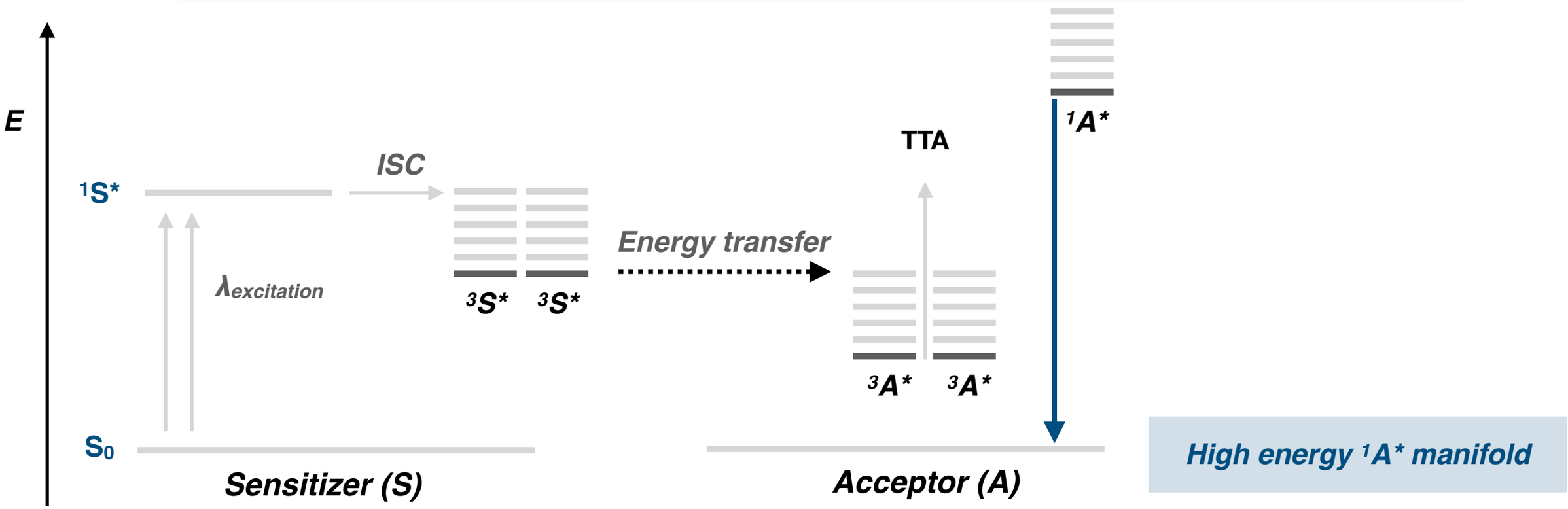
High energy $^1A^*$ manifold

Triplet-Triplet Annihilation (TTA) Upconversion

Singh-Rachford, T. N., Castellano, F. N. *Coord. Chem. Rev.* **2010**. *254*, 2560.

Understanding the process

The mechanism of TTA photon upconversion



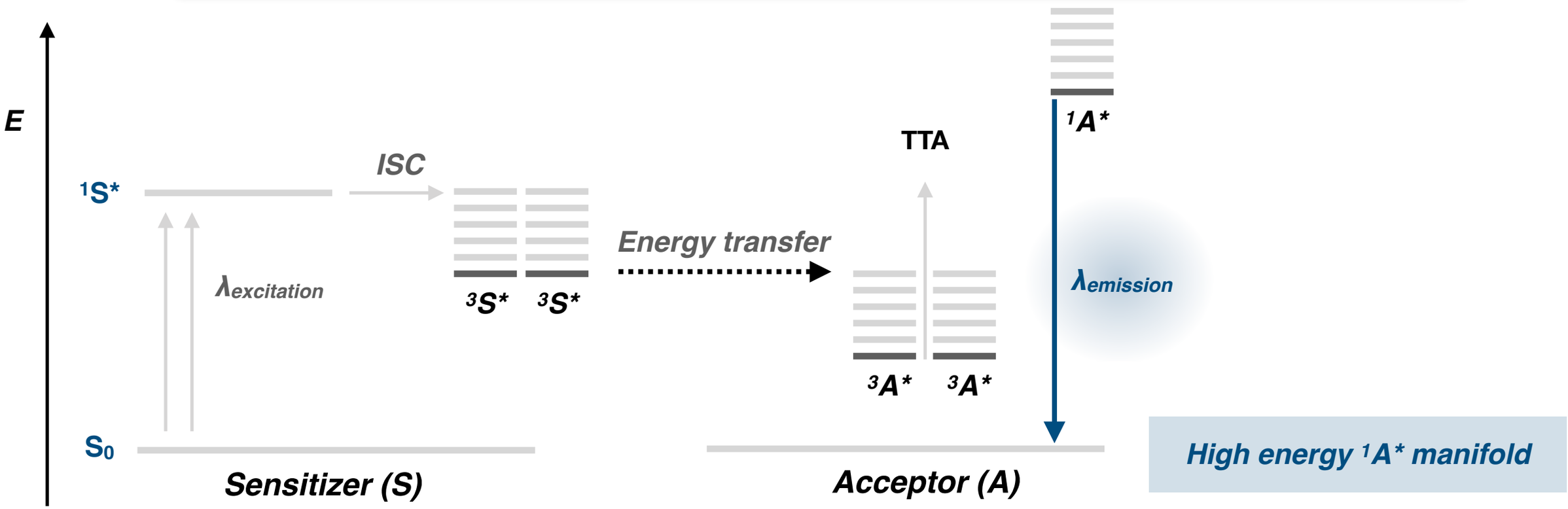
Triplet-Triplet Annihilation (TTA) Upconversion

*Upconverted **fluorescence** emission occurs from the **singlet state***

Singh-Rachford, T. N., Castellano, F. N. *Coord. Chem. Rev.* **2010**. *254*, 2560.

Understanding the process

The mechanism of TTA photon upconversion



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Understanding the process

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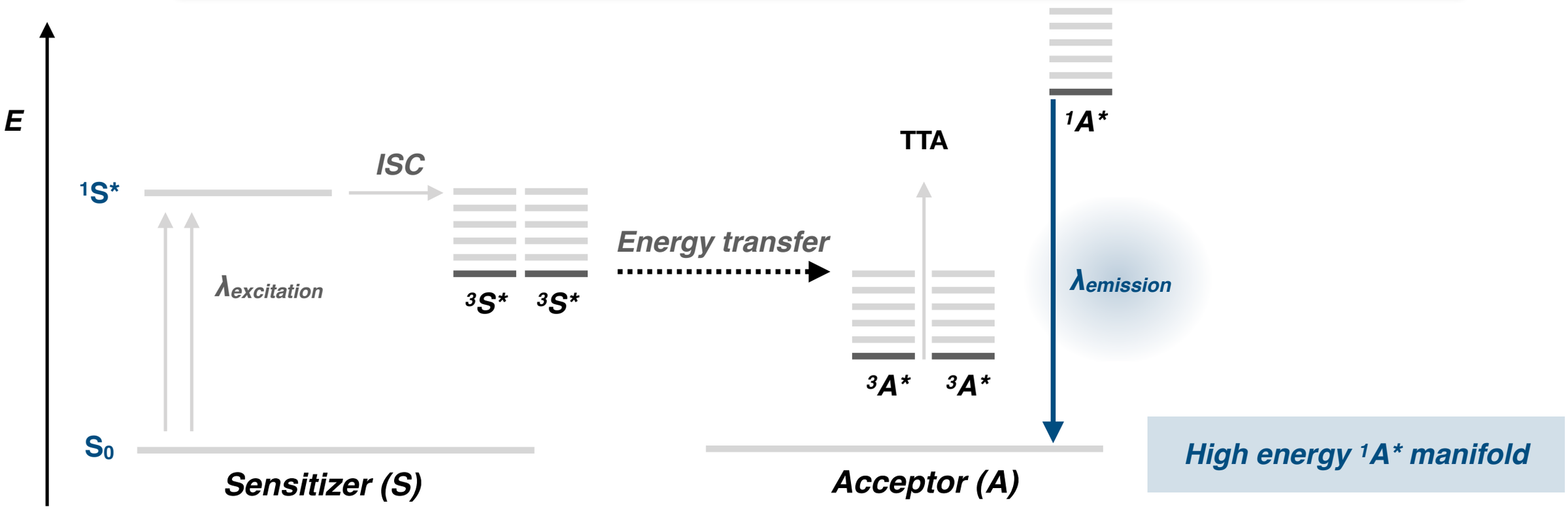

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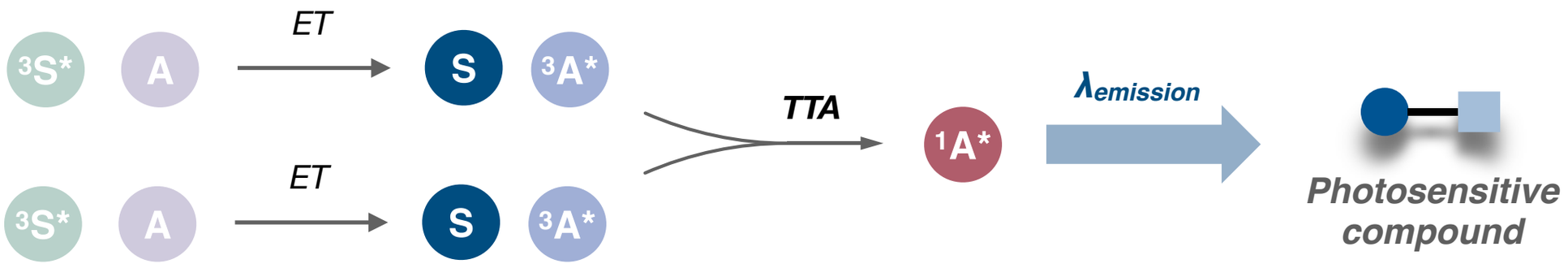

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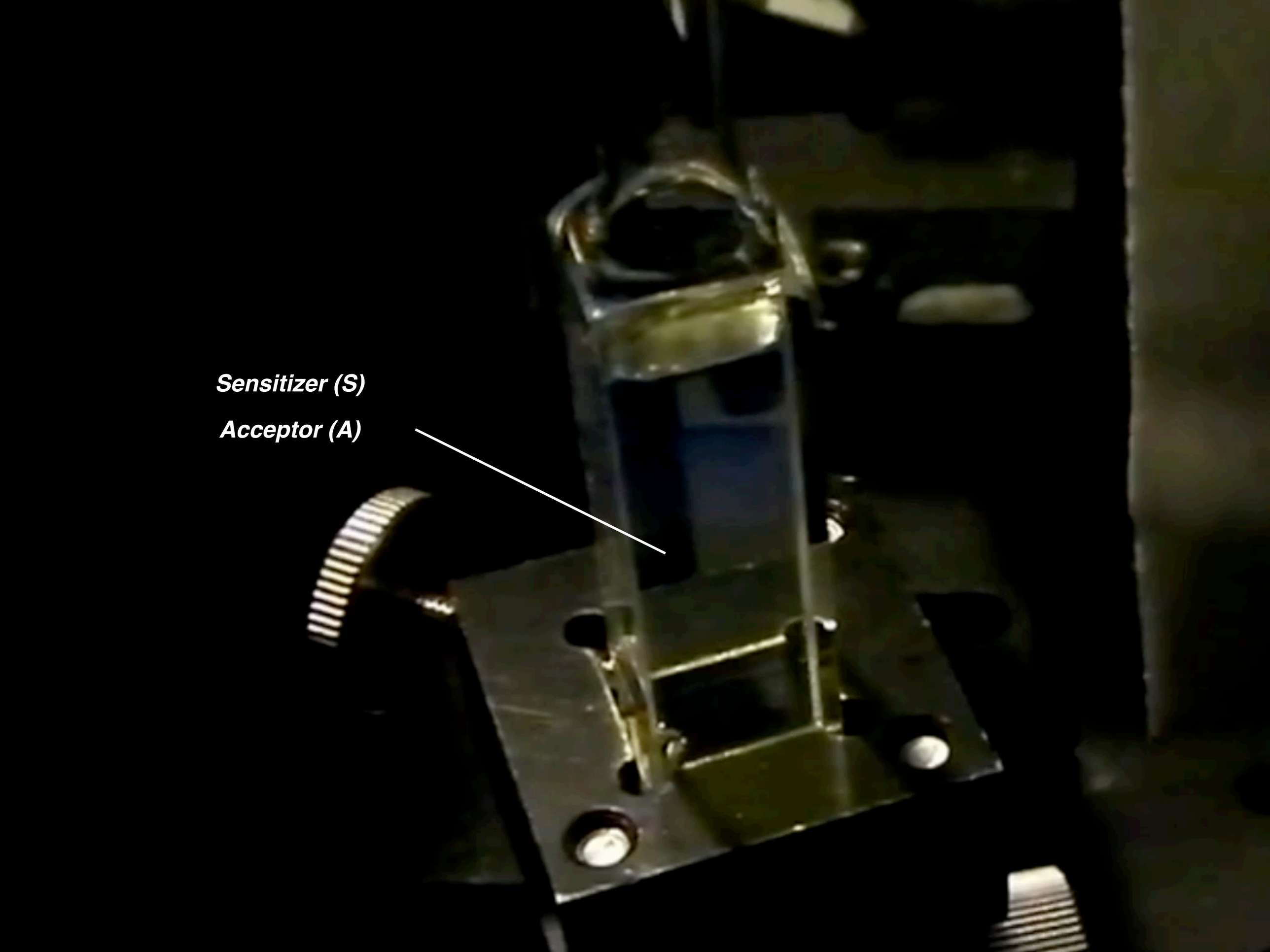
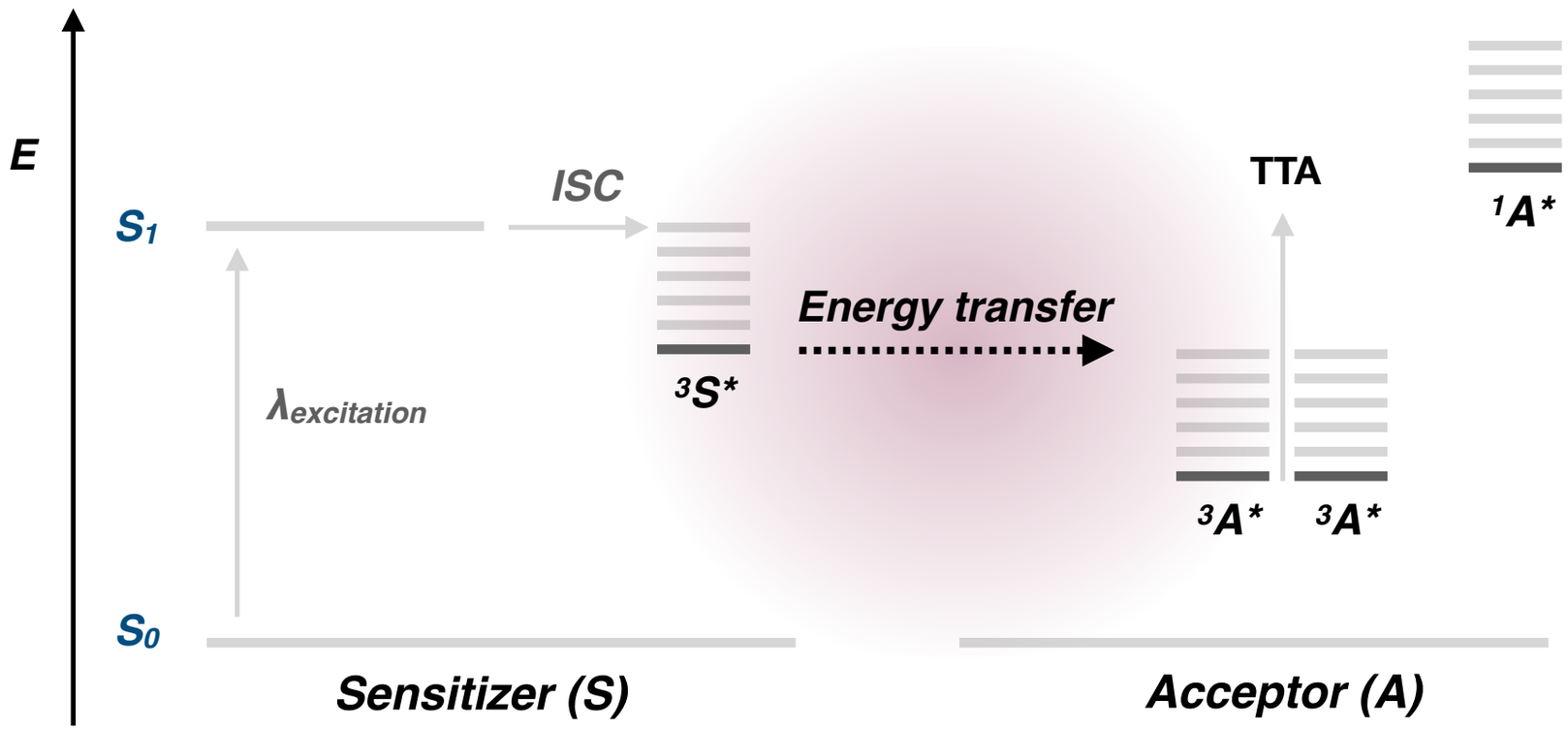

Sensitizer (S)
Acceptor (A)

Understanding the process

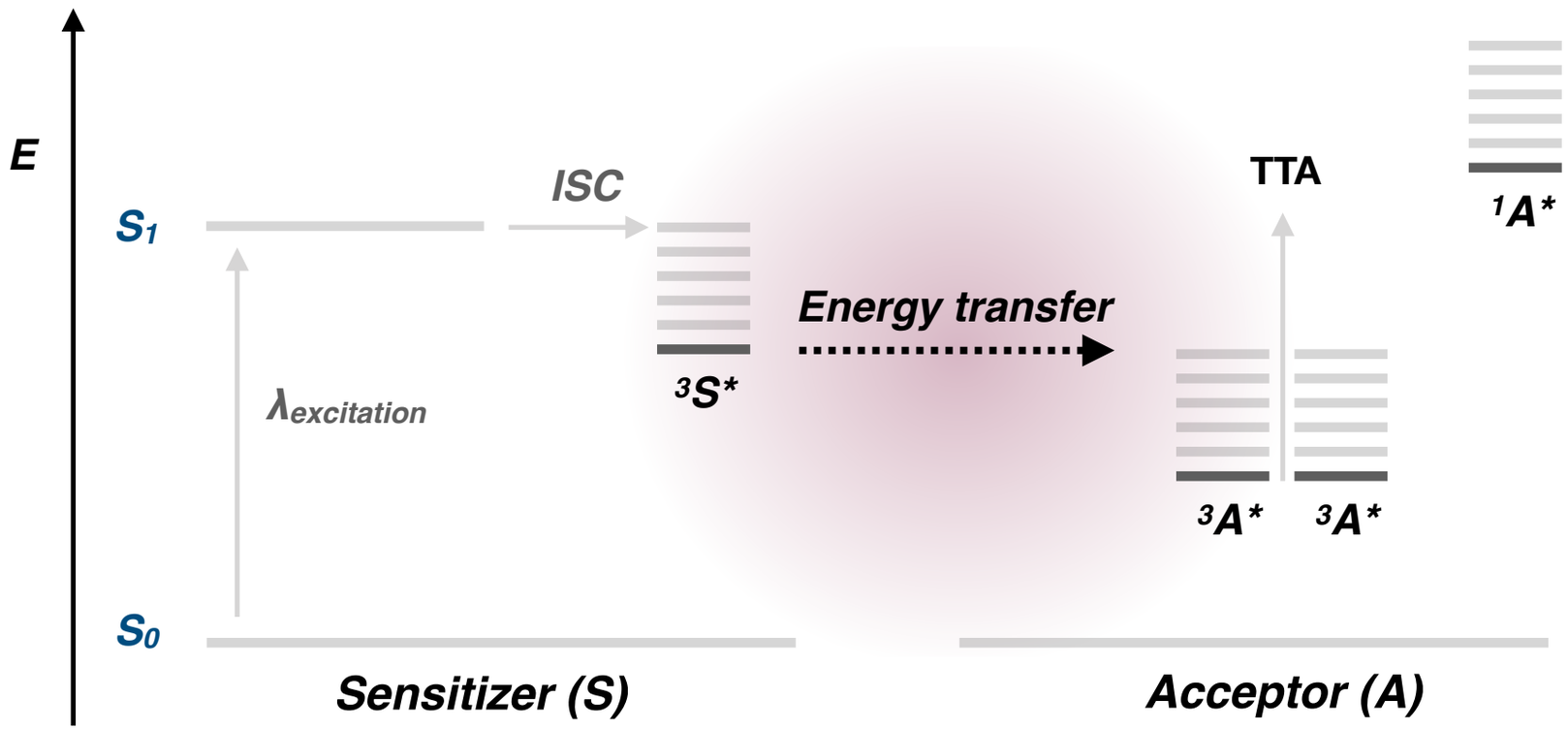
The mechanism of photon upconversion



Singh-Rachford, T. N., Castellano, F. N. *Coord. Chem. Rev.* **2010**. *254*, 2560.

Understanding the process

The mechanism of photon upconversion



Triplet-Triplet Annihilation (TTA) Upconversion

- *Upconversion via **triplet fusion** is limited to **direct activation** of the acceptor*

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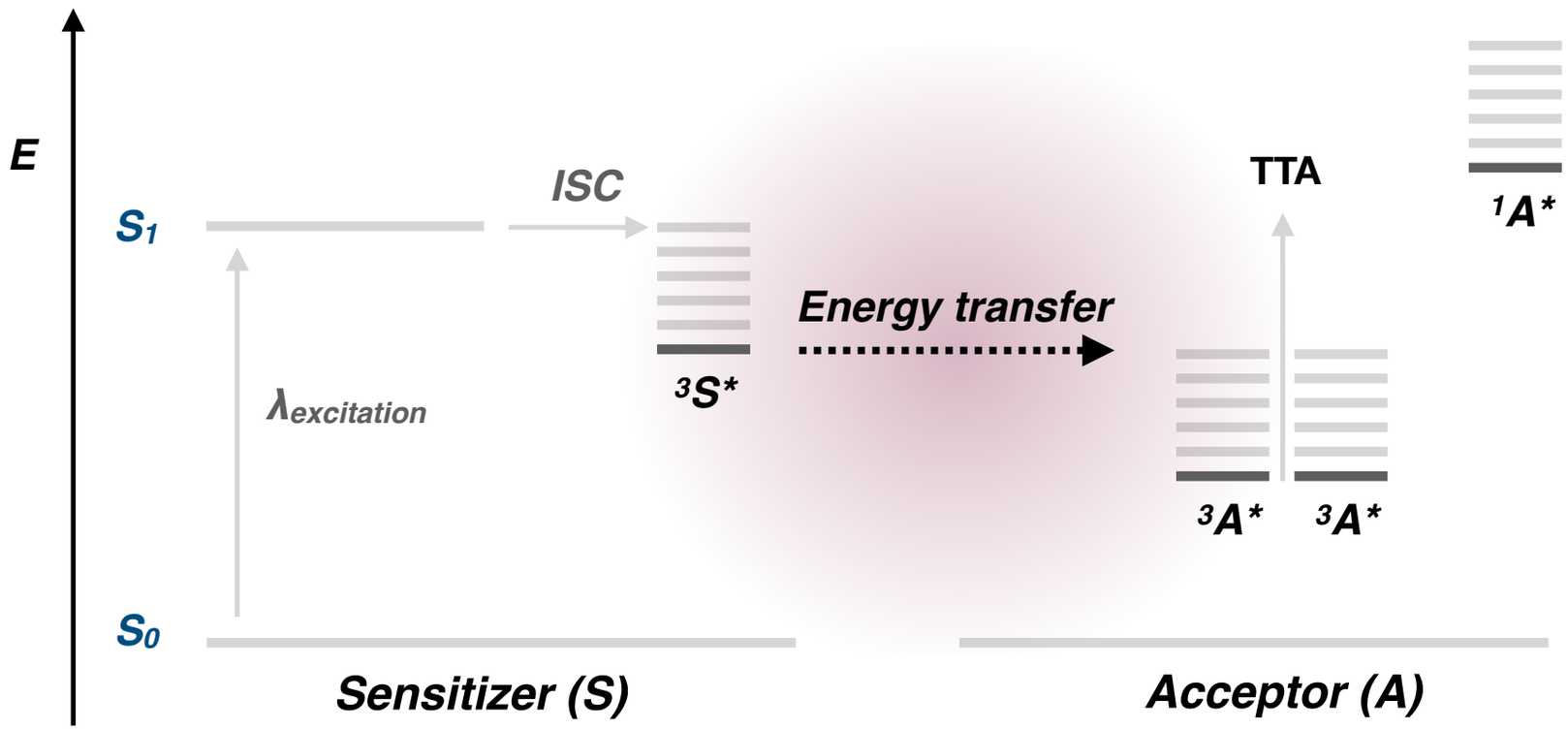
Understanding the process

The mechanism of photon upconversion



Triplet-Triplet Annihilation (TTA) Upconversion

- *Upconversion via **triplet fusion** is limited to **direct activation** of the acceptor*

A highly tunable acceptor is needed

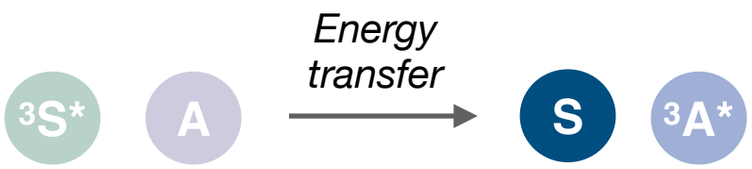
Singh-Rachford, T. N., Castellano, F. N. *Coord. Chem. Rev.* **2010**. *254*, 2560.

Upconversion applied in organic systems

Upconversion in Organic Materials

Upconversion applied in organic systems

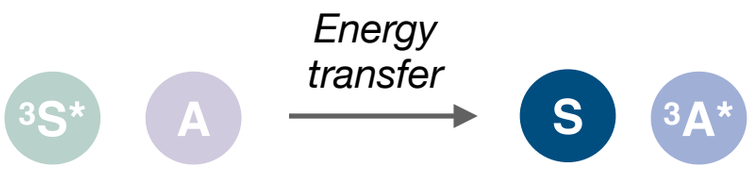
Upconversion in Organic Materials



Acceptor (A) = Organic substrate

Upconversion applied in organic systems

Upconversion in Organic Materials



Acceptor (A) = Organic substrate

Organic molecules = synthetically diverse

Upconversion applied in organic systems

Upconversion in Organic Materials

$^3S^*$ = **PdTNP**

Huang, L., Wu, W., Li, Y., Huang, K., Zeng, L., Lin, W., Han, G. *J. Am. Chem. Soc.* **2020**. *142*, 18460–18470.

Upconversion applied in organic systems

Upconversion in Organic Materials

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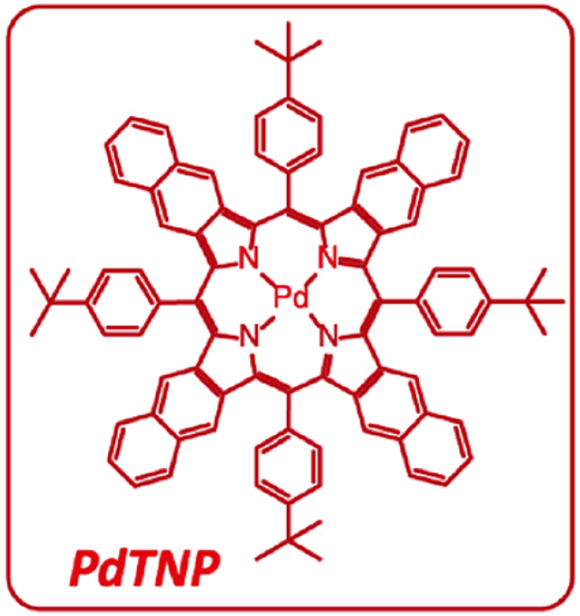

PdTNP

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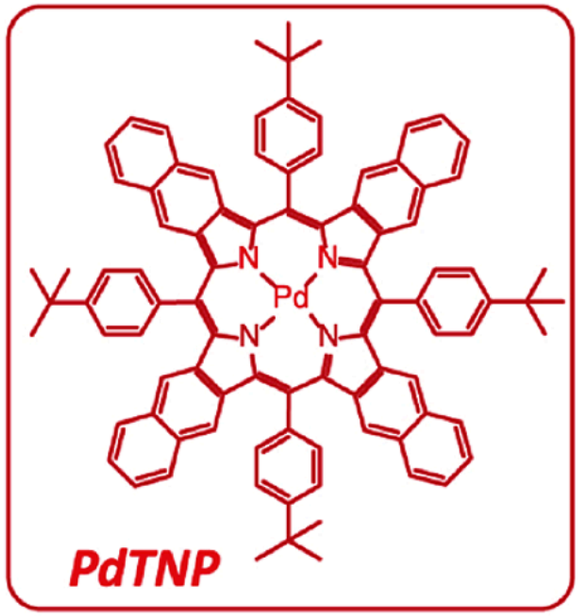

PdTNP

- **Long-lived triplet lifetime τ_T = 65 μs**

Huang, L., Wu, W., Li, Y., Huang, K., Zeng, L., Lin, W., Han, G. *J. Am. Chem. Soc.* **2020**. *142*, 18460–18470.

Upconversion applied in organic systems

Upconversion in Organic Materials

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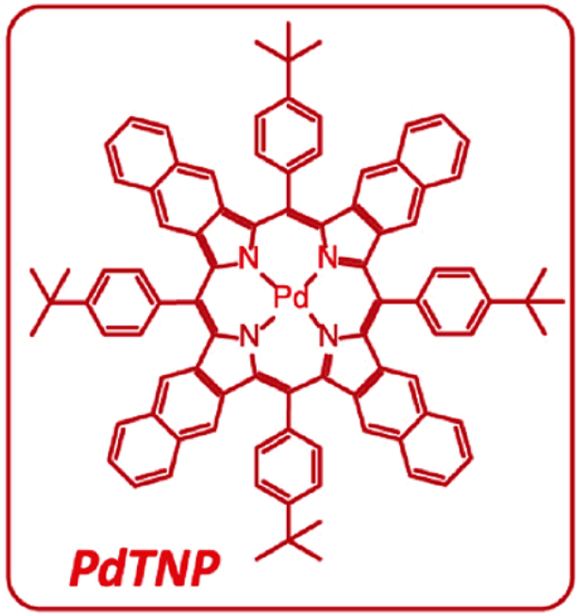


PdTNP

- **Long-lived triplet lifetime τ_T = 65 μs**
- **Goal: NIR to green light TTA UC**

Huang, L., Wu, W., Li, Y., Huang, K., Zeng, L., Lin, W., Han, G. *J. Am. Chem. Soc.* **2020**. *142*, 18460–18470.

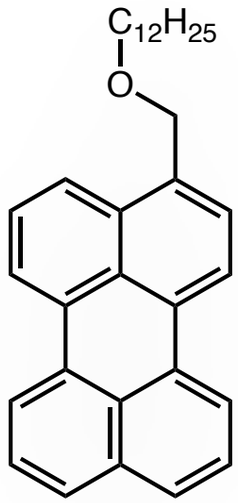
Upconversion applied in organic systems

Upconversion in Organic Materials

excitation = 653 nm

$^3S^*$ = **PdTNP**

A =



Py0

Huang, L., Wu, W., Li, Y., Huang, K., Zeng, L., Lin, W., Han, G. *J. Am. Chem. Soc.* **2020**. *142*, 18460–18470.

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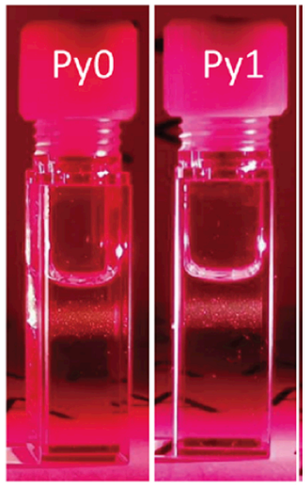

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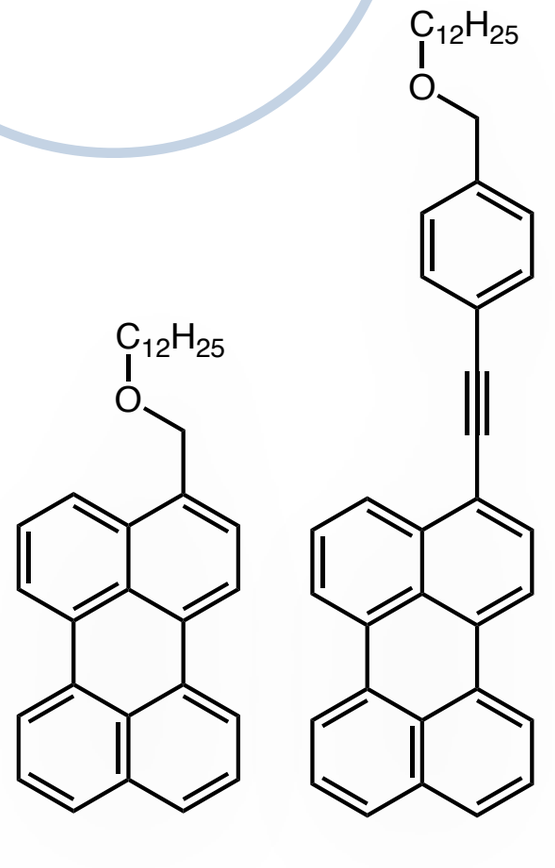

Py0 ***Py1***

conjugation in organic annihilator

Huang, L., Wu, W., Li, Y., Huang, K., Zeng, L., Lin, W., Han, G. *J. Am. Chem. Soc.* **2020**. *142*, 18460–18470.

Upconversion applied in organic systems

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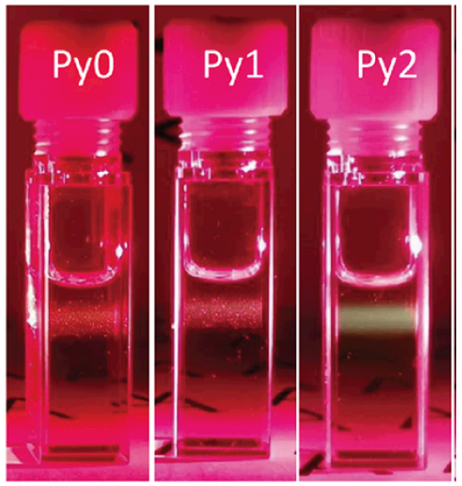

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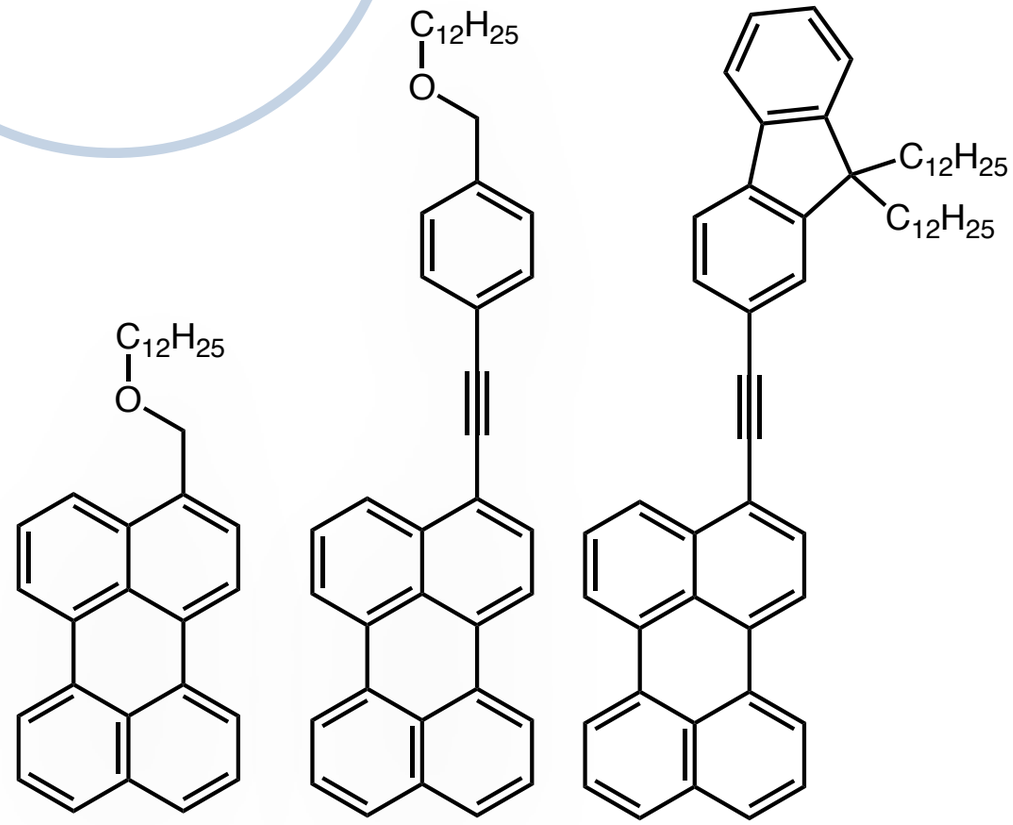


Py0 ***Py1*** ***Py2***

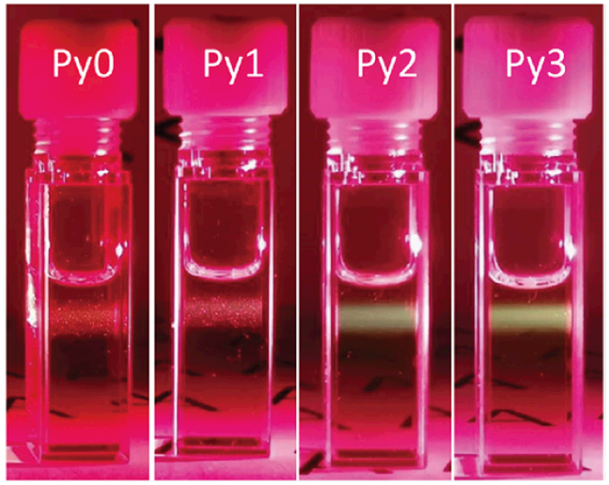
conjugation in organic annihilator

Huang, L., Wu, W., Li, Y., Huang, K., Zeng, L., Lin, W., Han, G. *J. Am. Chem. Soc.* **2020**. *142*, 18460–18470.

Upconversion applied in organic systems

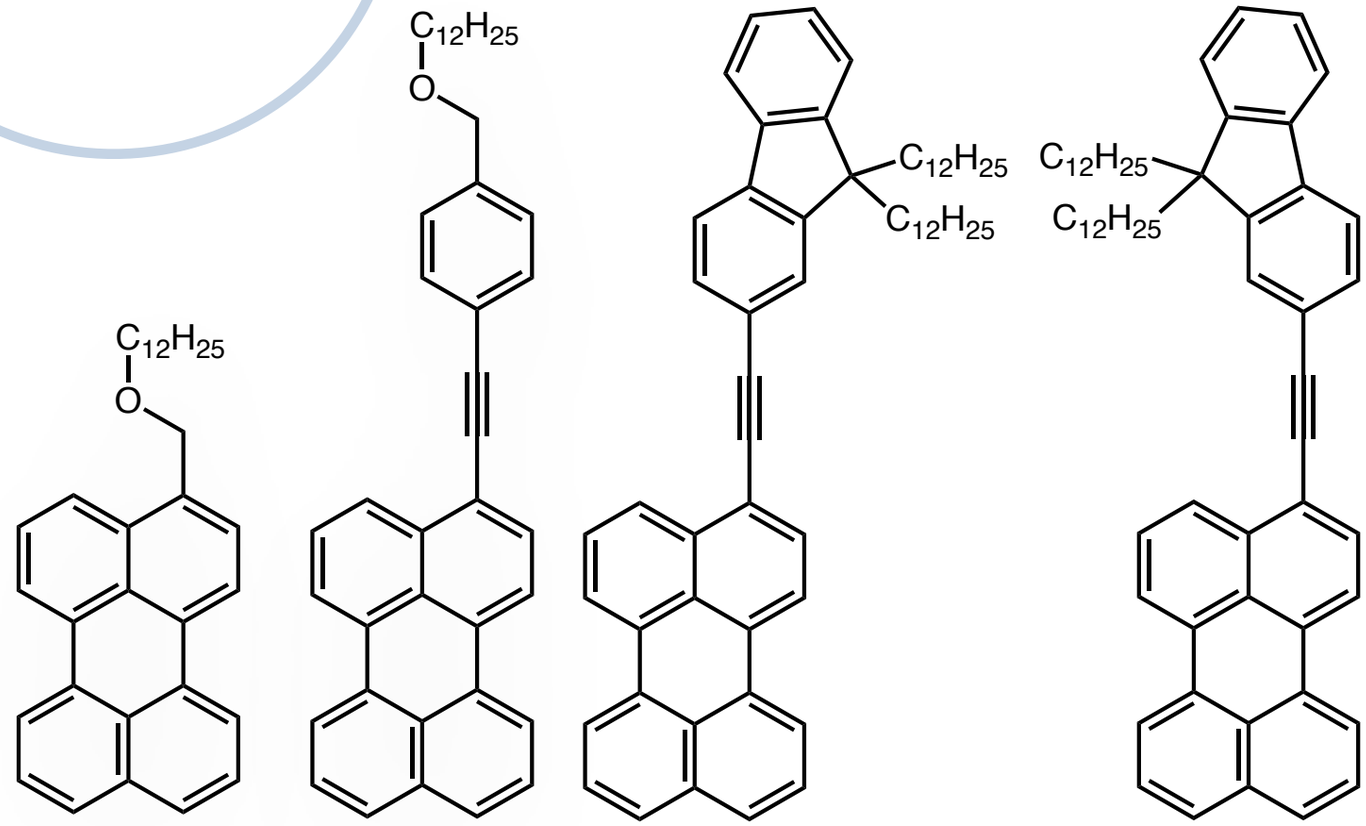
Upconversion in Organic Materials

excitation = 653 nm



$^3S^*$ = **PdTNP**

A =



Py0 ***Py1*** ***Py2*** ***Py3***

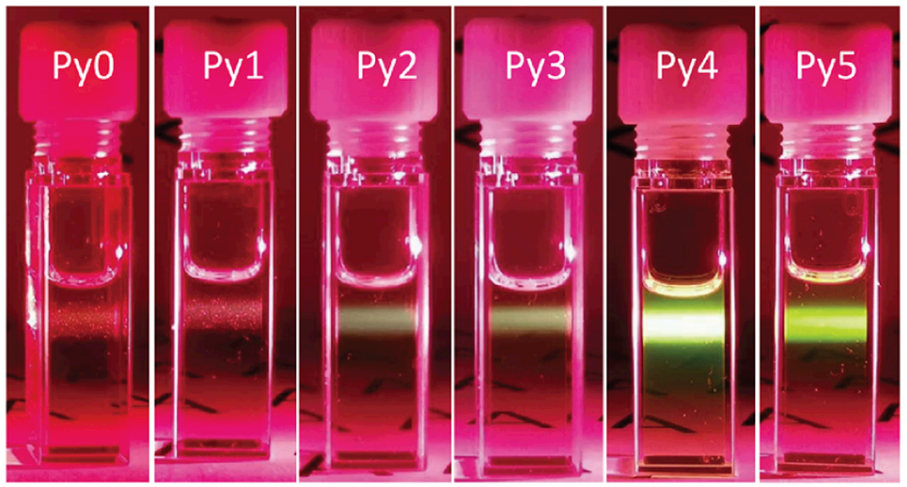
conjugation in organic annihilator

Huang, L., Wu, W., Li, Y., Huang, K., Zeng, L., Lin, W., Han, G. *J. Am. Chem. Soc.* **2020**. *142*, 18460–18470.

Upconversion applied in organic systems

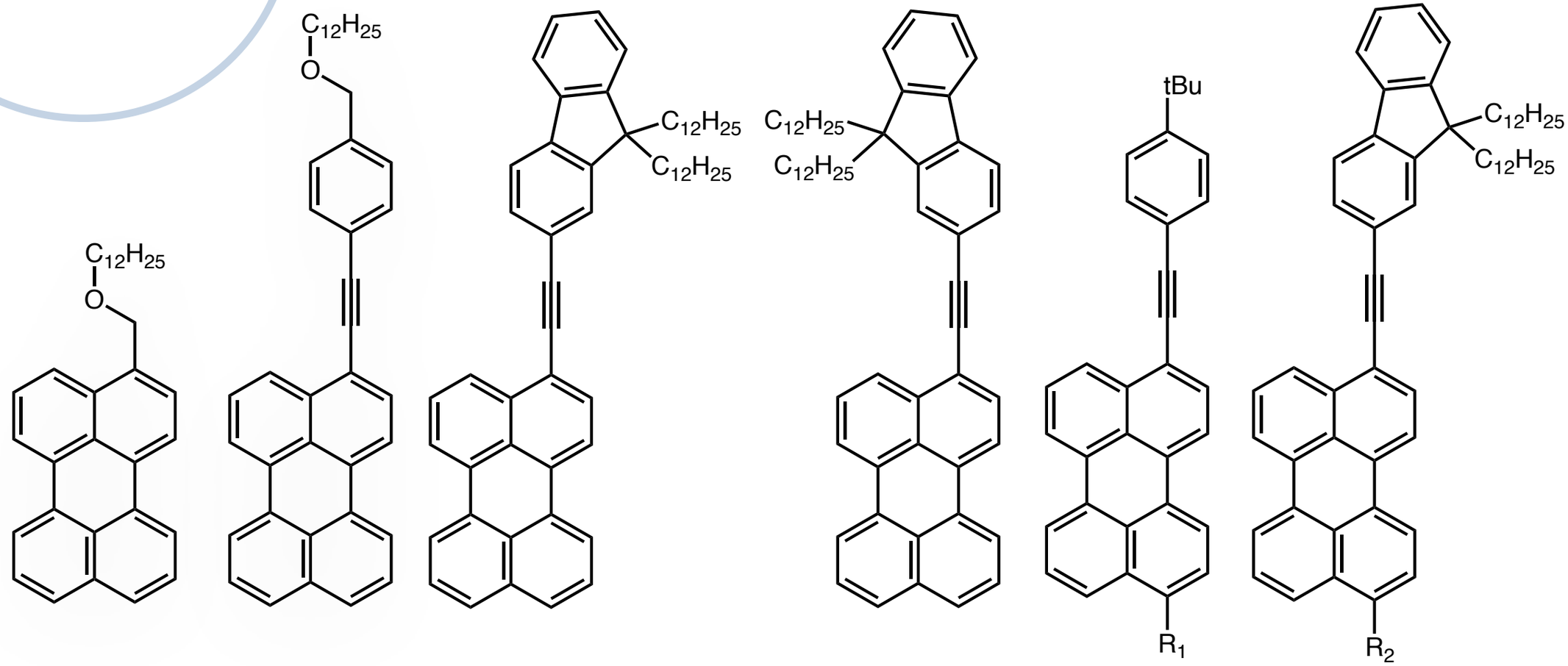
Upconversion in Organic Materials

excitation = 653 nm



$^3S^*$ = PdTNP

A =



Py0 ***Py1*** ***Py2*** ***Py3*** ***Py4*** ***Py5***

conjugation in organic annihilator

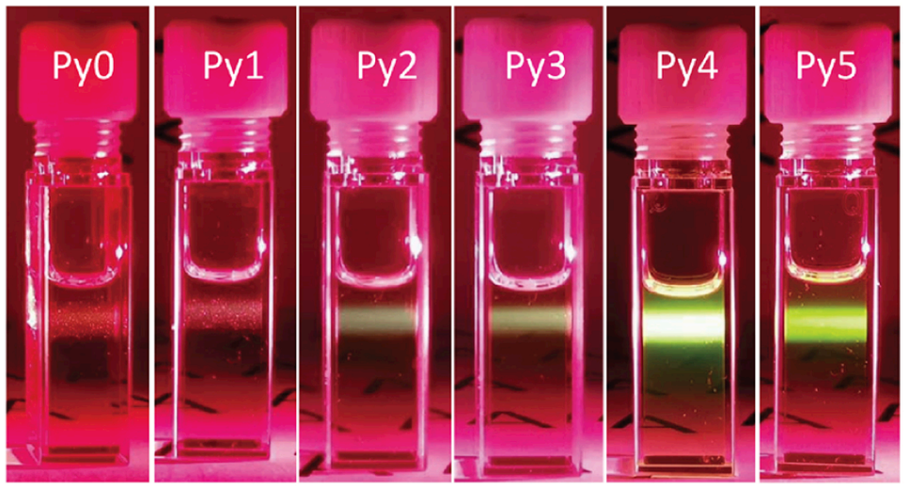
Huang, L., Wu, W., Li, Y., Huang, K., Zeng, L., Lin, W., Han, G. *J. Am. Chem. Soc.* **2020**. *142*, 18460–18470.

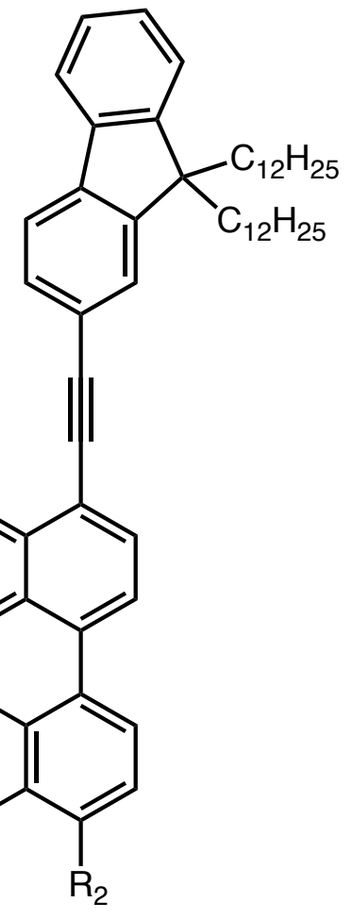
Upconversion applied in organic systems

Upconversion in Organic Materials

- ***NIR activated TTA upconversion***

excitation = 653 nm





Py5

$^3S^*$ = **PdTNP**

A =

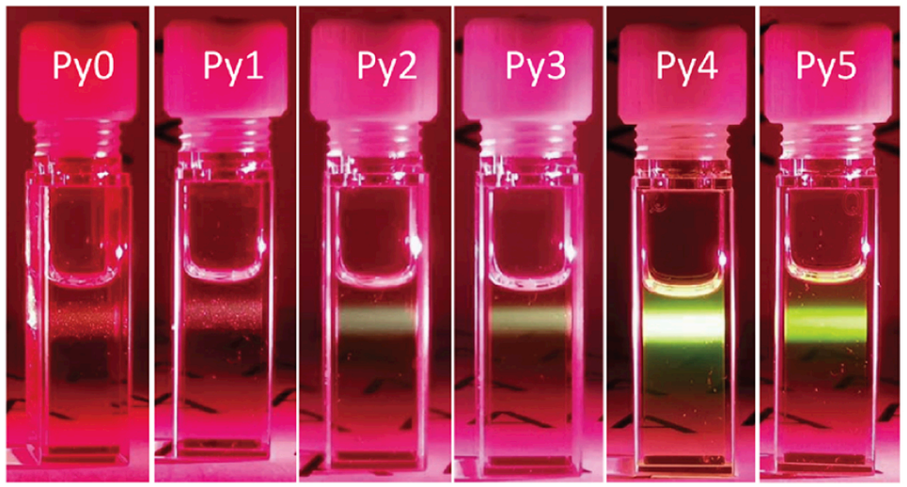
conjugation in organic annihilator

Huang, L., Wu, W., Li, Y., Huang, K., Zeng, L., Lin, W., Han, G. *J. Am. Chem. Soc.* **2020**. *142*, 18460–18470.

Upconversion applied in organic systems

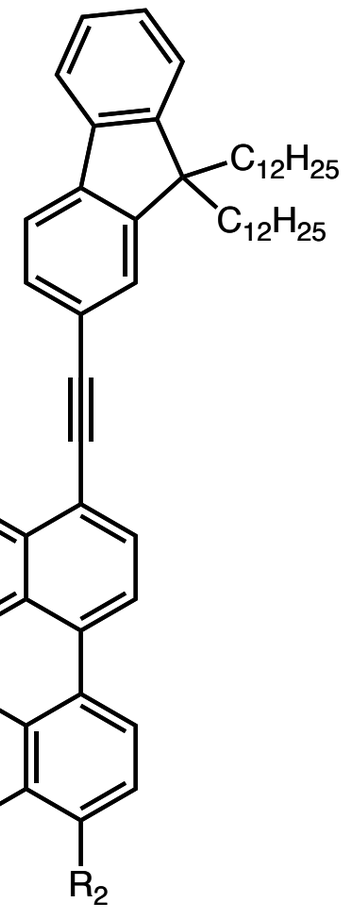
Upconversion in Organic Materials

excitation = 653 nm



- ***NIR activated TTA upconversion***

Φ_{UC} = 16.7% (653 nm)



$^3S^*$ = **PdTNP**

A = ***Py5***

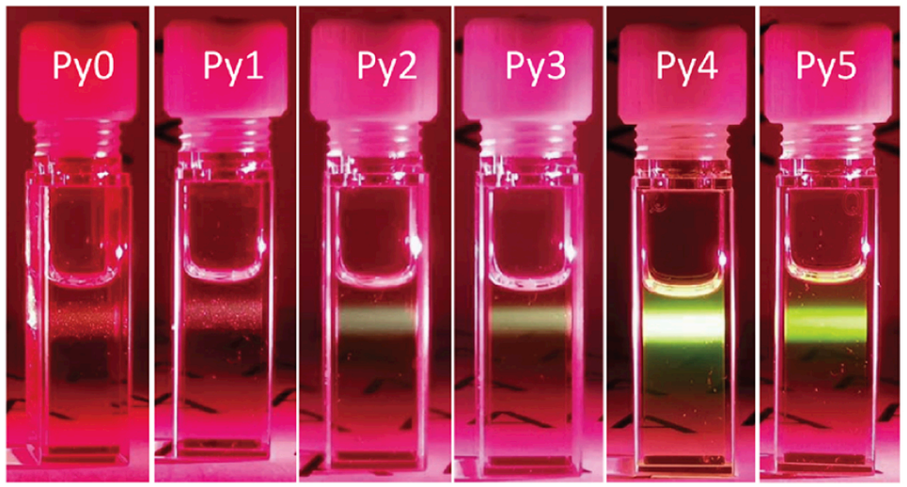
conjugation in organic annihilator

Huang, L., Wu, W., Li, Y., Huang, K., Zeng, L., Lin, W., Han, G. *J. Am. Chem. Soc.* **2020**. *142*, 18460–18470.

Upconversion applied in organic systems

Upconversion in Organic Materials

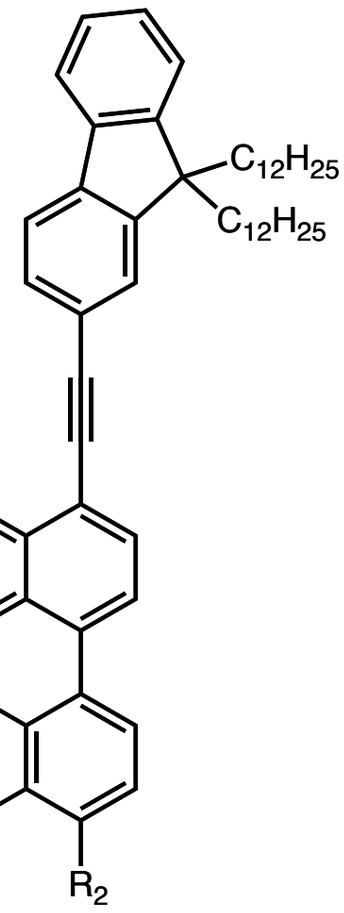
excitation = 653 nm



- ***NIR activated TTA upconversion***

  Φ_{UC} = 16.7% (653 nm)

- ***Highest recorded NIR to green TTA-UC pair***



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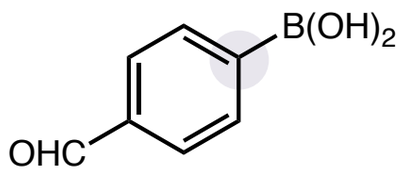
Upconversion applied in organic systems

- *TTA-UC applied to photoredox*



(0.5 mmol)

PdTNP/Py5/PhI(OAc)$_2$

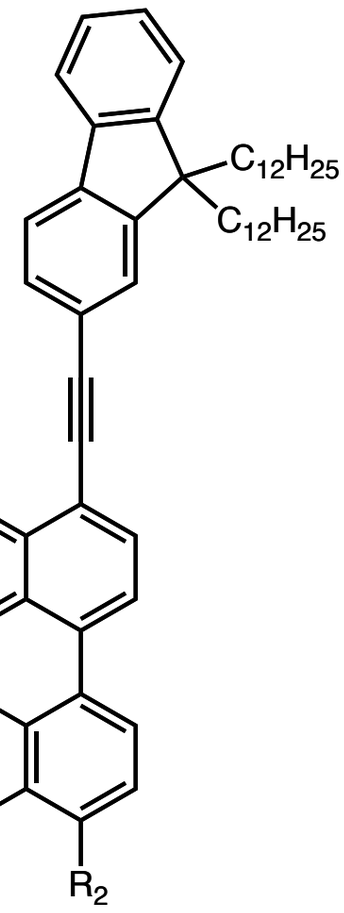
Eosin Y, DMF, K_2CO_3

λ =720 nm, r.t., 2 h

- ***NIR activated TTA upconversion***

Φ_{UC} = 16.7% (653 nm)

- ***Highest recorded NIR to green TTA-UC pair***



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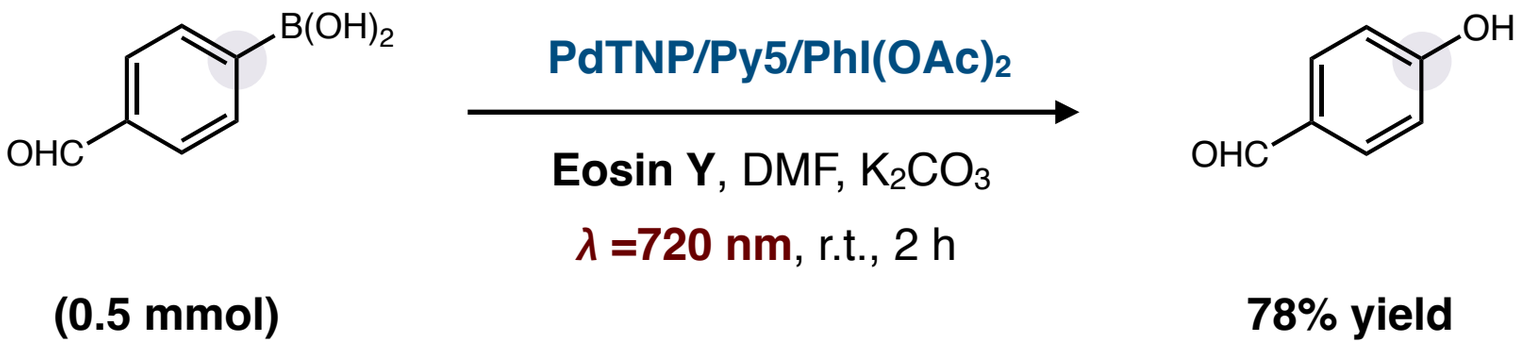


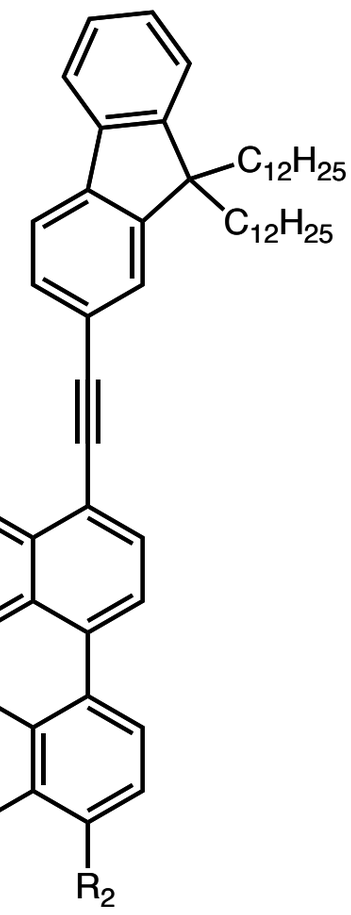
(0.5 mmol)

78% yield

- ***NIR activated TTA upconversion***

Φ_{UC} = 16.7% (653 nm)

- ***Highest recorded NIR to green TTA-UC pair***



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A = ***Py5***

conjugation in organic annihilator

Huang, L., Wu, W., Li, Y., Huang, K., Zeng, L., Lin, W., Han, G. *J. Am. Chem. Soc.* **2020**. *142*, 18460–18470.

Upconversion in Photocatalysis

***2 major considerations** in NIR/vis upconversion*

Upconversion in near-IR (NIR) and Visible light photocatalysis

Upconversion in Photocatalysis

Consideration 1

- *"Although irradiation with visible light is attractive for a number of reasons,* ***the longer the wavelength of absorption, the less energy the singlet and triplet excited states*** *will posses"*

Upconversion in near-IR (NIR) and Visible light photocatalysis

Romero, N. A., Nicewicz, D. A. *Chem. Rev.* **2016**, *116*, 10075–10166.

Upconversion in Photocatalysis

Consideration 1

- *"Although irradiation with visible light is attractive for a number of reasons,* ***the longer the wavelength of absorption, the less energy the singlet and triplet excited states*** *will posses"*

Upconversion in near-IR (NIR) and Visible light photocatalysis

Consideration 2

- *Molecules designed to* ***absorb in IR*** *do so at the* ***expense of triplet lifetime***

Alves, J., Feng, J., Nienhaus, L., Schmidt, T. W. *J. Mater. Chem. C.* **2022**, *10*, 7783–7798.

Romero, N. A., Nicewicz, D. A. *Chem. Rev.* **2016**, *116*, 10075–10166.

Tuning Sensitizer Energy Levels for Photoredox

Iron (III) sensitizer for organic annihilator TTA UC

Synthetic challenge:

Tune a 1st-row transition metal to access sensitizer reactivity under NIR

21	22	23	24	25	26	27	28	29	30
Sc	Ti	V	Cr	Mn	Fe	Co	Ni	Cu	Zn

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Previously: **Cu(I)**

Wellauer, J., Ziereisen, F., Sinha, N., Prescimone, A., Velic, A., Meyer, F., Wenger, O. S. *J. Am. Chem. Soc.* **2024**. *(As soon as publishable)*

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(good)

Wellauer, J., Ziereisen, F., Sinha, N., Prescimone, A., Velic, A., Meyer, F., Wenger, O. S. *J. Am. Chem. Soc.* **2024**. *(As soon as publishable)*

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(Don't want these)

Wellauer, J., Ziereisen, F., Sinha, N., Prescimone, A., Velic, A., Meyer, F., Wenger, O. S. *J. Am. Chem. Soc.* **2024**. *(As soon as publishable)*

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Luminescent CT excited states ⟵ *Previously:* **Cu(I)** $3d^{10}$ ⟶✕ ***Low lying metal-centered states***

Wellauer, J., Ziereisen, F., Sinha, N., Prescimone, A., Velic, A., Meyer, F., Wenger, O. S. *J. Am. Chem. Soc.* **2024**. *(As soon as publishable)*

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Wärnmark, K. et *al. Nature.* **2017,** *543,* 695–699.

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Iron (III) sensitizer for organic annihilator TTA UC

Synthetic challenge:

Tune a 1st-row transition metal to access sensitizer reactivity under NIR

Luminescent CT excited states ←—✕—— **Fe(II)** $3d^6$ ——→ ***Low lying metal-centered states***

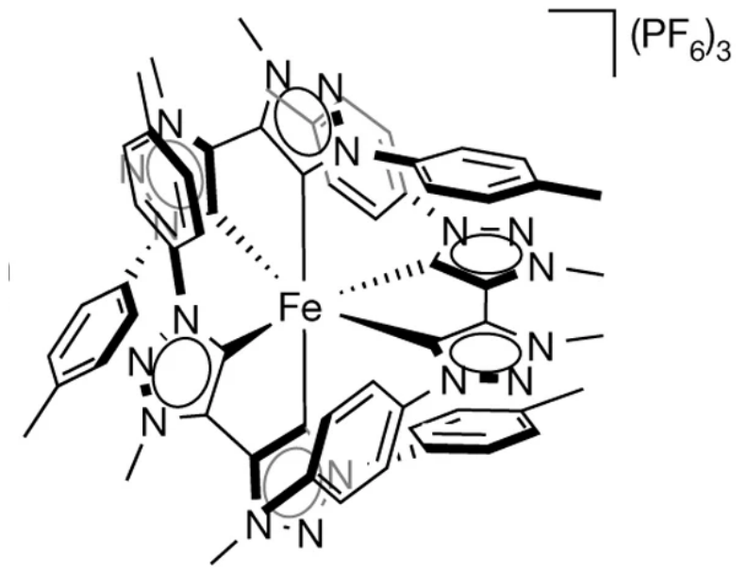
sub-picosecond CT excited-state lifetime

Wärnmark, K. et *al. Nature.* **2017,** *543,* 695–699.

Tuning Sensitizer Energy Levels for Photoredox

Iron (III) sensitizer for organic annihilator TTA UC

- ***Previously thought:***



Low-spin **Fe(III)** $3d^5$

Wärnmark, K. et *al. Nature.* **2017,** *543,* 695–699.

**in MeCN at 20 ºC*

Tuning Sensitizer Energy Levels for Photoredox

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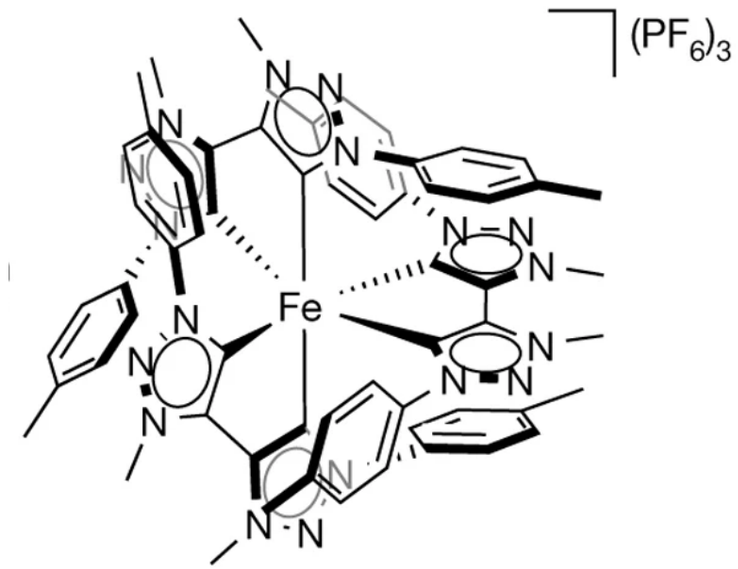

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- ***Luminescent*** *from* ***LMCT*** *excited state*

Wärnmark, K. et *al. Nature.* **2017,** *543,* 695–699.

**in MeCN at 20 ºC*

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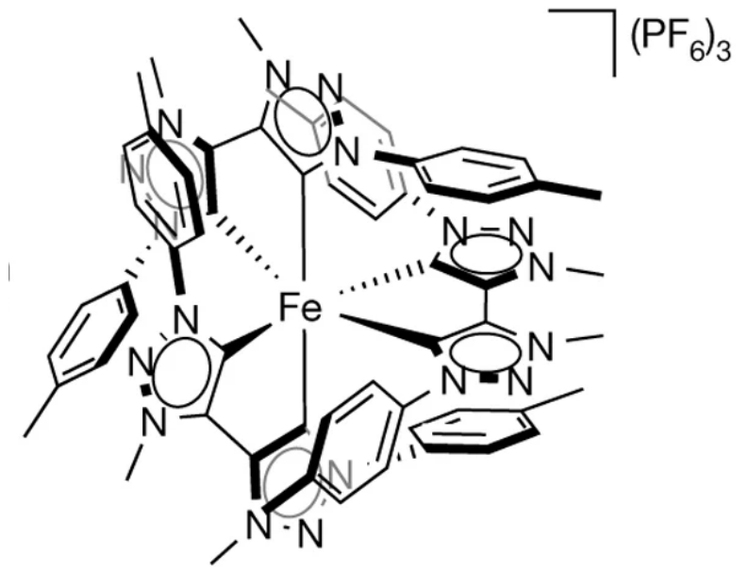

Low-spin **Fe(III)** $3d^5$

- ***Luminescent*** *from* ***LMCT*** *excited state*

$$\tau_{Excited\text{-}state} = 0.1\ ns^*$$

Wärnmark, K. et *al. Nature.* **2017,** *543,* 695–699.

**in MeCN at 20 ºC*

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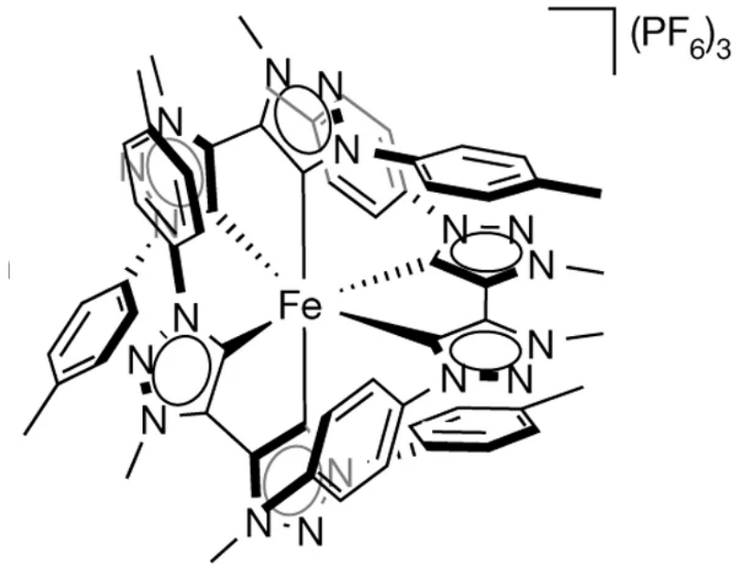

Low-spin **Fe(III)** $3d^5$

- ***Luminescent*** *from* ***LMCT*** *excited state*

$\tau_{Excited\text{-}state} = 0.1\ ns^*$

Alternative to:

Fe(II) $3d^6$

- ***MLCT***

Wärnmark, K. et *al. Nature.* **2017,** *543,* 695–699.

**in MeCN at 20 ºC*

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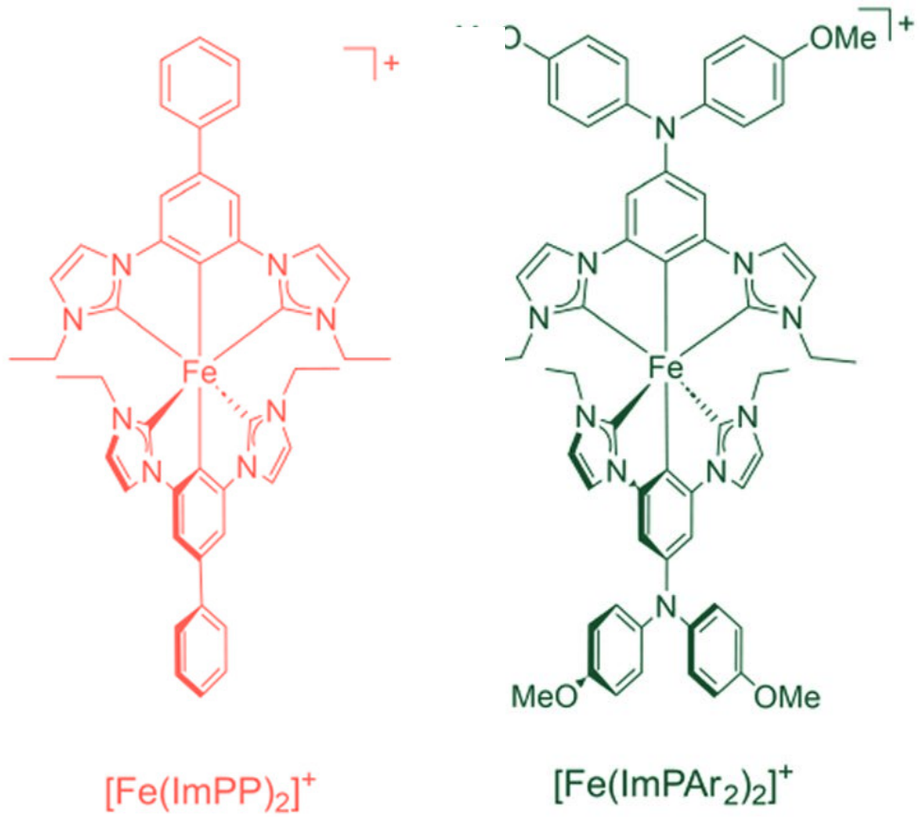
Iron (III) sensitizer for organic annihilator TTA UC



$[Fe(ImPP)_2]^+$ $[Fe(ImPAr_2)_2]^+$

Low-spin **Fe(III)** $3d^5$

Wellauer, J., Ziereisen, F., Sinha, N., Prescimone, A., Velic, A., Meyer, F., Wenger, O. S. *J. Am. Chem. Soc.* **2024**. *(As soon as publishable)*

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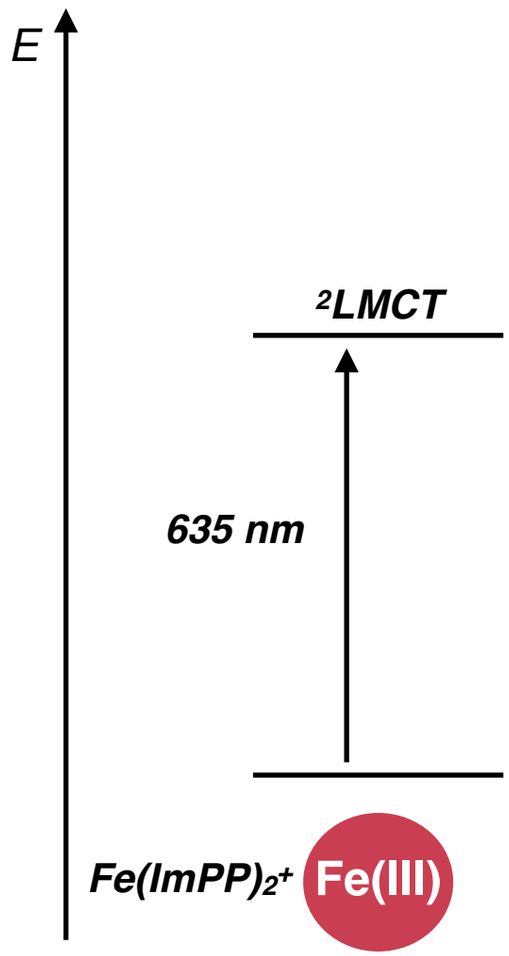

Iron (III) sensitizer $Fe(ImPP)_2^+$

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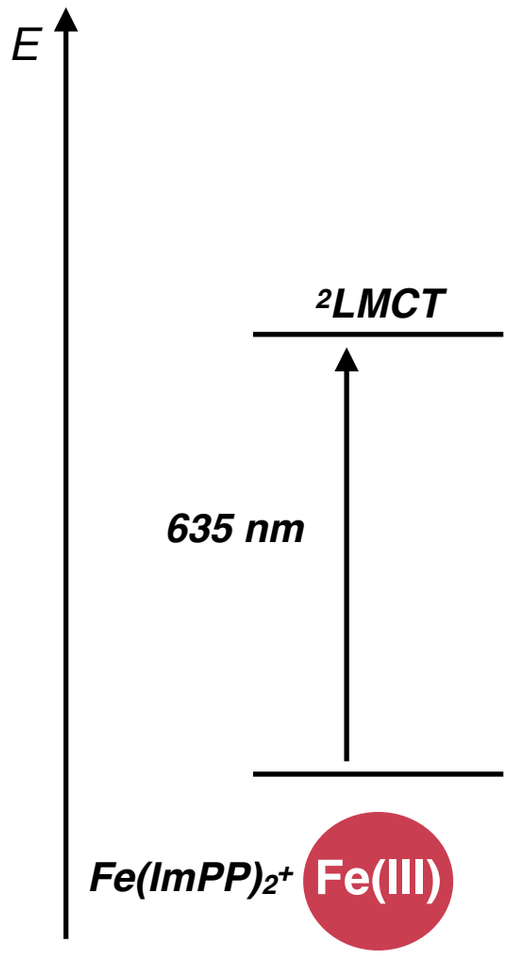

Iron (III) sensitizer $Fe(ImPP)_2^+$

$\tau_{Excited\text{-}state} \sim$ ***267 ps***

Wellauer, J., Ziereisen, F., Sinha, N., Prescimone, A., Velic, A., Meyer, F., Wenger, O. S. *J. Am. Chem. Soc.* **2024**. *(As soon as publishable)*

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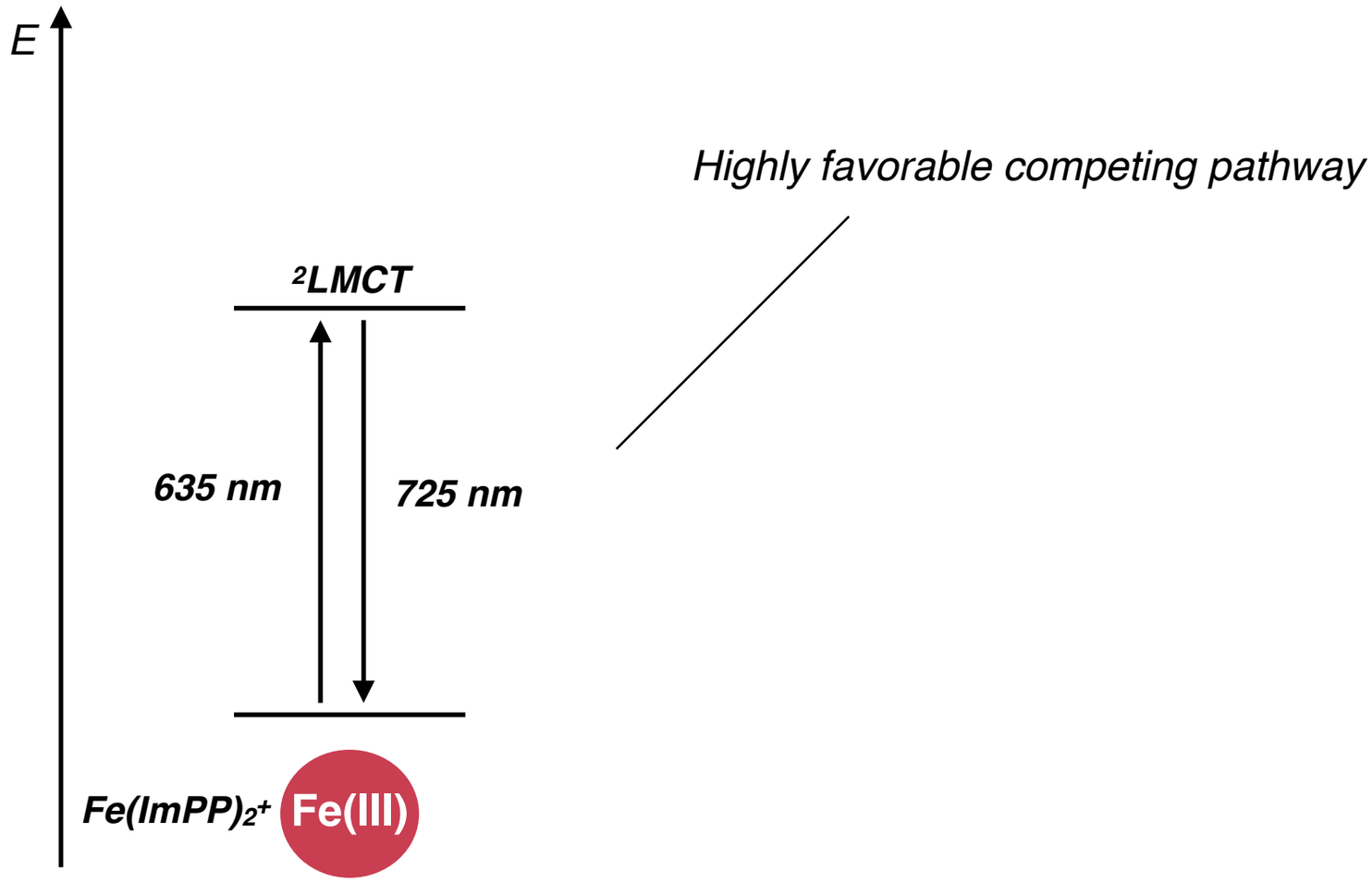

Iron (III) sensitizer $Fe(ImPP)_2^+$

$\tau_{Excited\text{-}state}$ ~ ***267 ps***

- ***red-light emission***

Wellauer, J., Ziereisen, F., Sinha, N., Prescimone, A., Velic, A., Meyer, F., Wenger, O. S. *J. Am. Chem. Soc.* **2024**. *(As soon as publishable)*

Tuning Sensitizer Energy Levels for Photoredox

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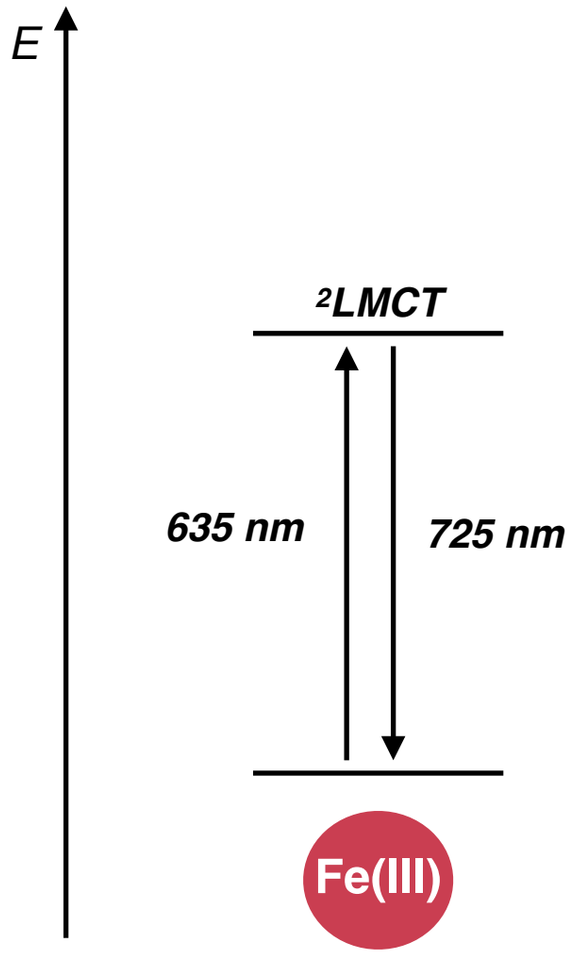

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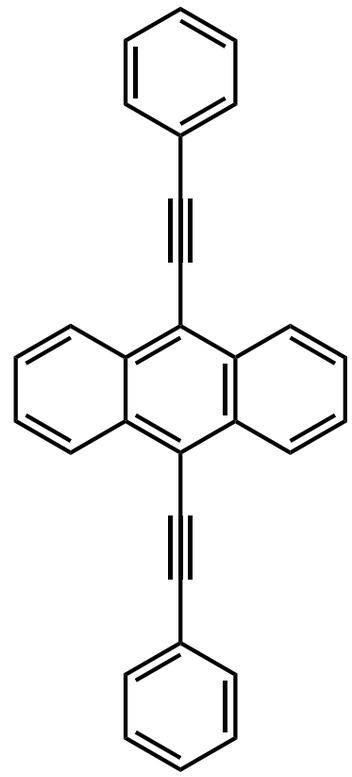

9,10-bis(phenylethynyl)anthracene (BPEA)

Organic annihilator

Wellauer, J., Ziereisen, F., Sinha, N., Prescimone, A., Velic, A., Meyer, F., Wenger, O. S. *J. Am. Chem. Soc.* **2024**. *(As soon as publishable)*

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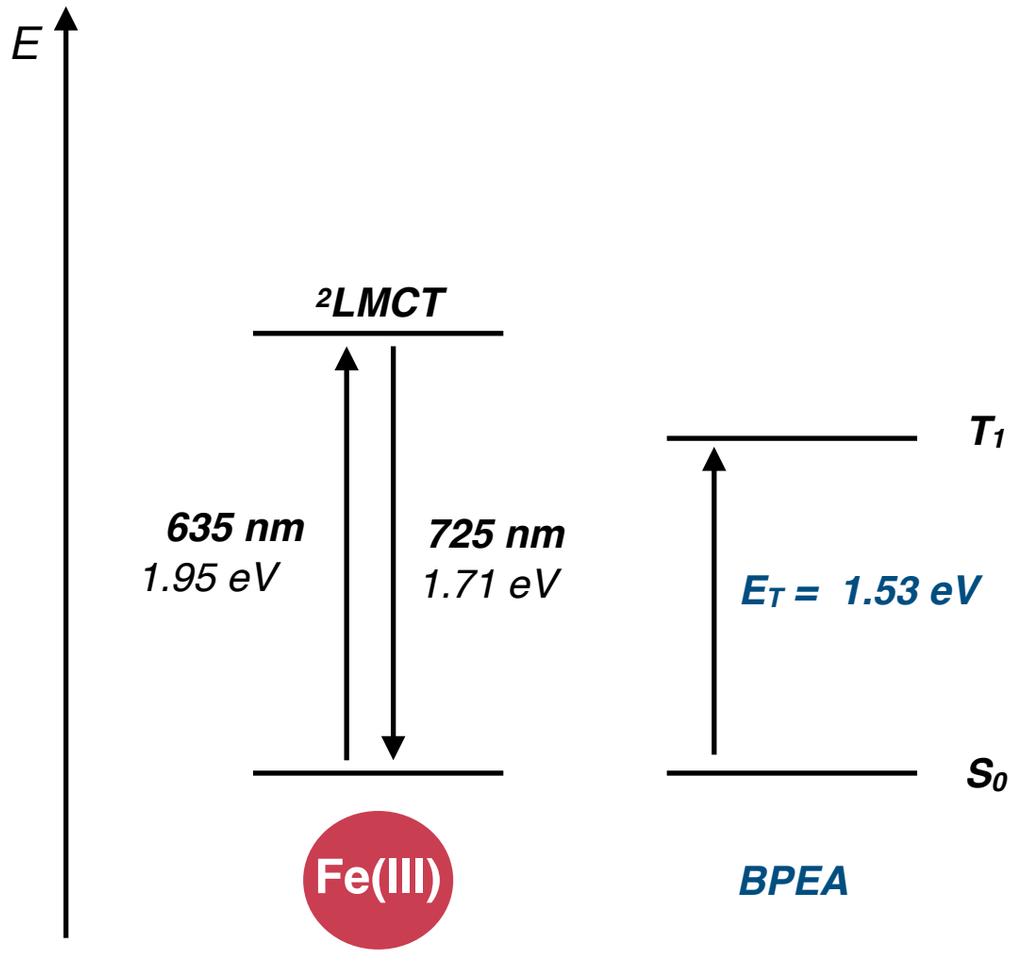

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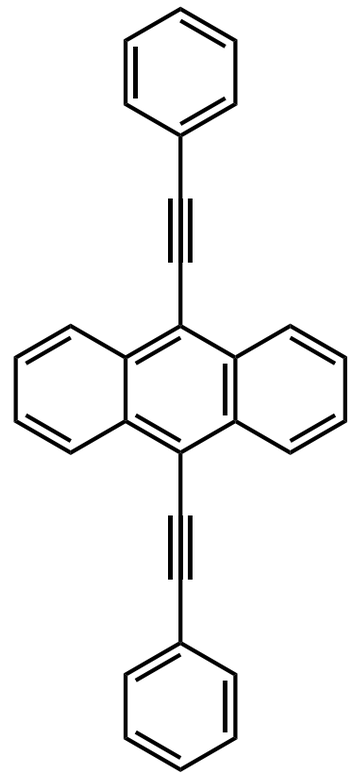

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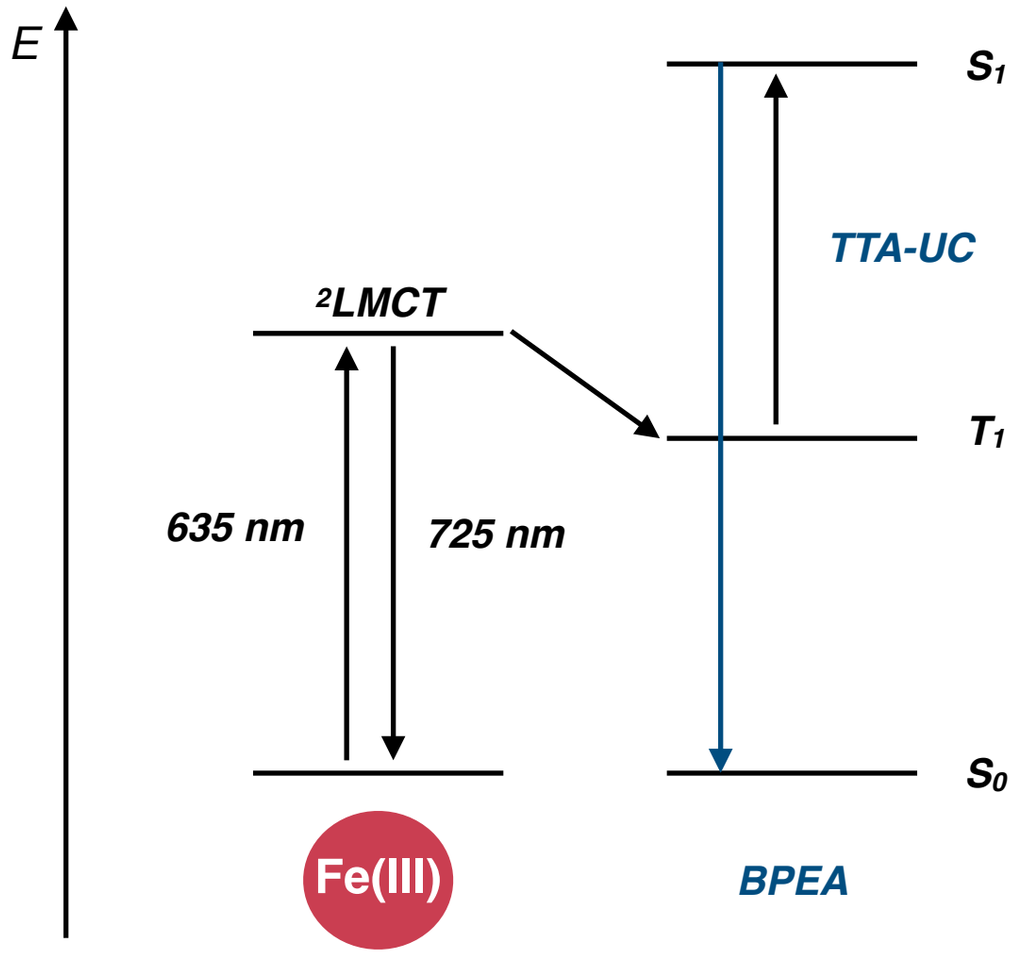

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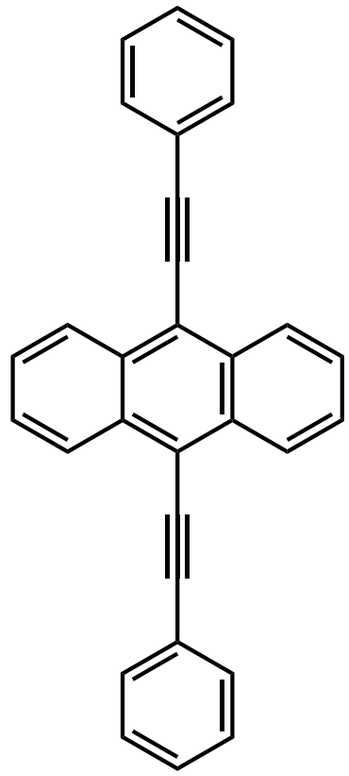

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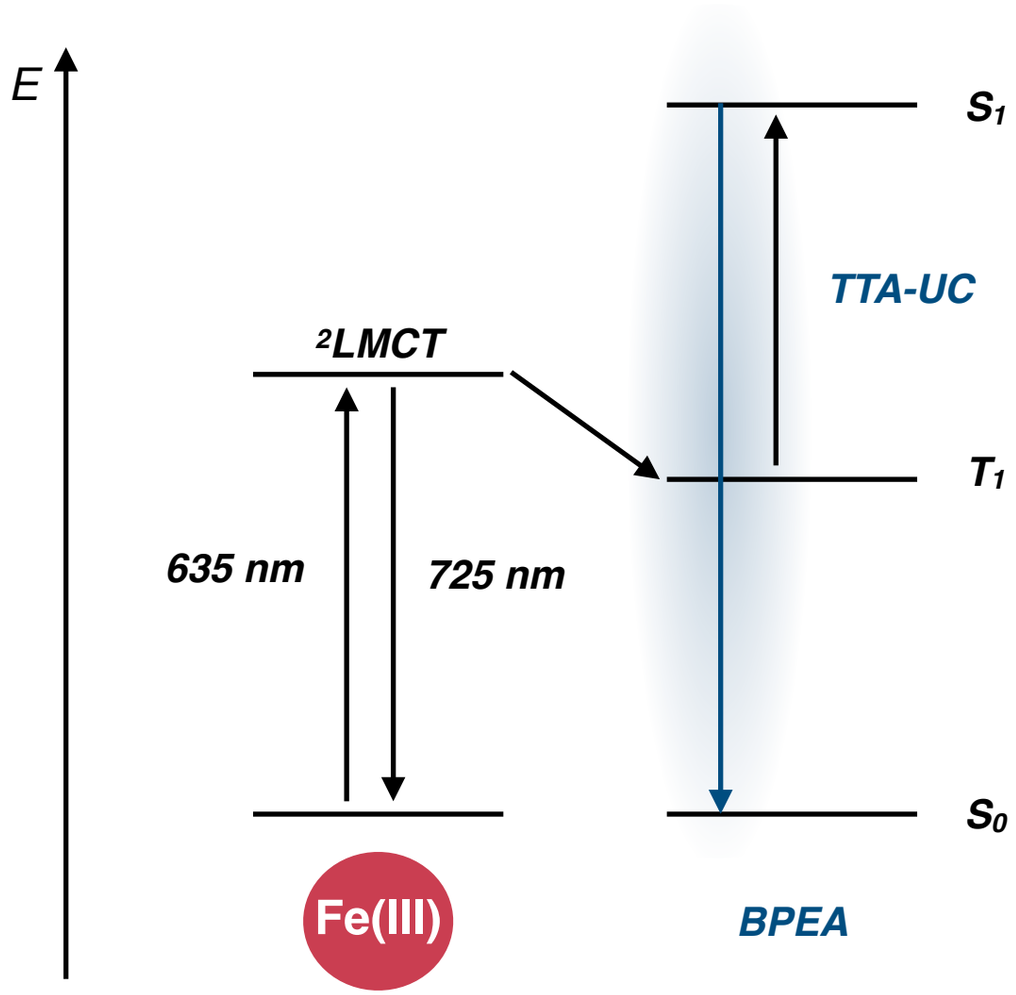

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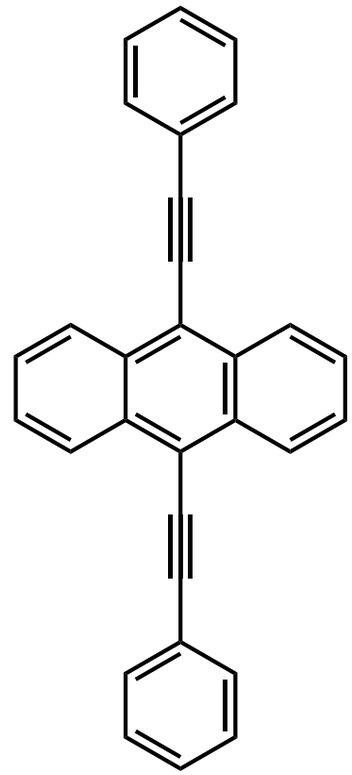
TTA-UC induced blue light emission



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Upconversion applied in organic systems

Upconversion in Organic Materials

2 key mechanisms:

- ***Triplet-Triplet Annihilation*** ✓
- ***Energy Pooling***

Upconversion applied in organic systems

Upconversion in Organic Materials

Cooperative Energy Pooling (CEP)

- *energy transfer mechanism*

Weingarten, D. H., LaCount, M. D., van de Lagemaat J., Rumbles, G., Leuko M. T., Shaheen, S. E. *Nat. Commun.* **2017**. *8*, 14808.

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Cooperative Energy Pooling (CEP)

- *energy transfer mechanism*
- *lowest-lying singlet excitations*

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Cooperative Energy Pooling (CEP)

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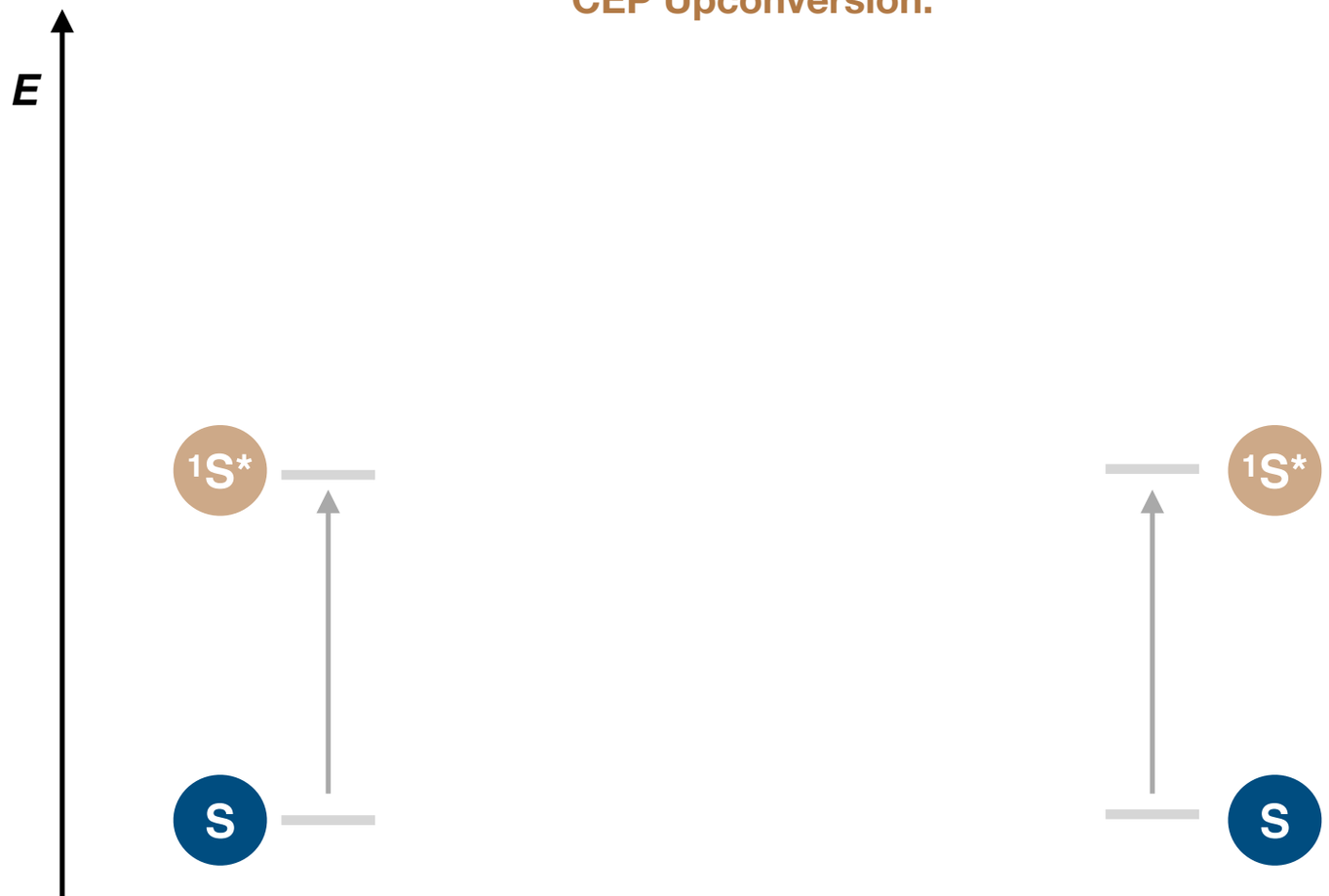
CEP Upconversion:



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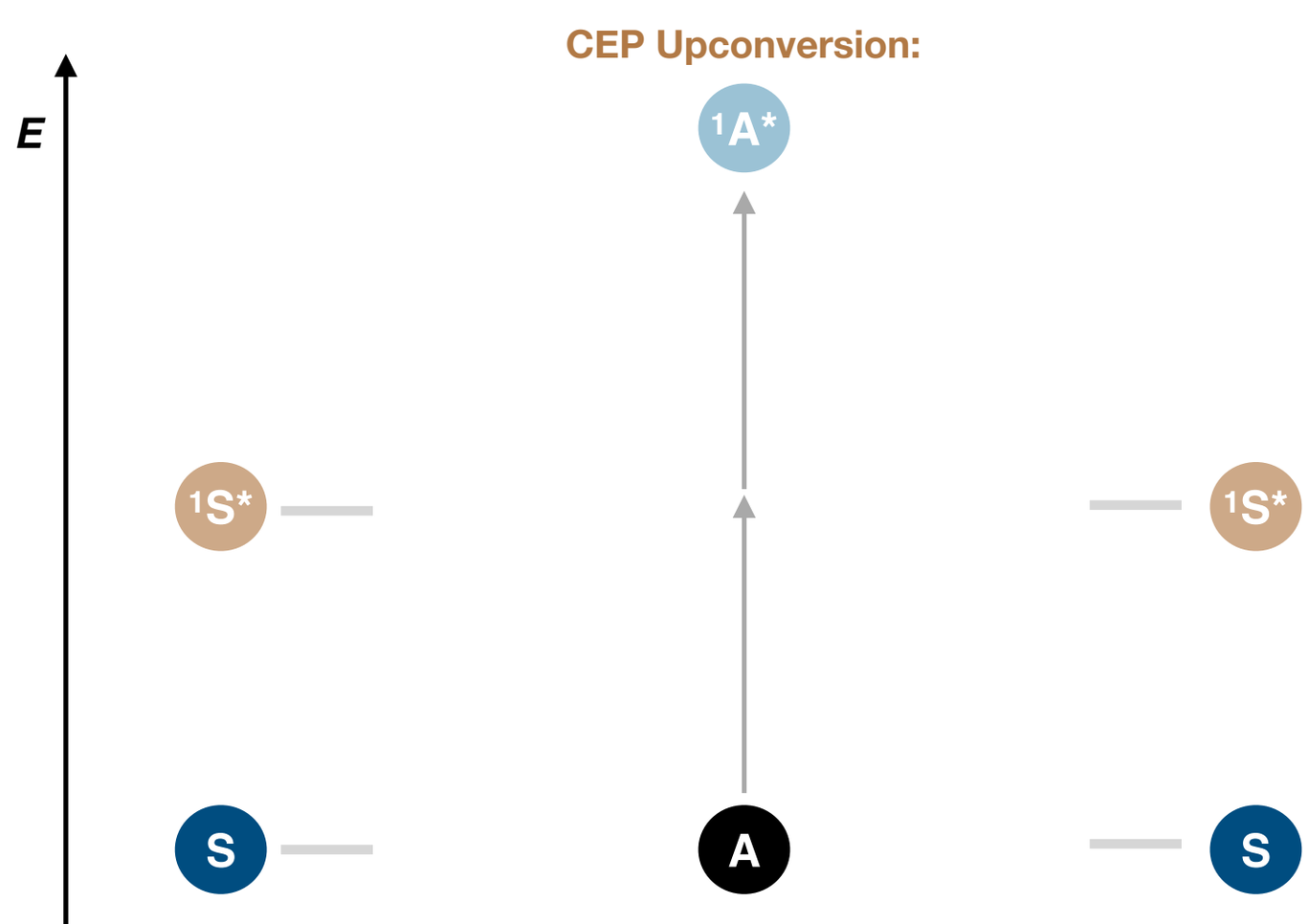

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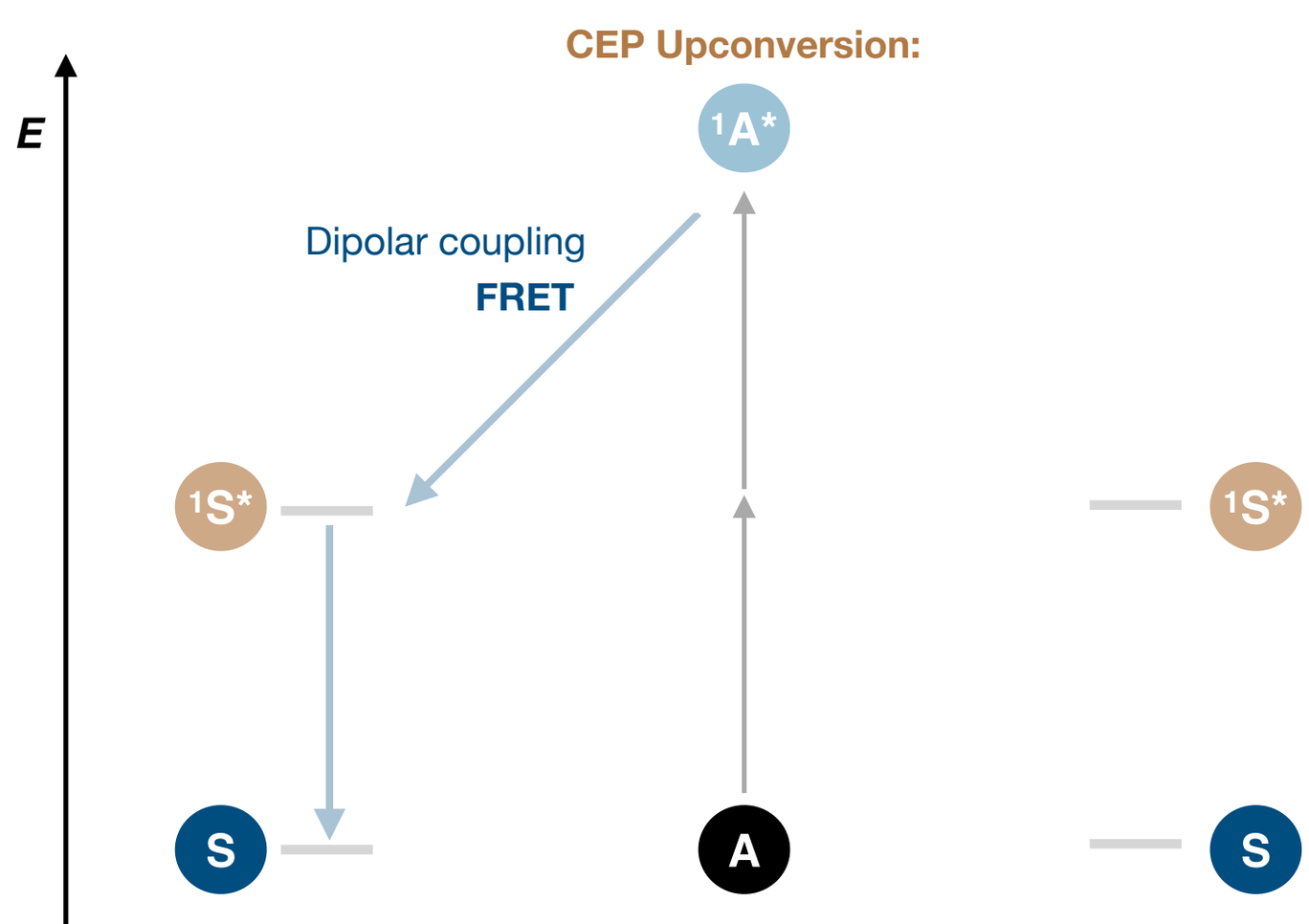

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Upconversion in Organic Materials

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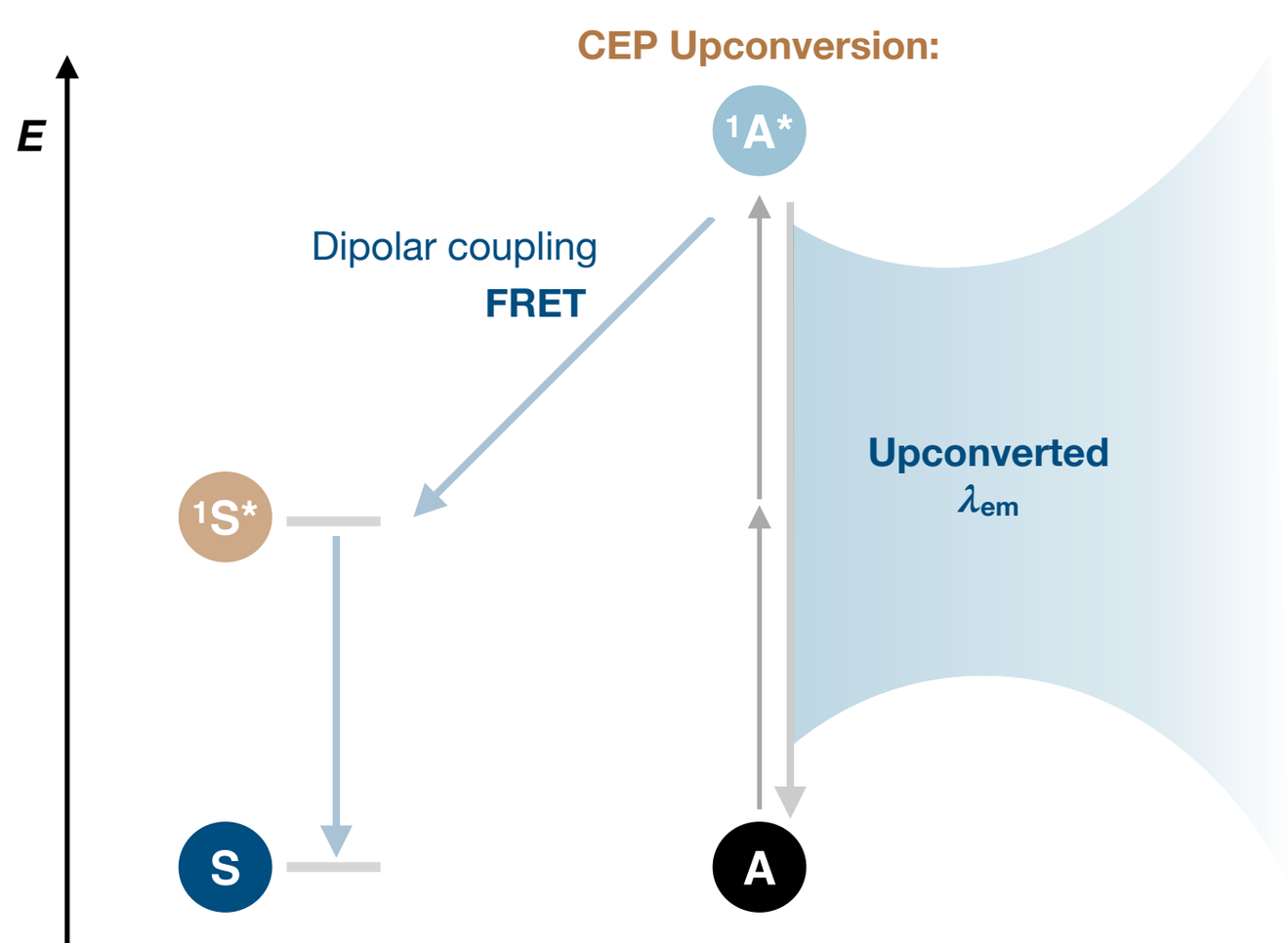

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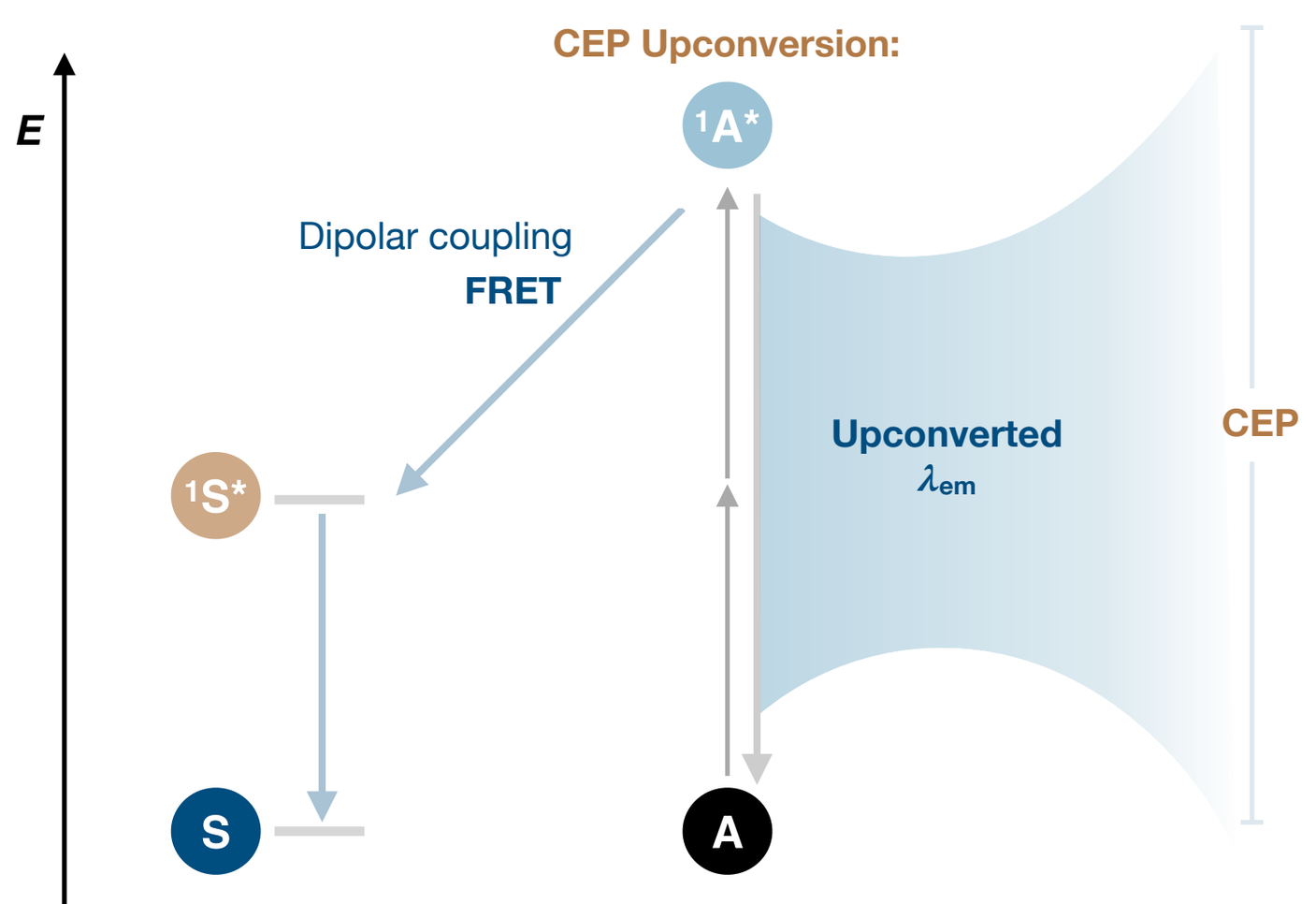

- ***Potential towards selective photochemical reactivity***

Upconversion using near-IR (NIR) light

Chen, G., Giu, H., Prasad, P. N., Chen, X. *Chem. Rev.* **2014**, *114*, 5161–5214.

Biological tissues *have an optical transparency window in NIR range*

~ 700-1100 nm

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- *Reduced photodamage effects*

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Upconversion using near-IR (NIR) light

- *Reduced photodamage effects*
- *Deeper light penetration*

Chen, G., Giu, H., Prasad, P. N., Chen, X. *Chem. Rev.* **2014**, *114*, 5161–5214.

Upconversion applied in organic systems

Hydrogel upconversion

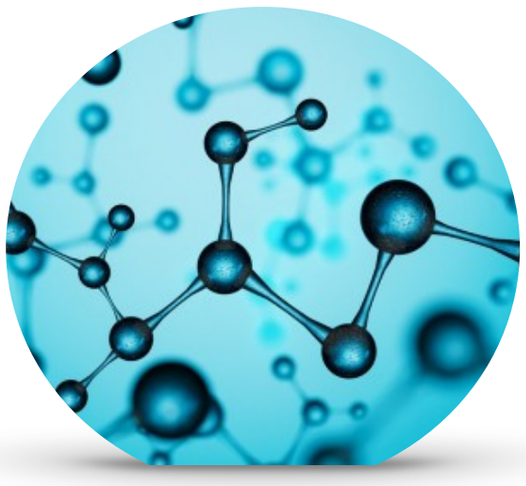
Can you apply upconversion to therapeutics?

Upconversion applied in organic systems

Hydrogel upconversion

The utility of hydrogels:

3D biocompatible scaffold



Li, W., Hu, J., Chen, C., Li, X., Zhang, H., Xin, Y., Tian, Q., Wang, S. *Regen. Ther.* **2023**, *24*, 459–471.

Upconversion applied in organic systems

Hydrogel upconversion

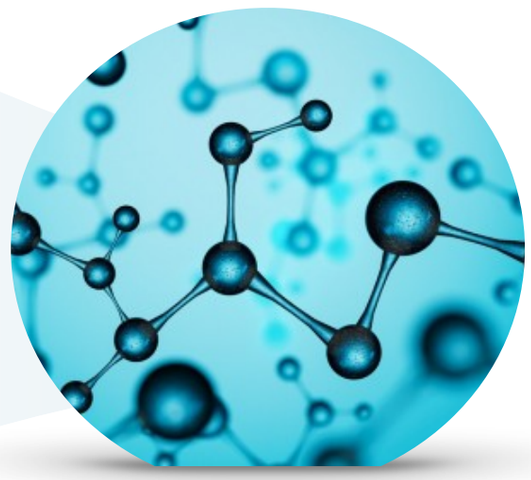
The utility of hydrogels:

Hydrophobic polymers

+

Water-soluble polymers

3D biocompatible scaffold



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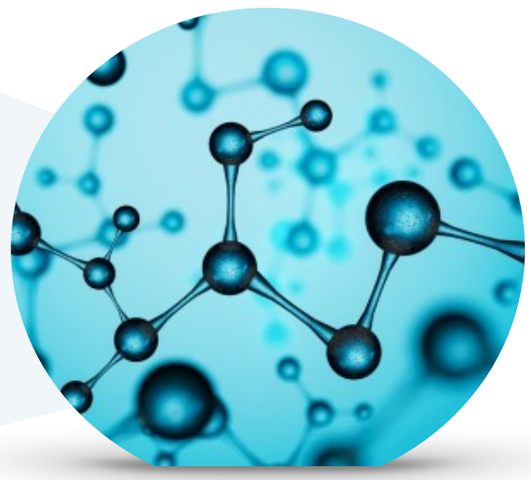

- *Control drug and protein delivery*

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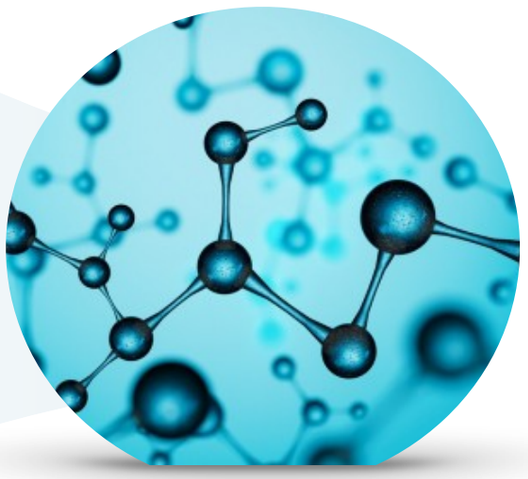
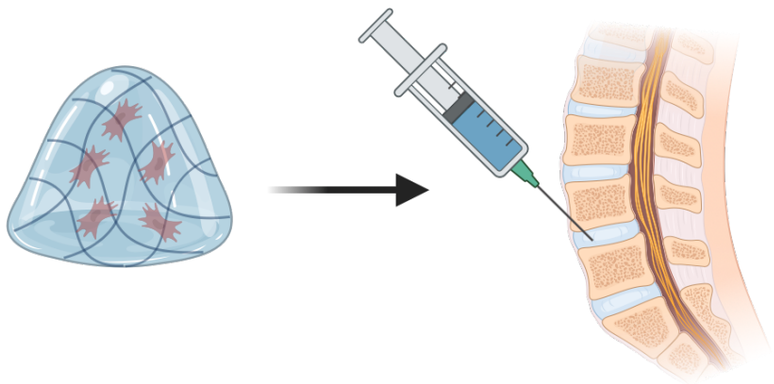


- *Control drug and protein delivery*
- *The most widely used scaffolds to* ***regenerate damaged tissue***



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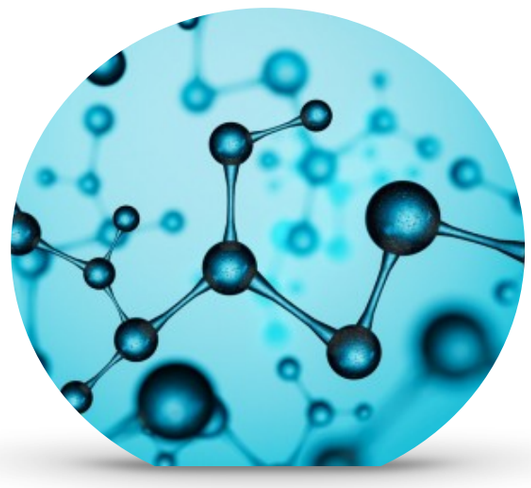
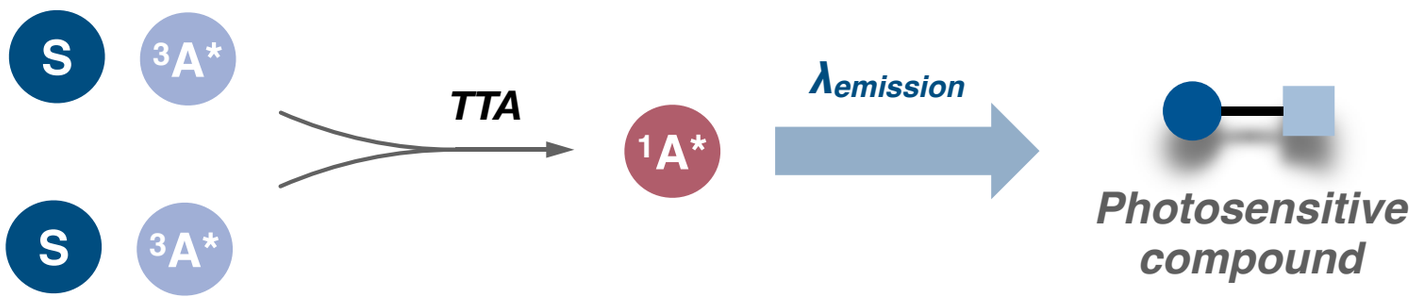


Triplet-Triplet Annihilation (TTA) Upconversion



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Upconversion applied in organic systems

Hydrogel upconversion

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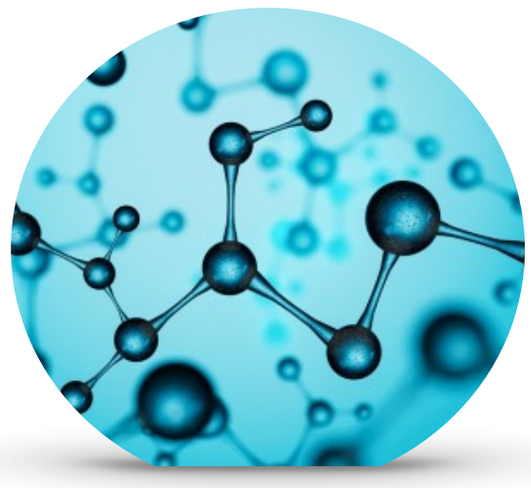

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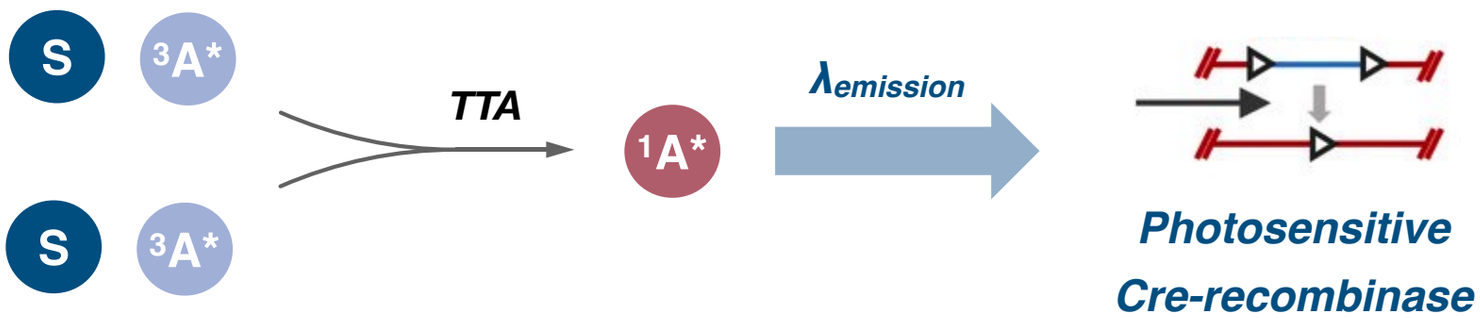

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Upconversion applied in organic systems

Hydrogel upconversion

Design considerations:

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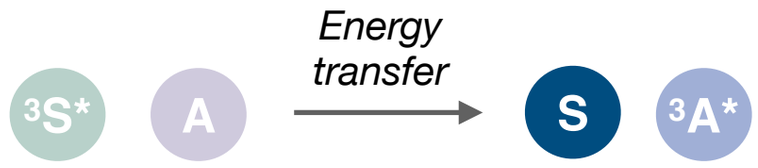

Acceptor (A) = Organic substrate

Sasaki, Y., Oshikawa, M., Bharmoria, P., Kouno, H., Hayashi-Takagi, A., Sato, M., Ajioka, I., Yanai, N., Kimisuka, N. *Angew. Chem. Int. Ed.* **2019**. *58*, 17827–17833.

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Hydrogel upconversion

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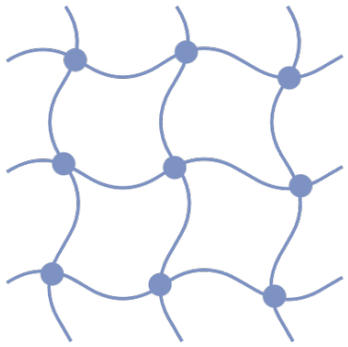
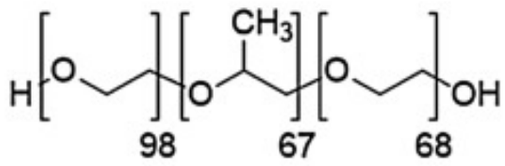


Viscous hydrogel matrix:



Pluronic F127

Sasaki, Y., Oshikawa, M., Bharmoria, P., Kouno, H., Hayashi-Takagi, A., Sato, M., Ajioka, I., Yanai, N., Kimisuka, N. *Angew. Chem. Int. Ed.* **2019**. *58*, 17827–17833.

Upconversion applied in organic systems

Hydrogel upconversion

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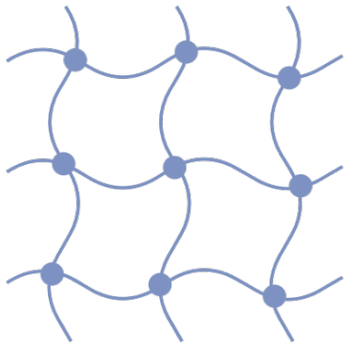

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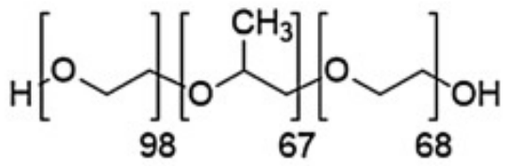

Pluronic F127

- **Suppresses O_2 diffusion**

Sasaki, Y., Oshikawa, M., Bharmoria, P., Kouno, H., Hayashi-Takagi, A., Sato, M., Ajioka, I., Yanai, N., Kimisuka, N. *Angew. Chem. Int. Ed.* **2019**. *58*, 17827–17833.

Upconversion applied in organic systems

Hydrogel upconversion

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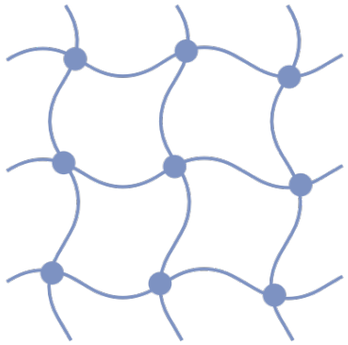

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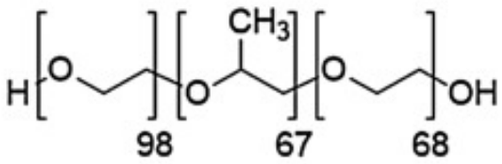

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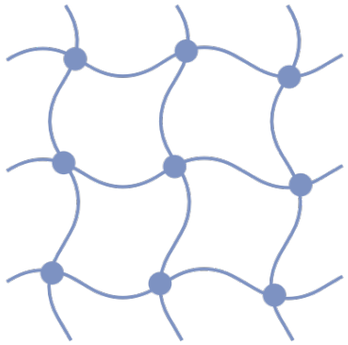
Sasaki, Y., Oshikawa, M., Bharmoria, P., Kouno, H., Hayashi-Takagi, A., Sato, M., Ajioka, I., Yanai, N., Kimisuka, N. *Angew. Chem. Int. Ed.* **2019**. *58*, 17827–17833.

Upconversion applied in organic systems

Hydrogel upconversion

Design considerations:

3D biocompatible scaffold



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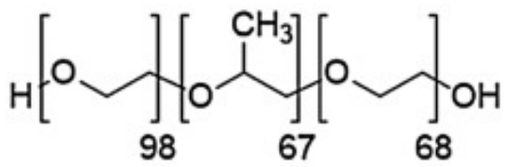

Pluronic F127

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#2. $\tau_{excited}$ sensitizer too short to enable collision with acceptors

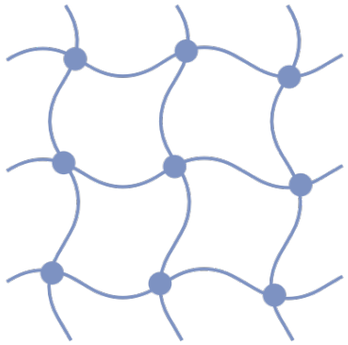
Sasaki, Y., Oshikawa, M., Bharmoria, P., Kouno, H., Hayashi-Takagi, A., Sato, M., Ajioka, I., Yanai, N., Kimisuka, N. *Angew. Chem. Int. Ed.* **2019**. *58*, 17827–17833.

Upconversion applied in organic systems

Hydrogel upconversion

Design considerations:

3D biocompatible scaffold



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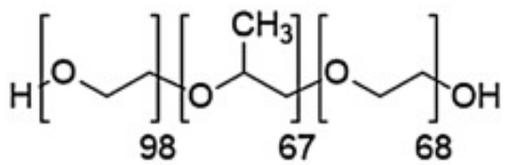

Pluronic F127

- **Suppresses O_2 diffusion**

#2. $\tau_{excited}$ sensitizer too short to enable collision with acceptors

Consideration 2

- *Molecules designed to **absorb in IR** do so at the **expense of triplet lifetime***

Sasaki, Y., Oshikawa, M., Bharmoria, P., Kouno, H., Hayashi-Takagi, A., Sato, M., Ajioka, I., Yanai, N., Kimisuka, N. *Angew. Chem. Int. Ed.* **2019**. *58*, 17827–17833.

Upconversion applied in organic systems

Hydrogel upconversion: Energy transfer via triplet lifetime manipulation

Design considerations:

- ***Elongate sensitizer triplet lifetime***

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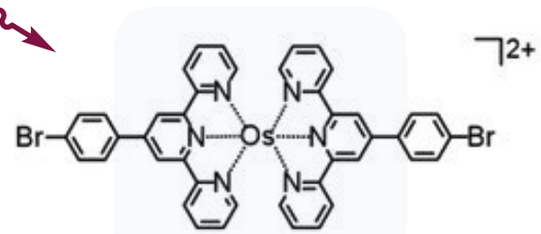
NIR



$Os(peptpy)_2^{2+}$

τ~0.2 μs

S

Sasaki, Y., Oshikawa, M., Bharmoria, P., Kouno, H., Hayashi-Takagi, A., Sato, M., Ajioka, I., Yanai, N., Kimisuka, N. *Angew. Chem. Int. Ed.* **2019**. *58*, 17827–17833.

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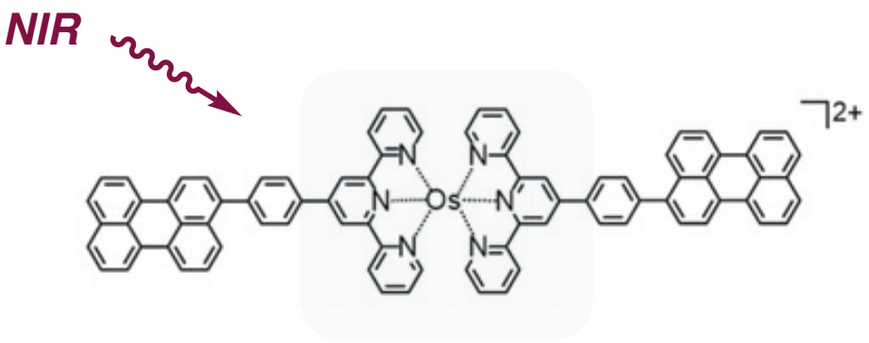

Donor $Os(peptpy)_2^{2+}$

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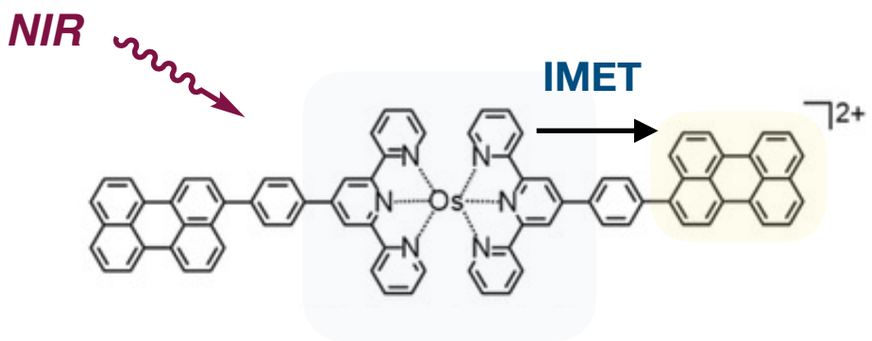

Donor $Os(peptpy)_2^{2+}$

S

Intramolecular energy transfer (IMET)

Sasaki, Y., Oshikawa, M., Bharmoria, P., Kouno, H., Hayashi-Takagi, A., Sato, M., Ajioka, I., Yanai, N., Kimisuka, N. *Angew. Chem. Int. Ed.* **2019**. *58*, 17827–17833.

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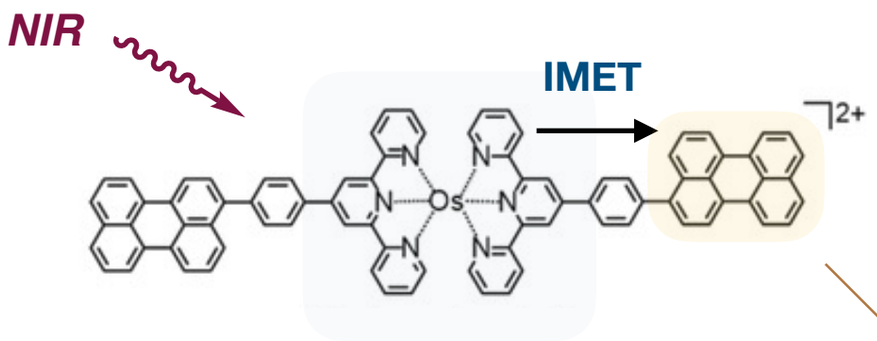

Donor $Os(peptpy)_2^{2+}$

Triplet-pooling phenyl perylene units

S

Sasaki, Y., Oshikawa, M., Bharmoria, P., Kouno, H., Hayashi-Takagi, A., Sato, M., Ajioka, I., Yanai, N., Kimisuka, N. *Angew. Chem. Int. Ed.* **2019**. *58*, 17827–17833.

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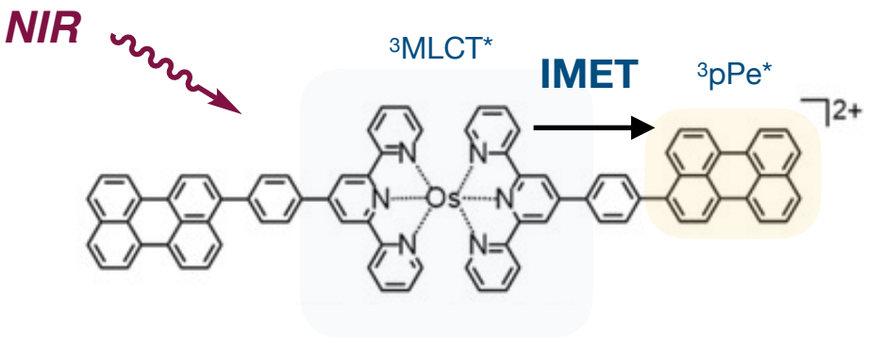
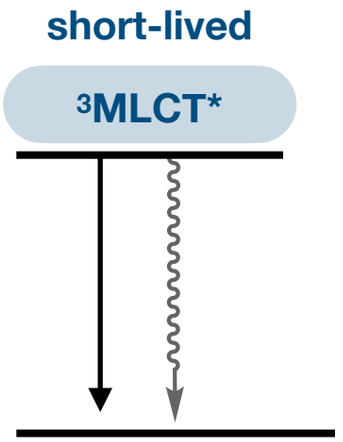


Donor Os(peptpy)$_2^{2+}$



Os(ptpy)$_2^{2+}$

^{3}S*

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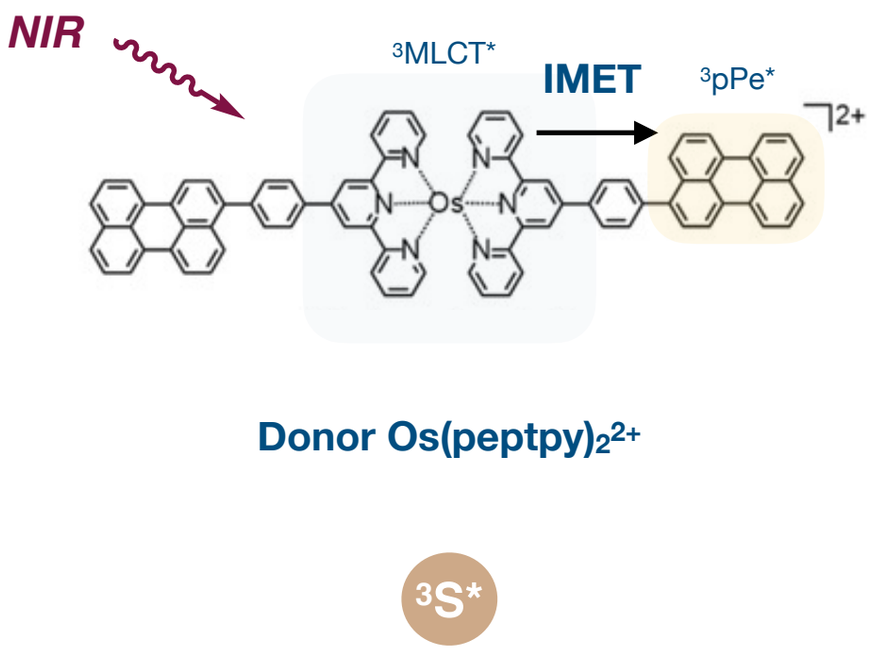

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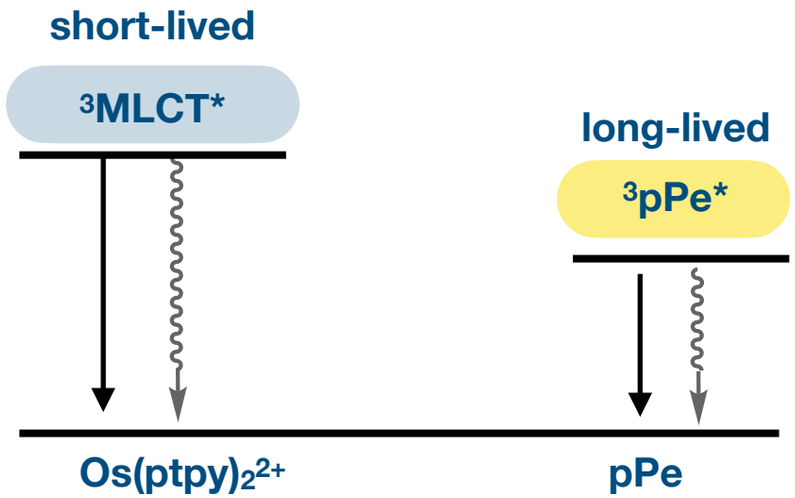

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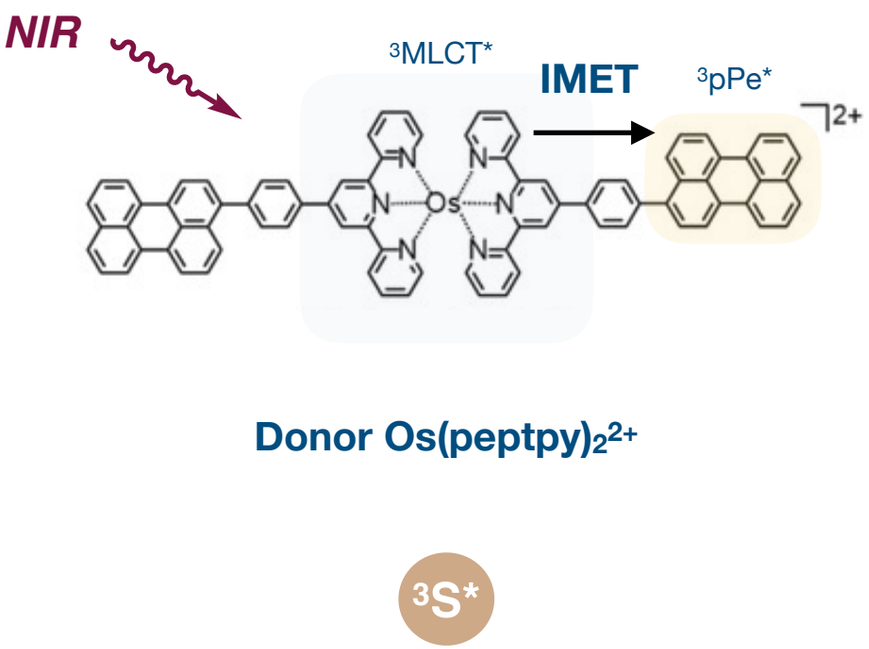

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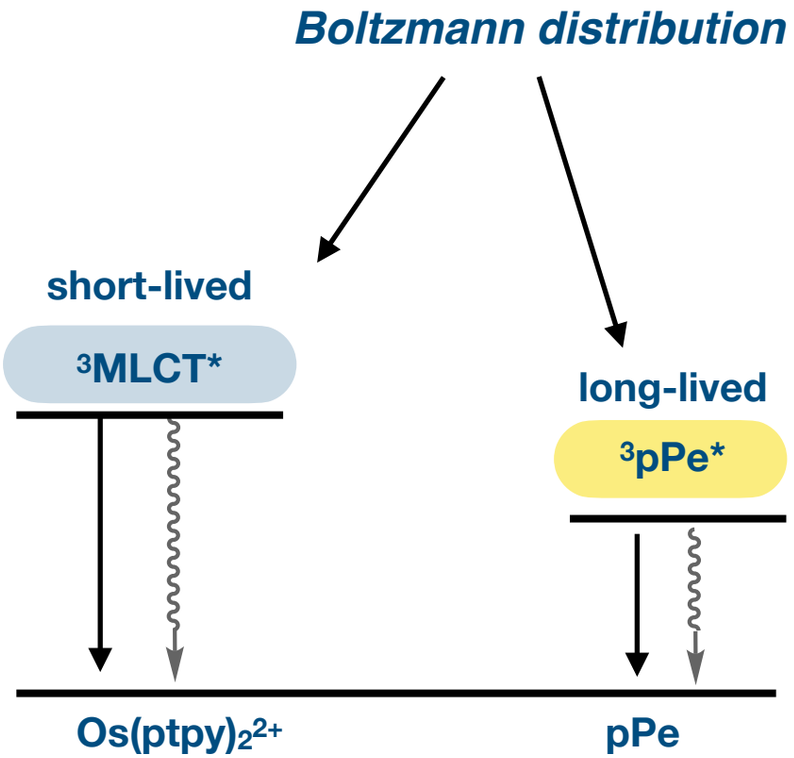

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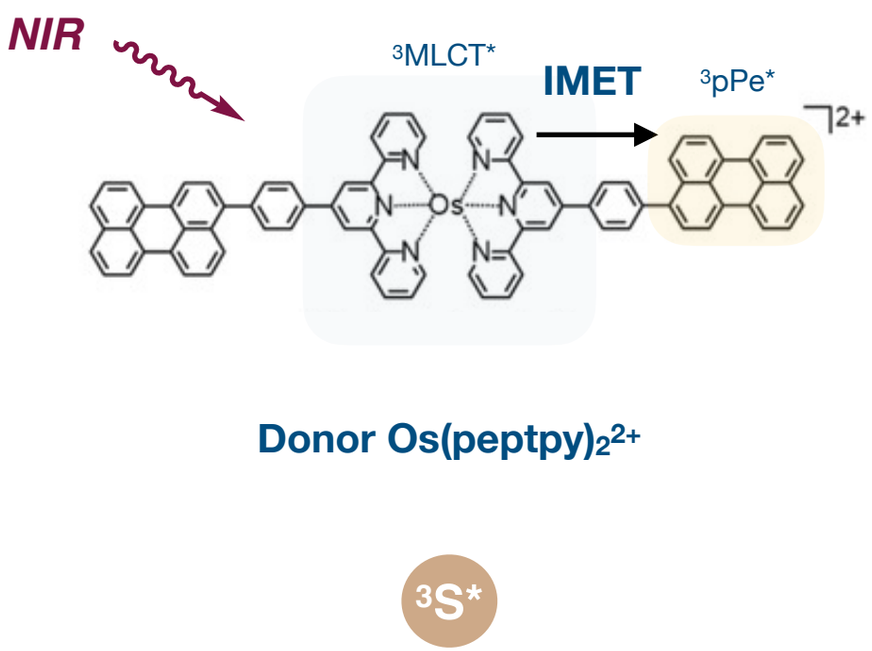
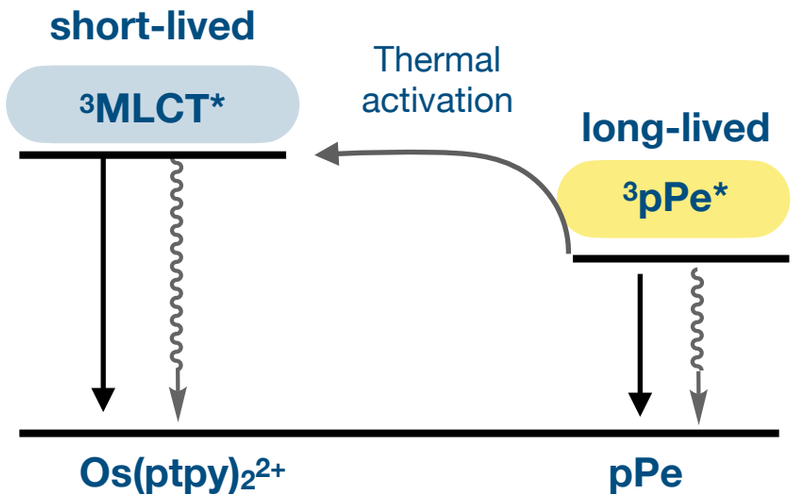


Donor Os(peptpy)$_2^{2+}$



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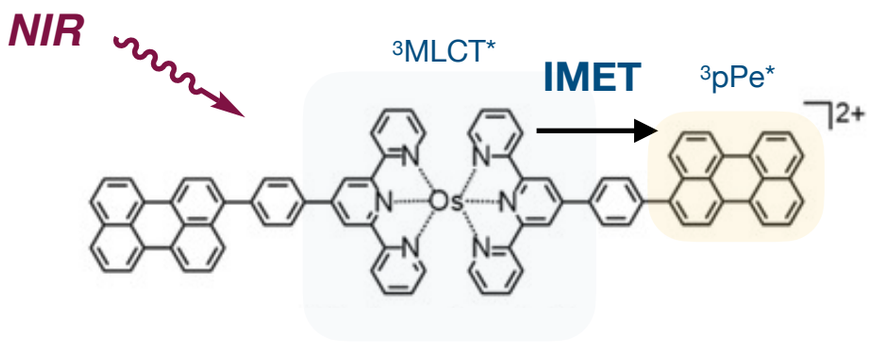

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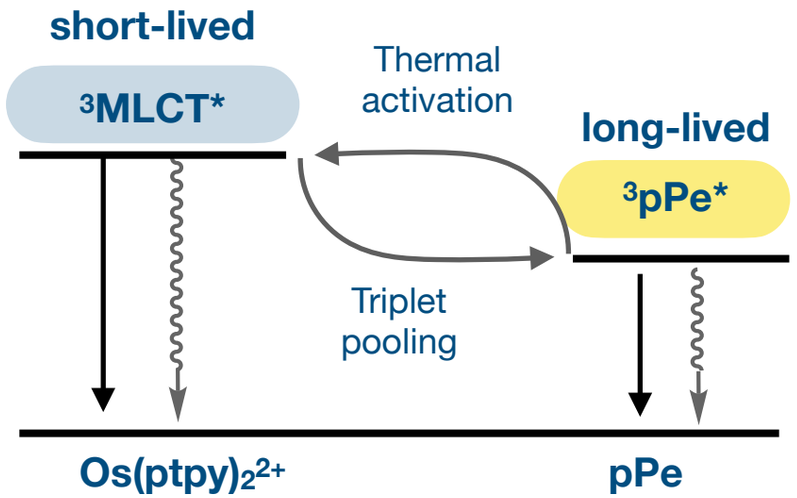

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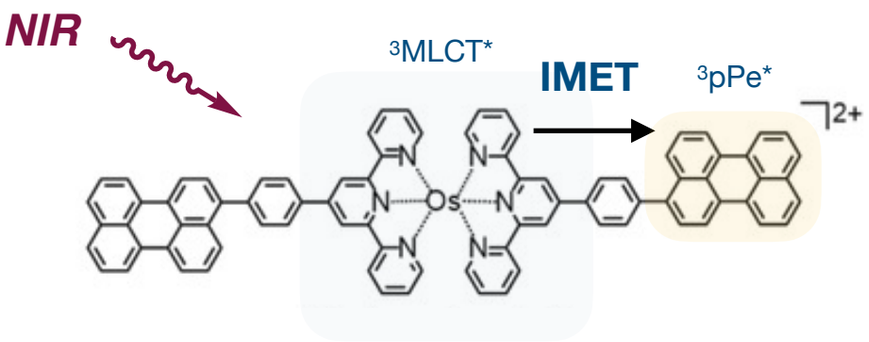
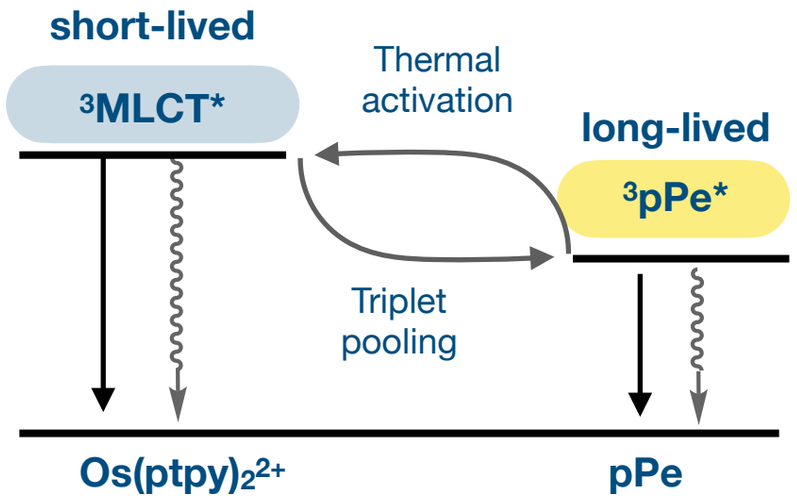


Donor Os(peptpy)$_2^{2+}$



^{3}S*

- **Excited state thermal equilibrium between ^{3}MLCT and ^{3}pPe***

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Hydrogel upconversion: Energy transfer via triplet lifetime manipulation

Design considerations:

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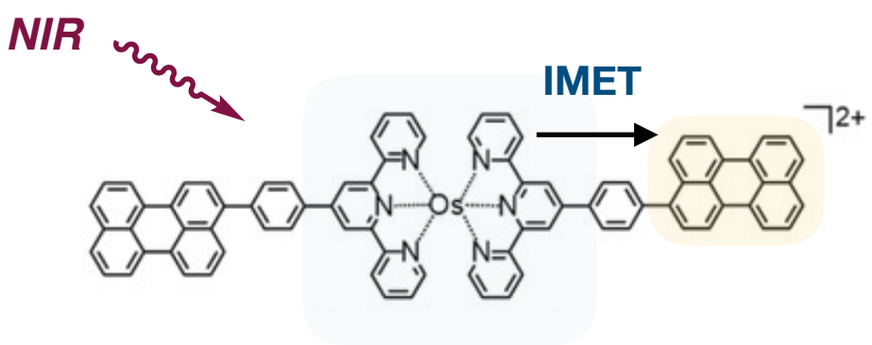

Donor $Os(peptpy)_2^{2+}$

$^3S^*$

Elongated net excited state lifetime

τ~0.2 μs

Sasaki, Y., Oshikawa, M., Bharmoria, P., Kouno, H., Hayashi-Takagi, A., Sato, M., Ajioka, I., Yanai, N., Kimisuka, N. *Angew. Chem. Int. Ed.* **2019**. *58*, 17827–17833.

Upconversion applied in organic systems

Hydrogel upconversion: Energy transfer via triplet lifetime manipulation

Design considerations:

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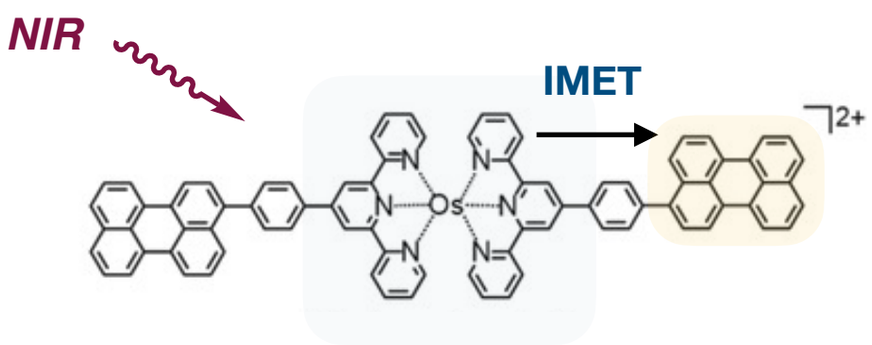


Donor $Os(peptpy)_2^{2+}$

$^3S^*$

Elongated net excited state lifetime

τ~0.2 μs ⟶ **τ~23 μs**

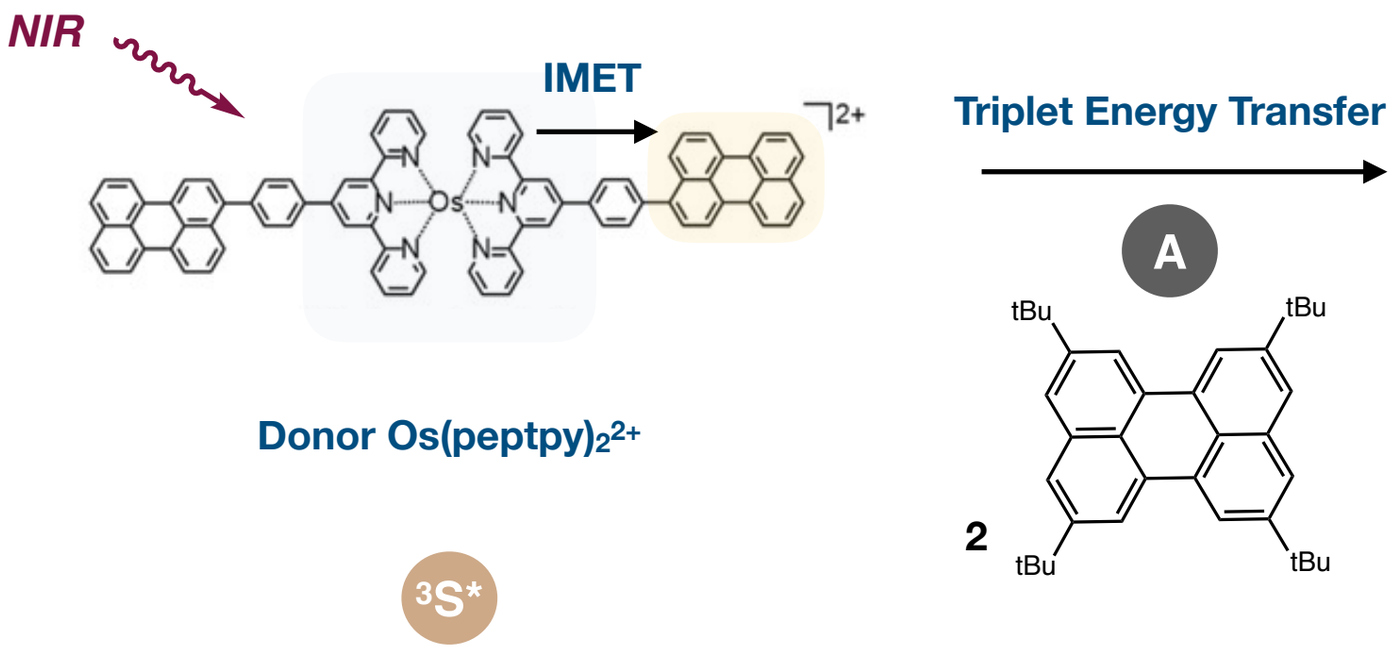
Sasaki, Y., Oshikawa, M., Bharmoria, P., Kouno, H., Hayashi-Takagi, A., Sato, M., Ajioka, I., Yanai, N., Kimisuka, N. *Angew. Chem. Int. Ed.* **2019**. *58*, 17827–17833.

Upconversion applied in organic systems

Hydrogel upconversion: Energy transfer via triplet lifetime manipulation

Design considerations:

- ***Elongate sensitizer triplet lifetime***



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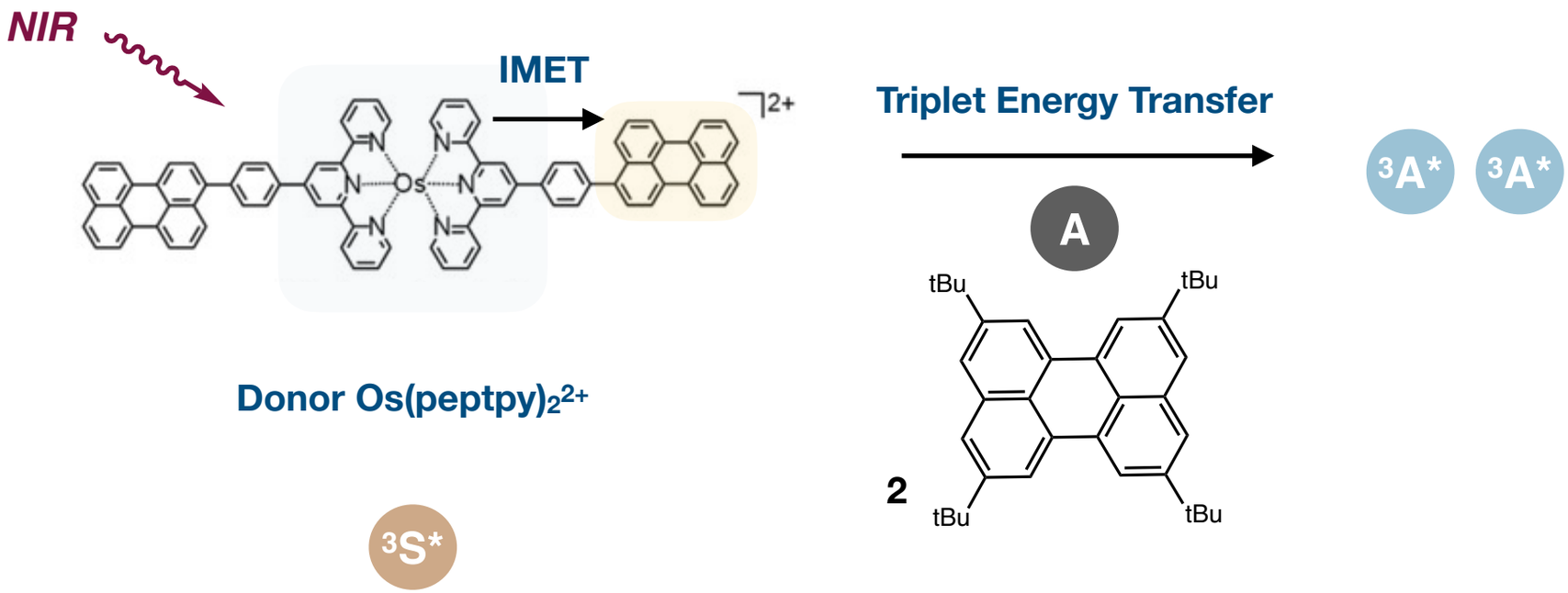

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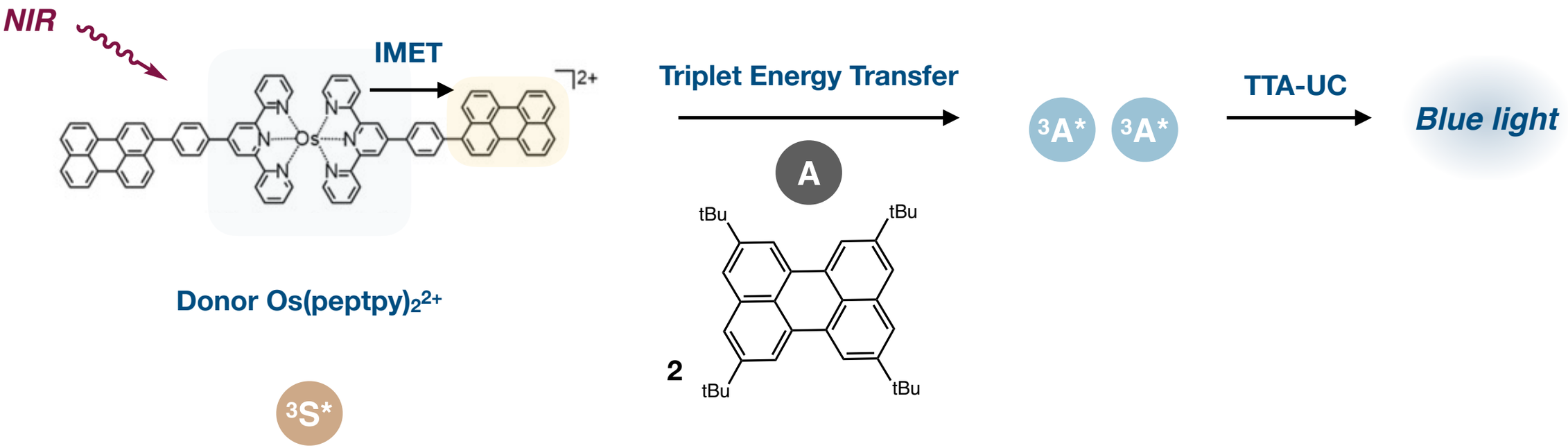

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TTA-UC in hydrogel scaffolds

Blue light induced signal activation:

Blue light

Interface TTA-UC with photoactivatable switch

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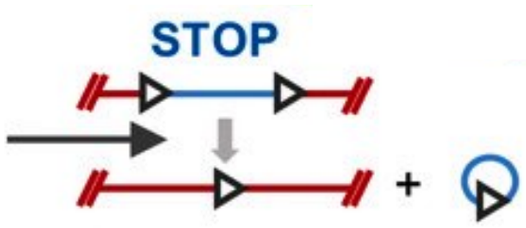
Blue light → ***Cre recombinase***



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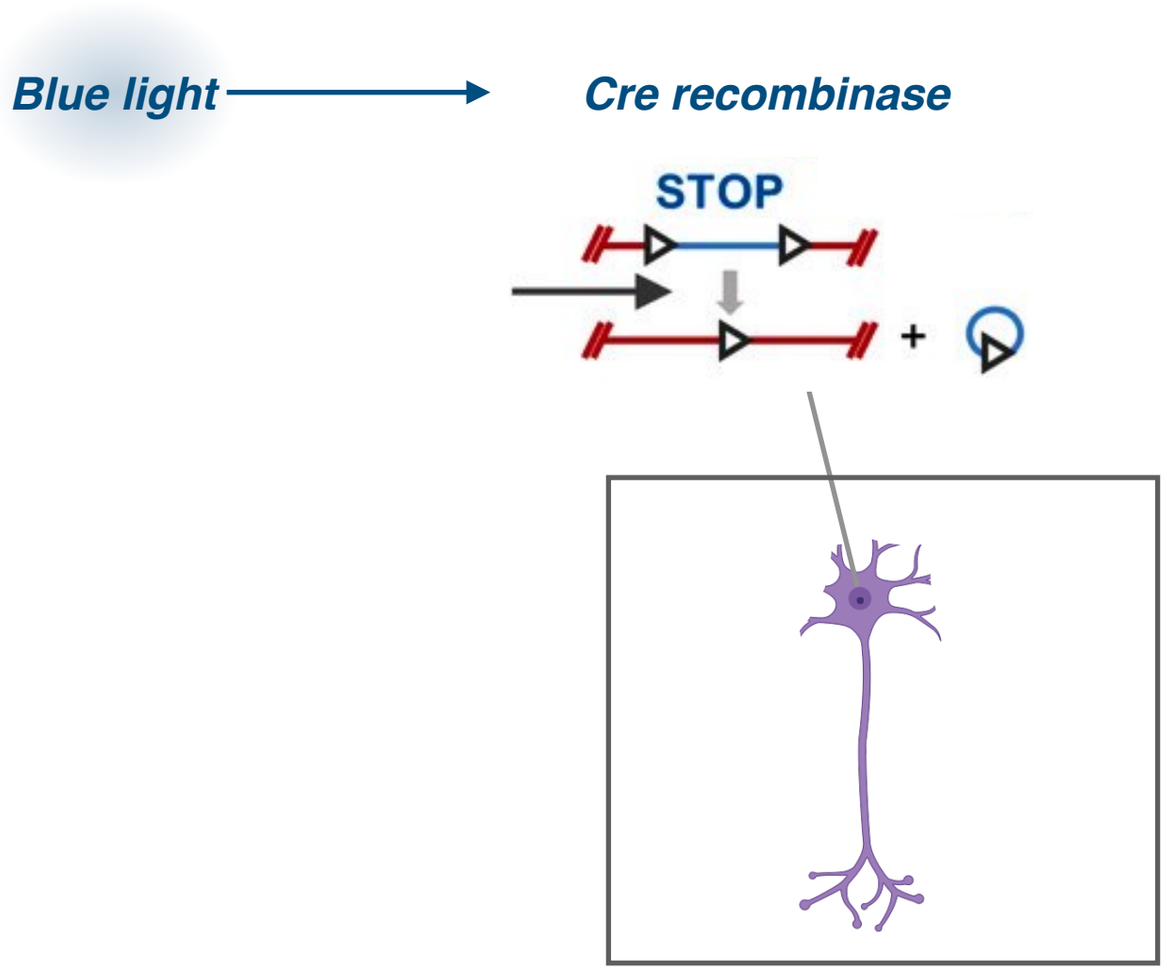

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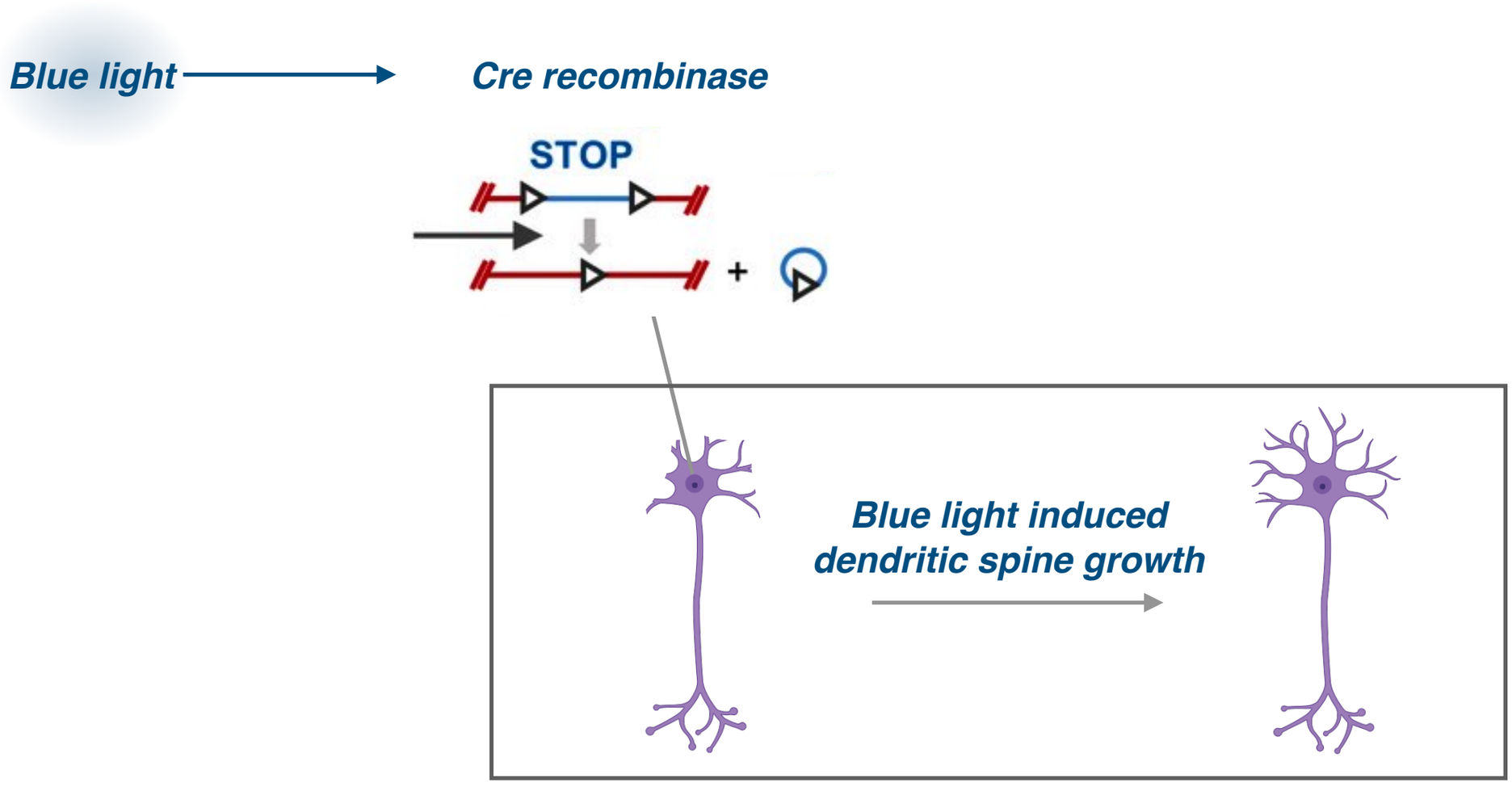

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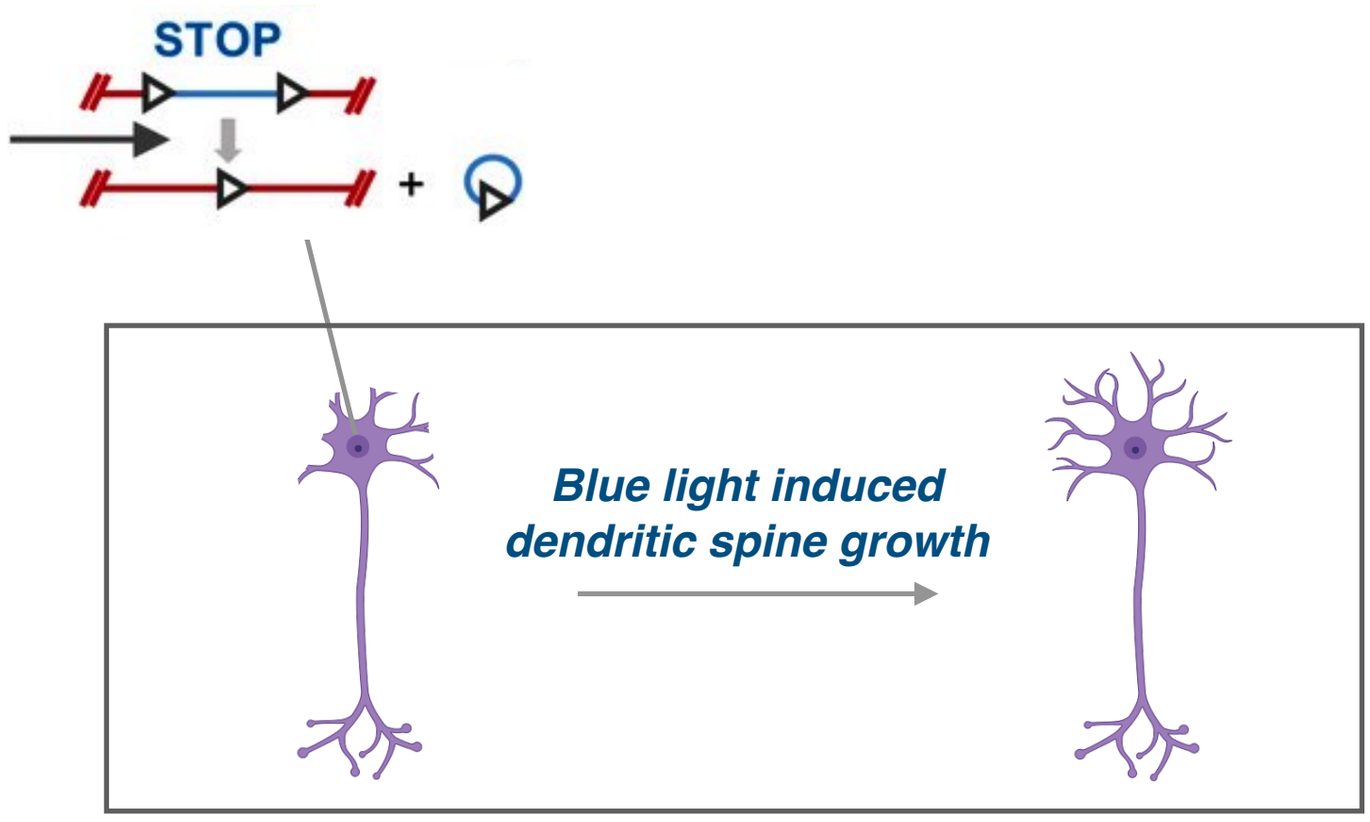


Neuronal activity acts as a read out to success of method

Sasaki, Y., Oshikawa, M., Bharmoria, P., Kouno, H., Hayashi-Takagi, A., Sato, M., Ajioka, I., Yanai, N., Kimisuka, N. *Angew. Chem. Int. Ed.* **2019**. *58*, 17827–17833.

Processes of Upconversion

Upconversion in Organic Materials

Upconversion in Inorganic Materials

- *How does upconversion occur in **inorganic** systems?*

Processes of Upconversion

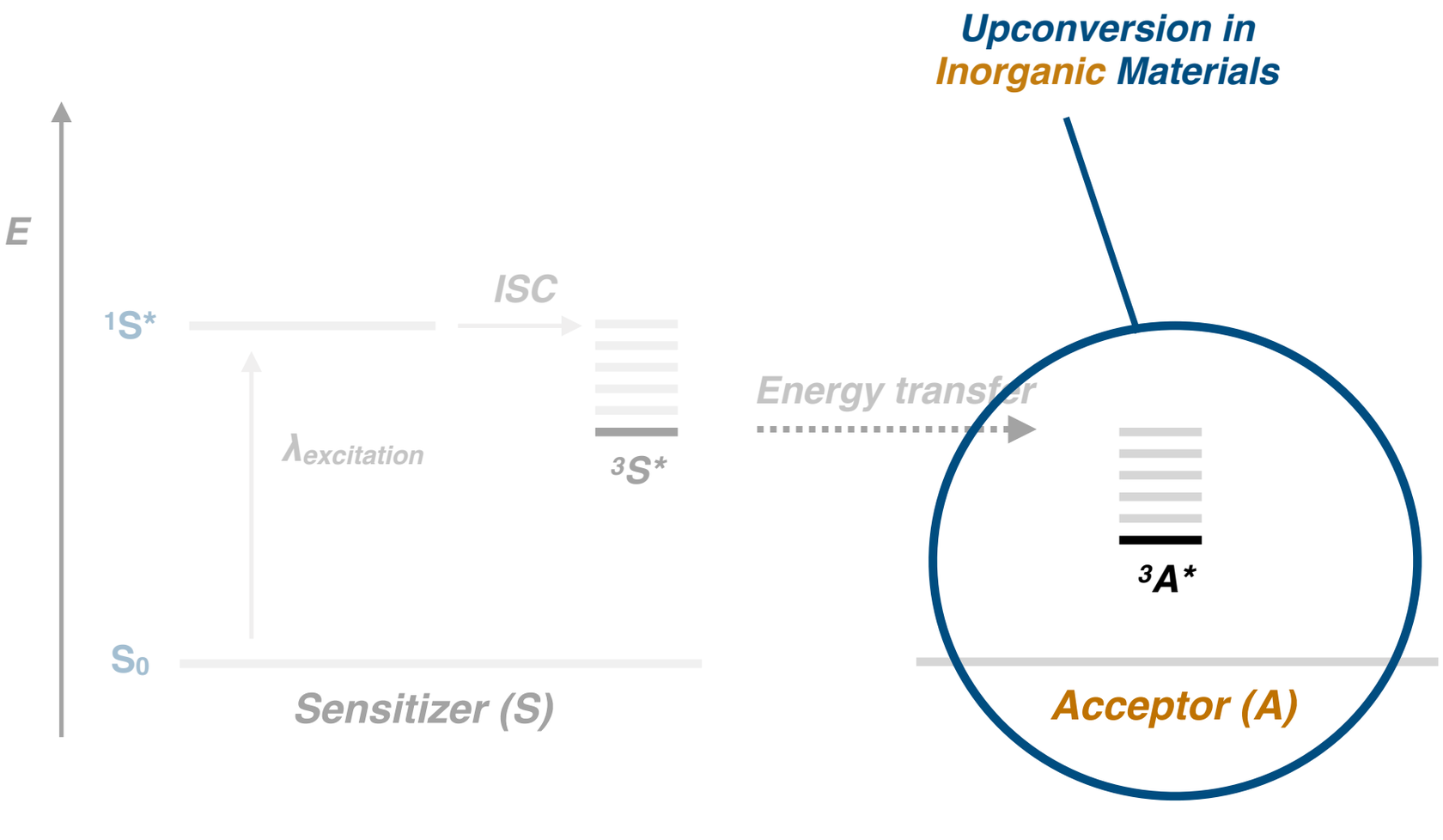
Upconversion in Organic Materials

Upconversion in Inorganic Materials

- ***Energy transfer, cross relaxation***
- ***Excited-State Absorption***
- ***Photon Avalanche***

Upconversion in Inorganic Systems

Lanthanide annihilators



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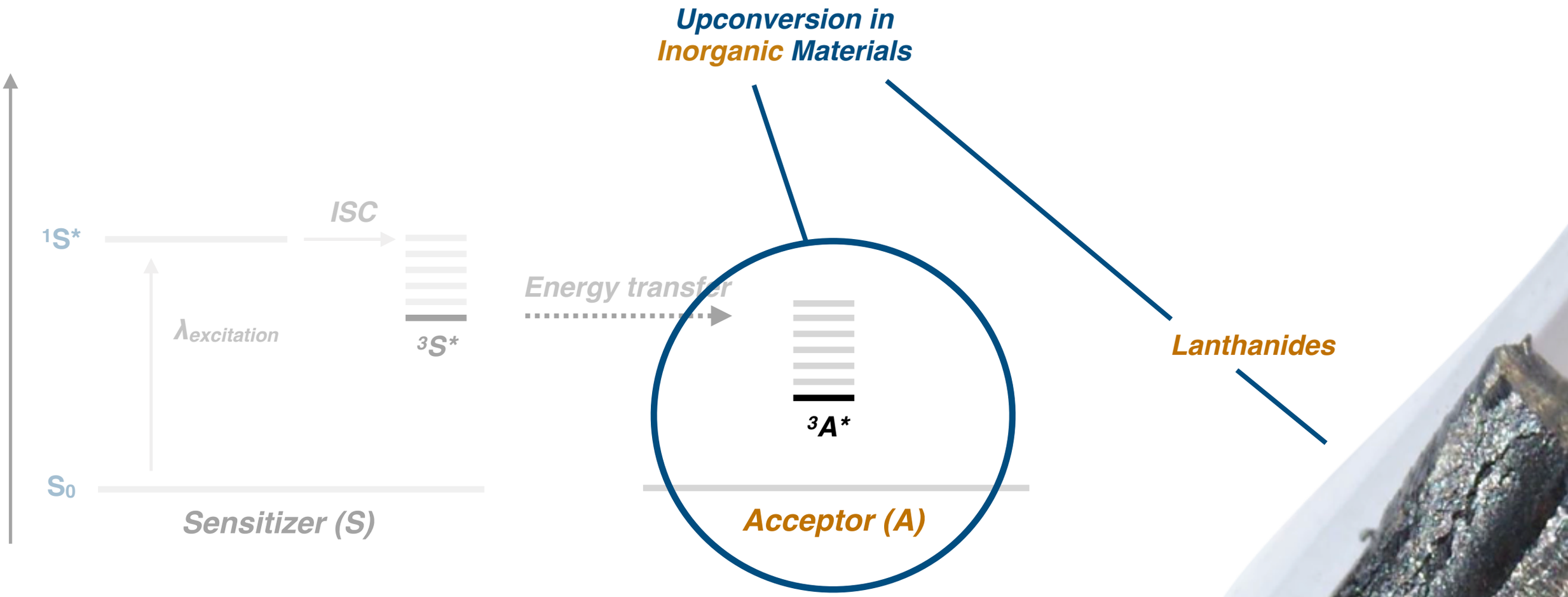

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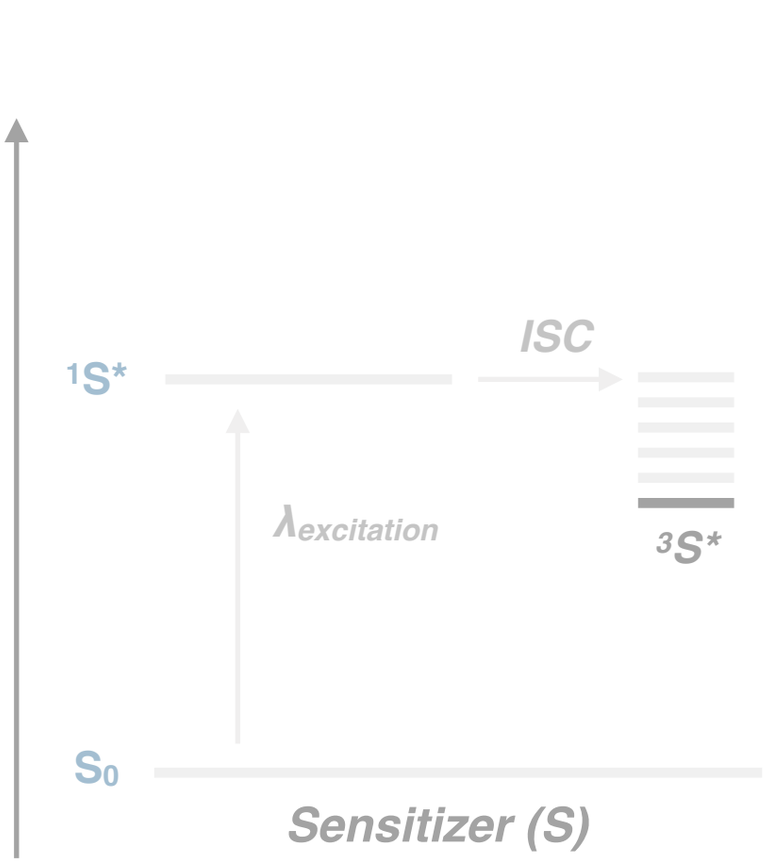

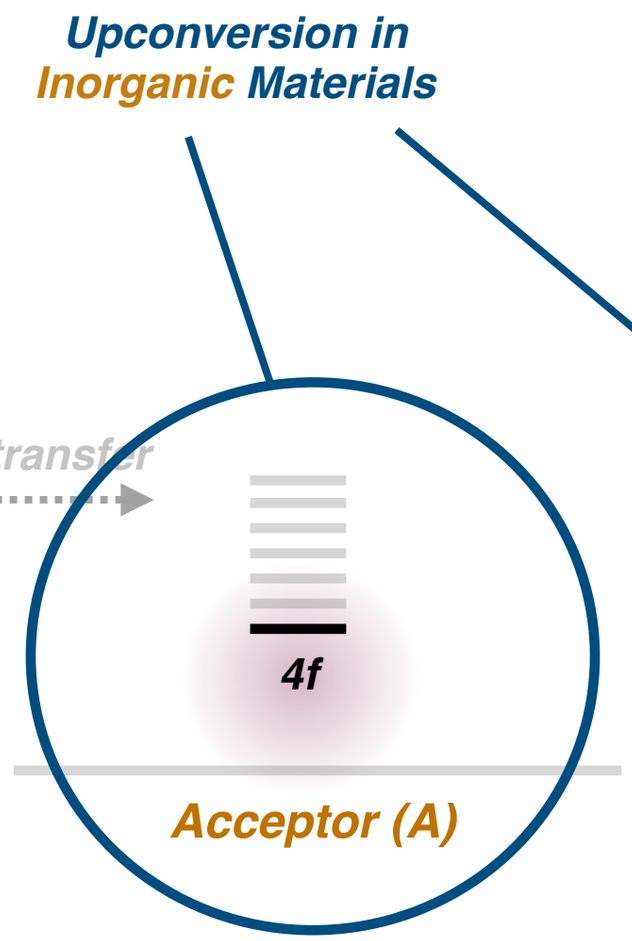

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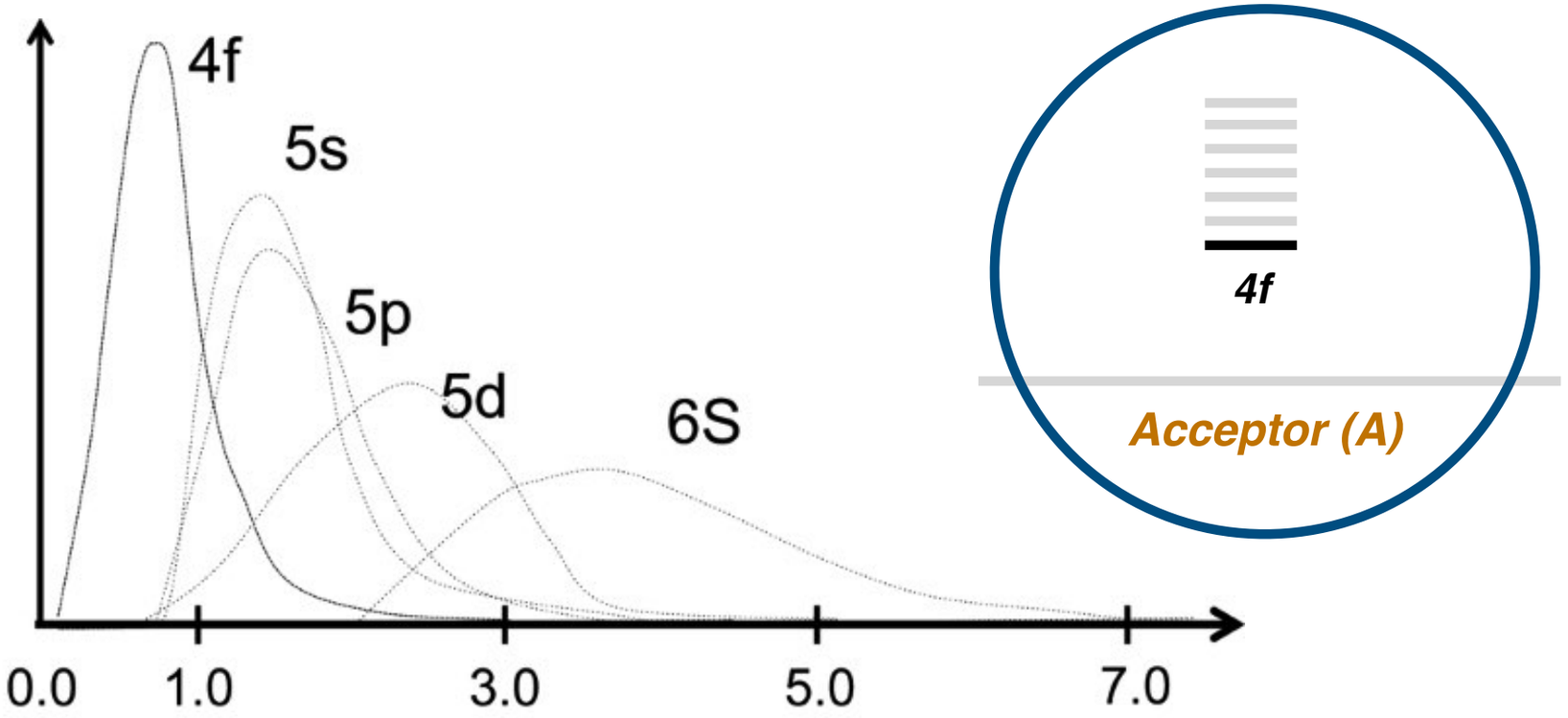

Hasegawa, Y., Kitagawa, Y., Nakanishi, T. *NPG. Asia. Mat.* **2018**. *10*, 52–70.

Safdar, M., Ghazy, A., Lastusaari, M., Karppinen, M. *J. Mat. Chem.* **2020**. *8*, 6946–6965.

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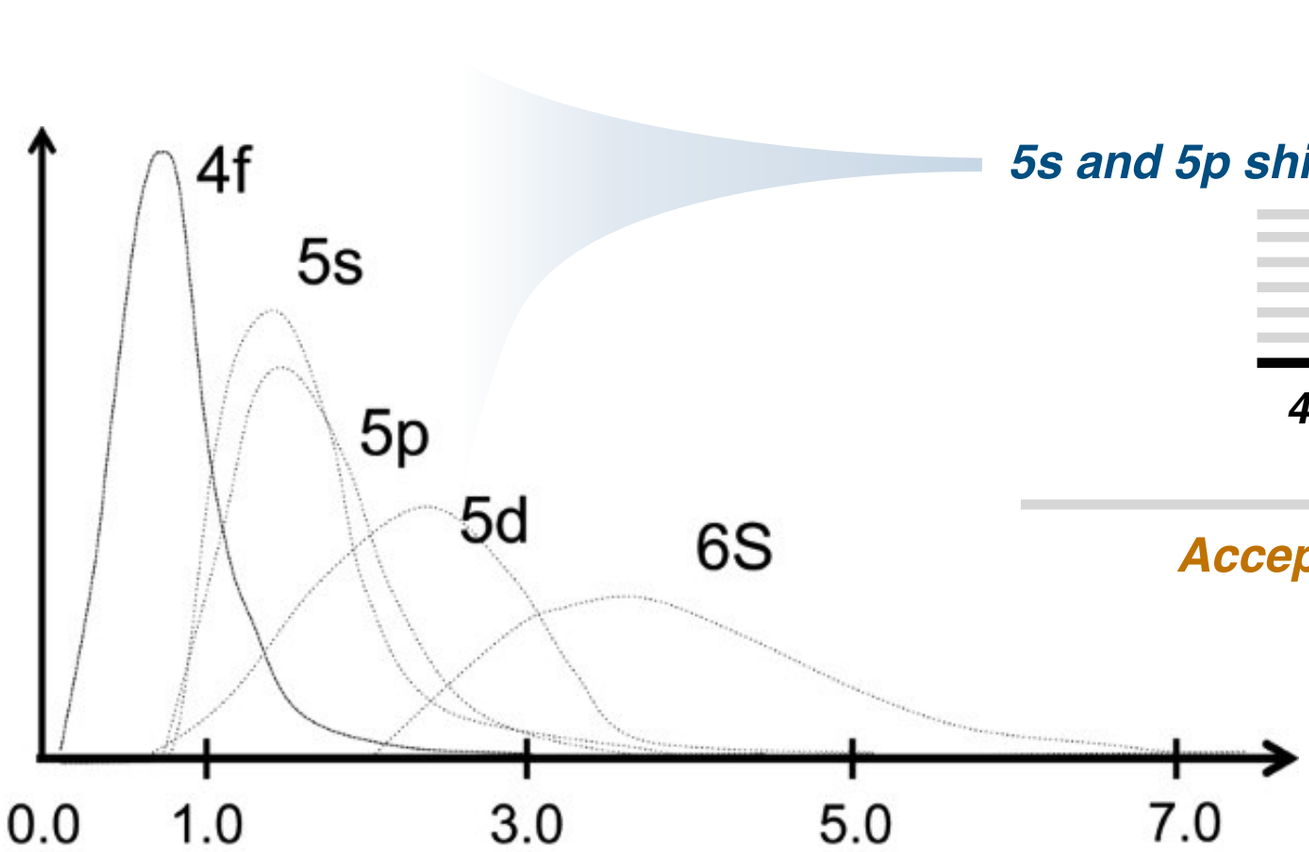

5s and 5p shield 4f orbitals

Acceptor (A)

Lanthanides

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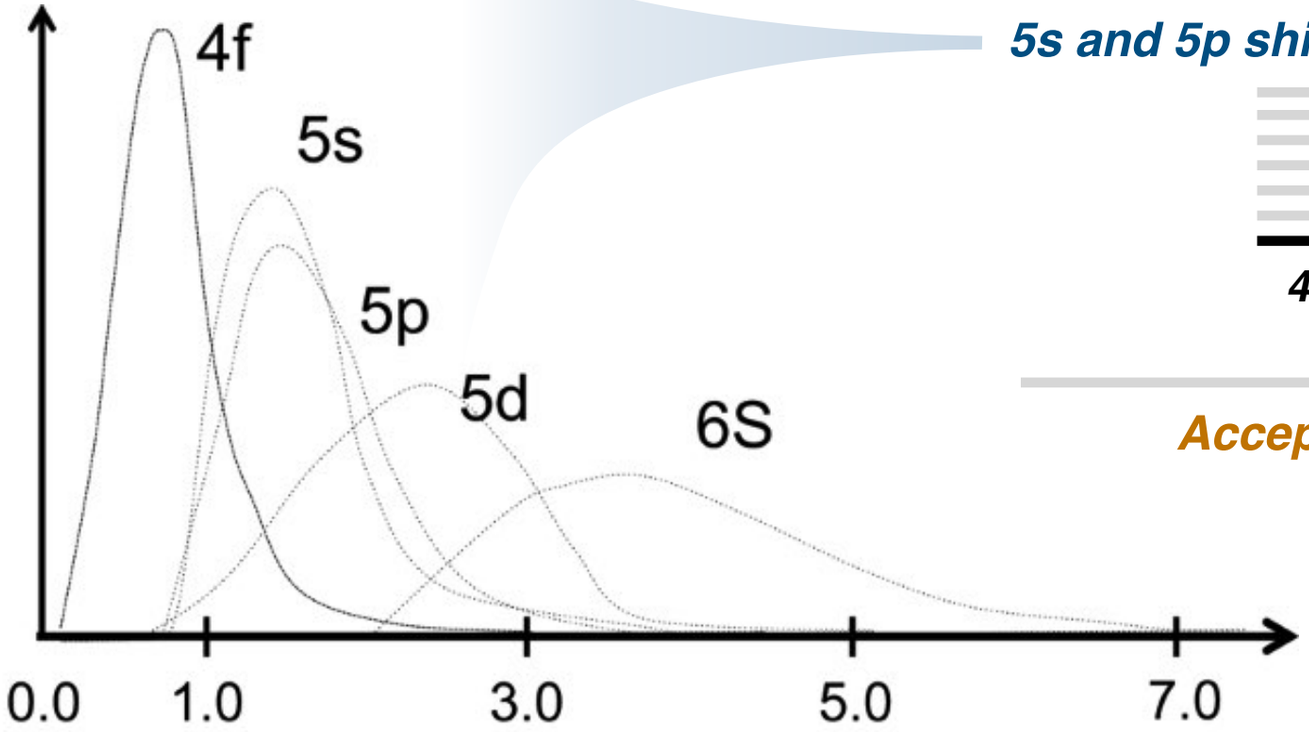
Upconversion in Inorganic Systems

Lanthanide annihilators

1. Stabilized electronic configuration

Narrow-band emission spectra

5s and 5p shield 4f orbitals



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Upconversion in Inorganic Systems

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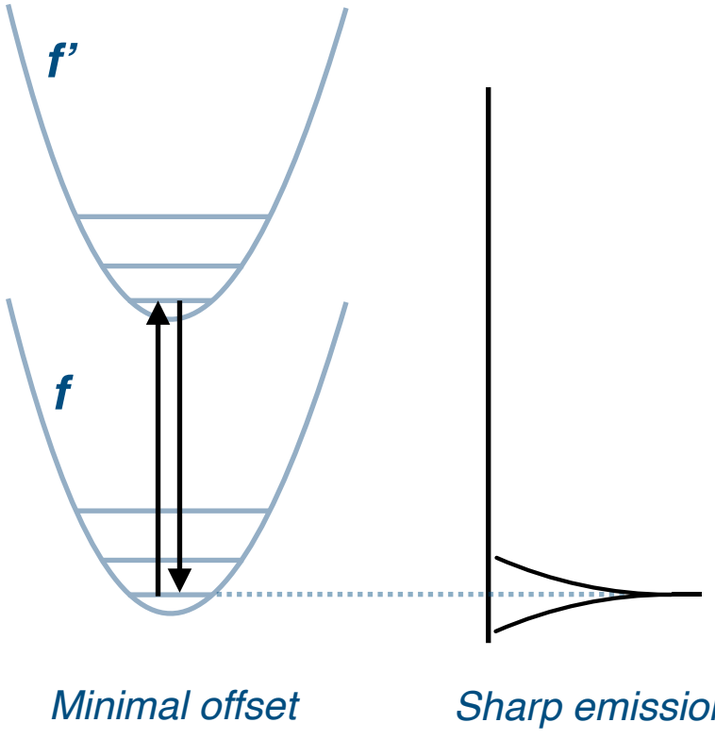

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Upconversion in Inorganic Systems

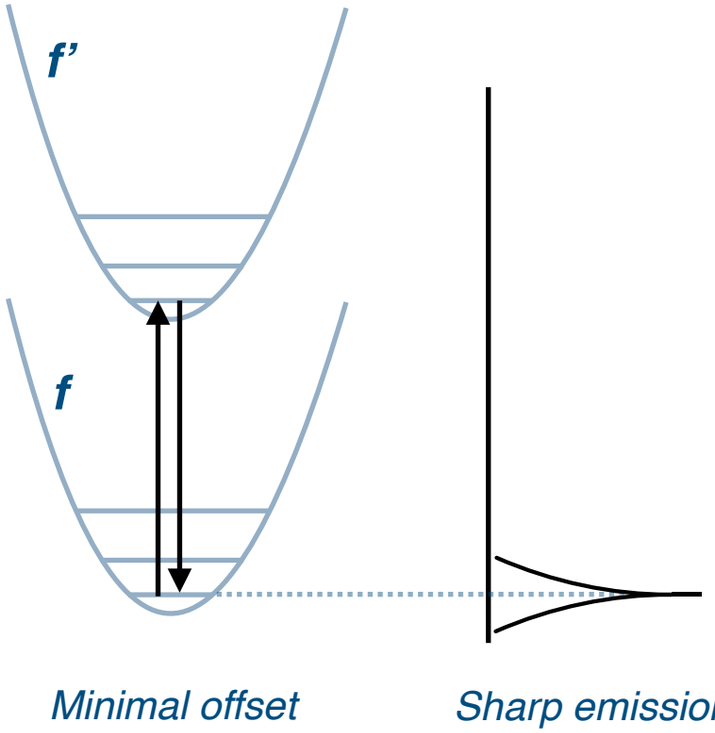
Lanthanide annihilators

1. ***Stabilized electronic configuration***

Narrow-band emission spectra

2. ***f-f transitions are spin-forbidden***

Long excited state lifetimes



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Upconversion in Inorganic Systems

Solid state upconversion

Upconversion was identified as a parasitic process

In competition with laser activity

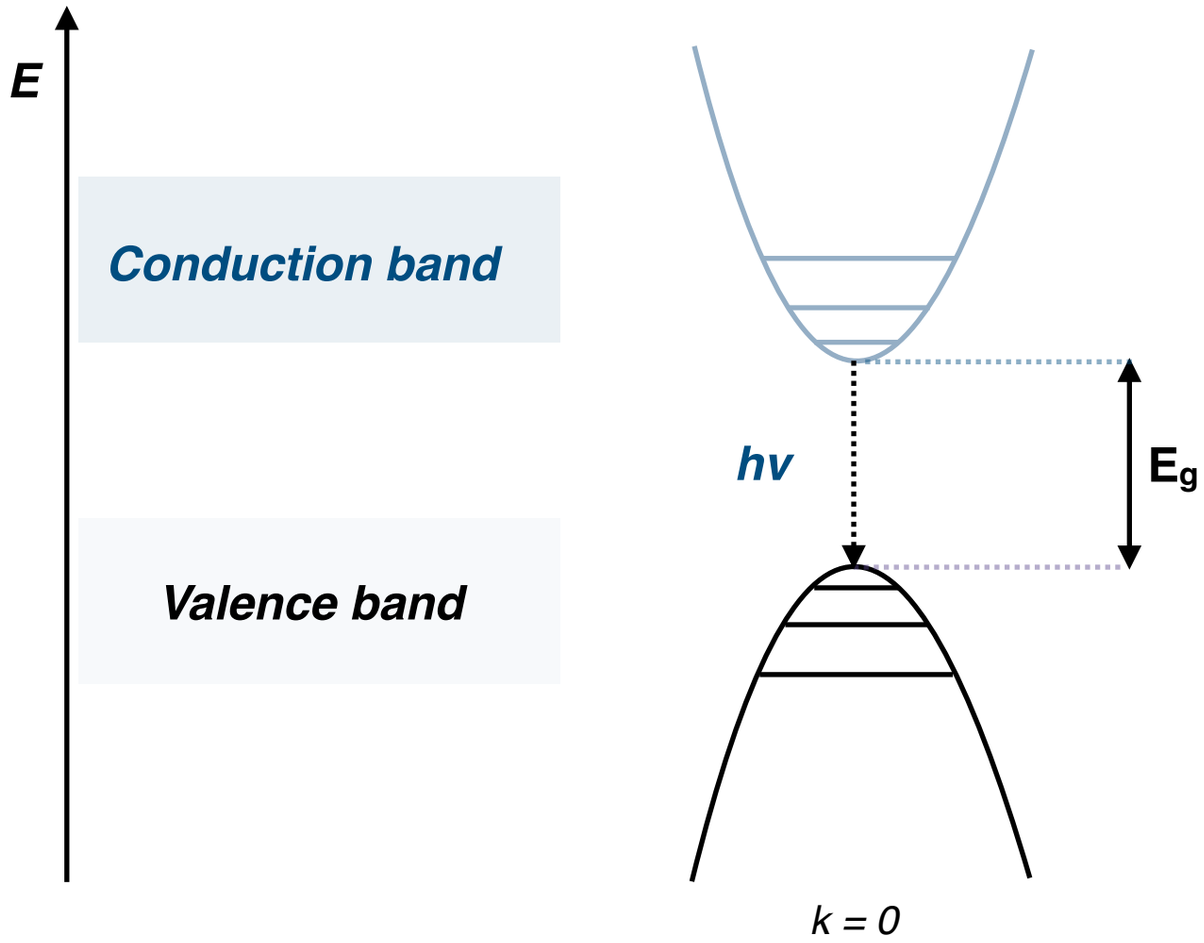
1960s
Discovery of lasers

Nadort, A., Zhao, J., Gold's, E. M. *Nanoscale.* **2016**. *8*, 13099–13130.

Upconversion in Inorganic Systems

Solid state upconversion

Laser activity:



Direct band gap structure

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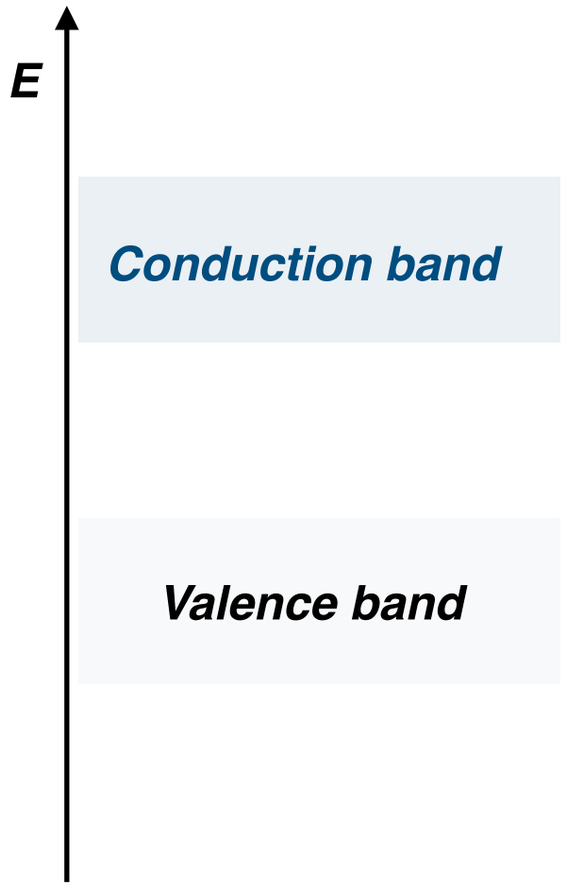

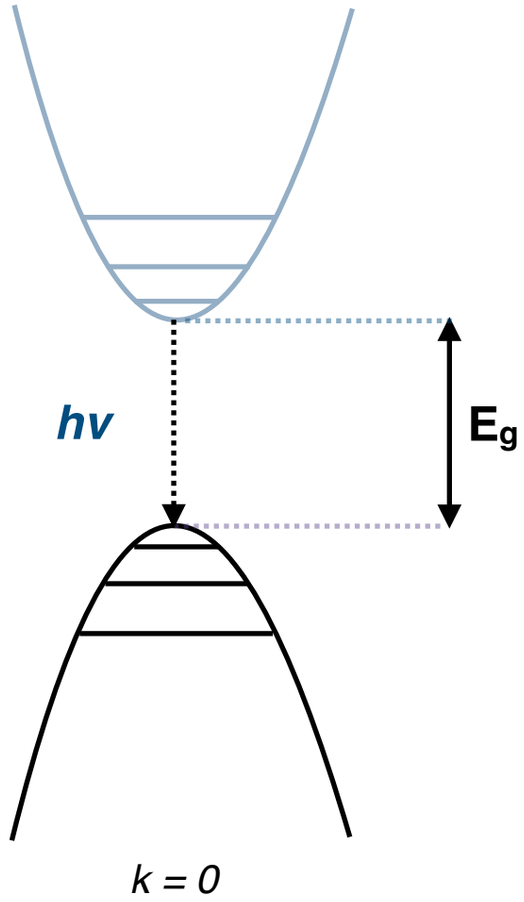

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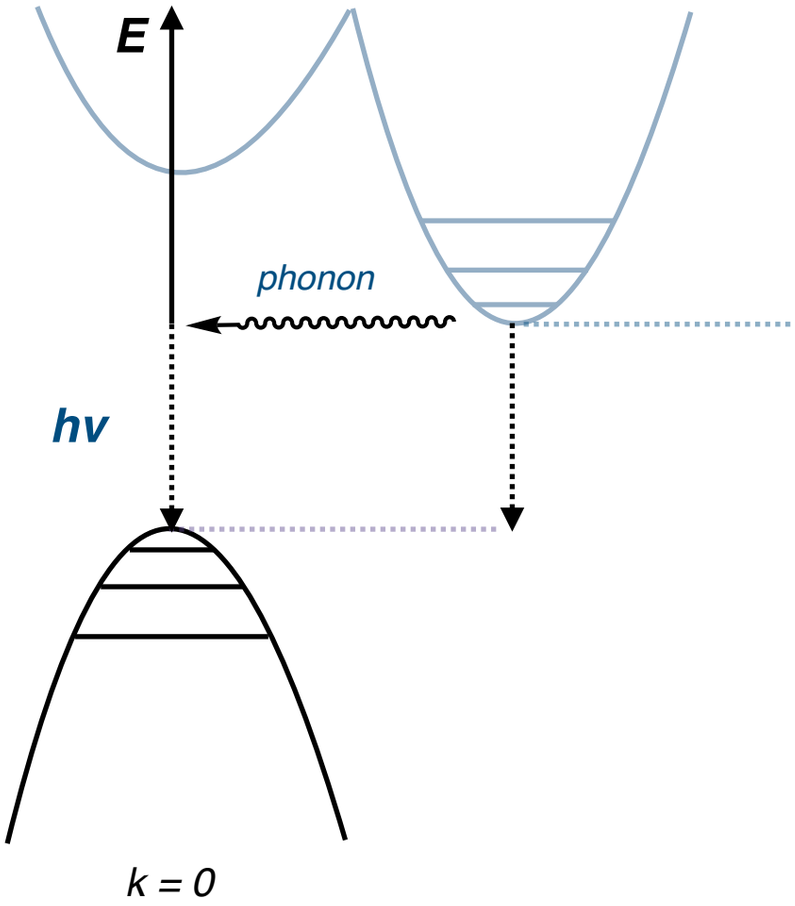

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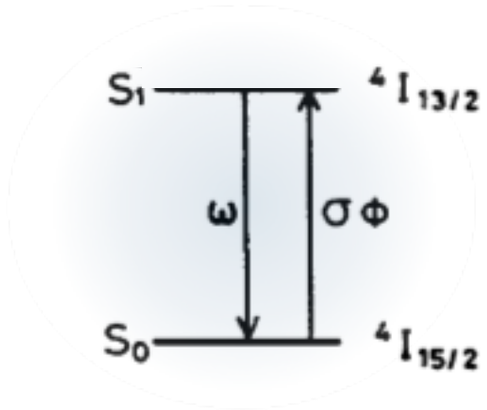
Upconversion in Inorganic Systems

Solid state upconversion

Energy Transfer Upconversion



Upconversion competes with direct radiative decay

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Upconversion in Inorganic Systems

Solid state upconversion

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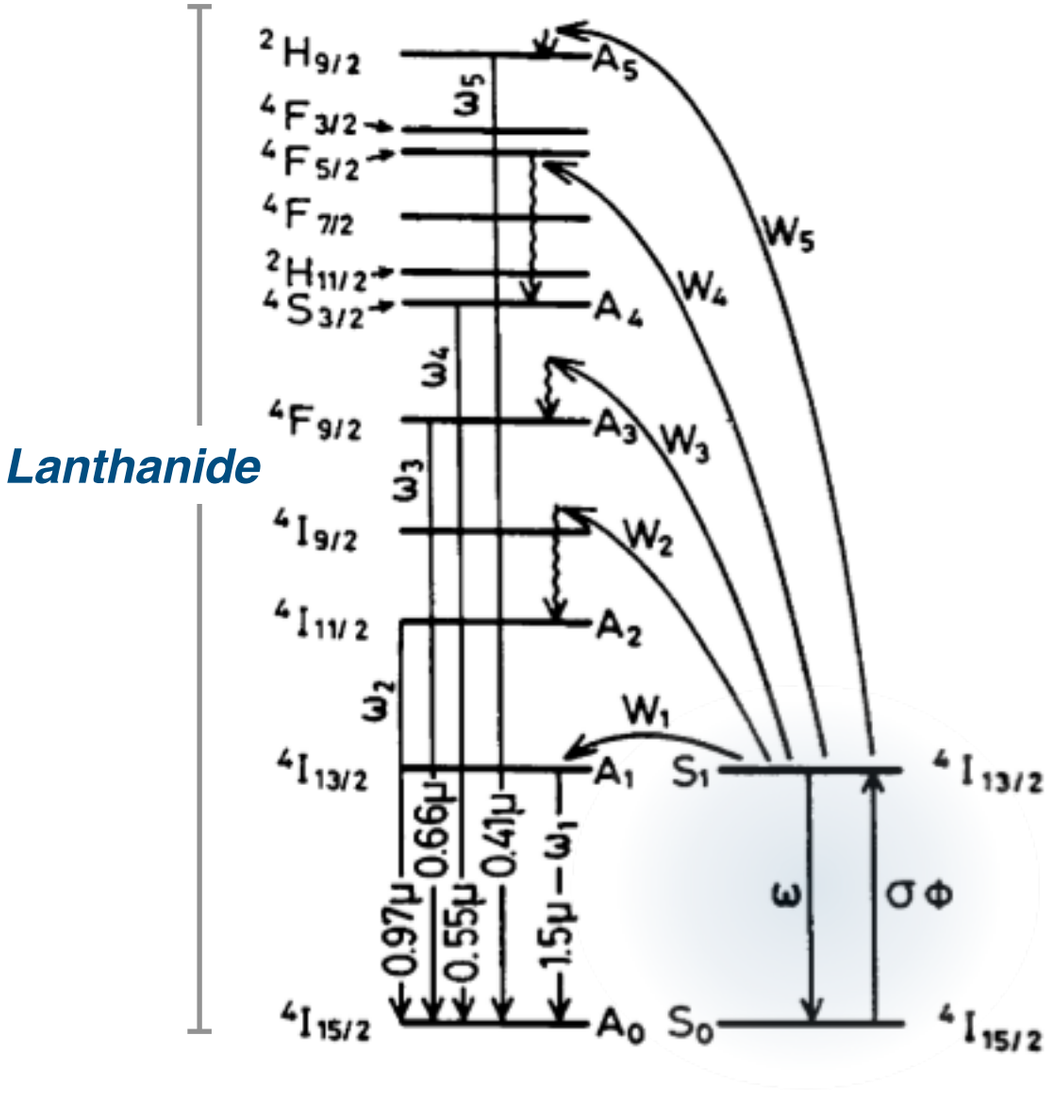

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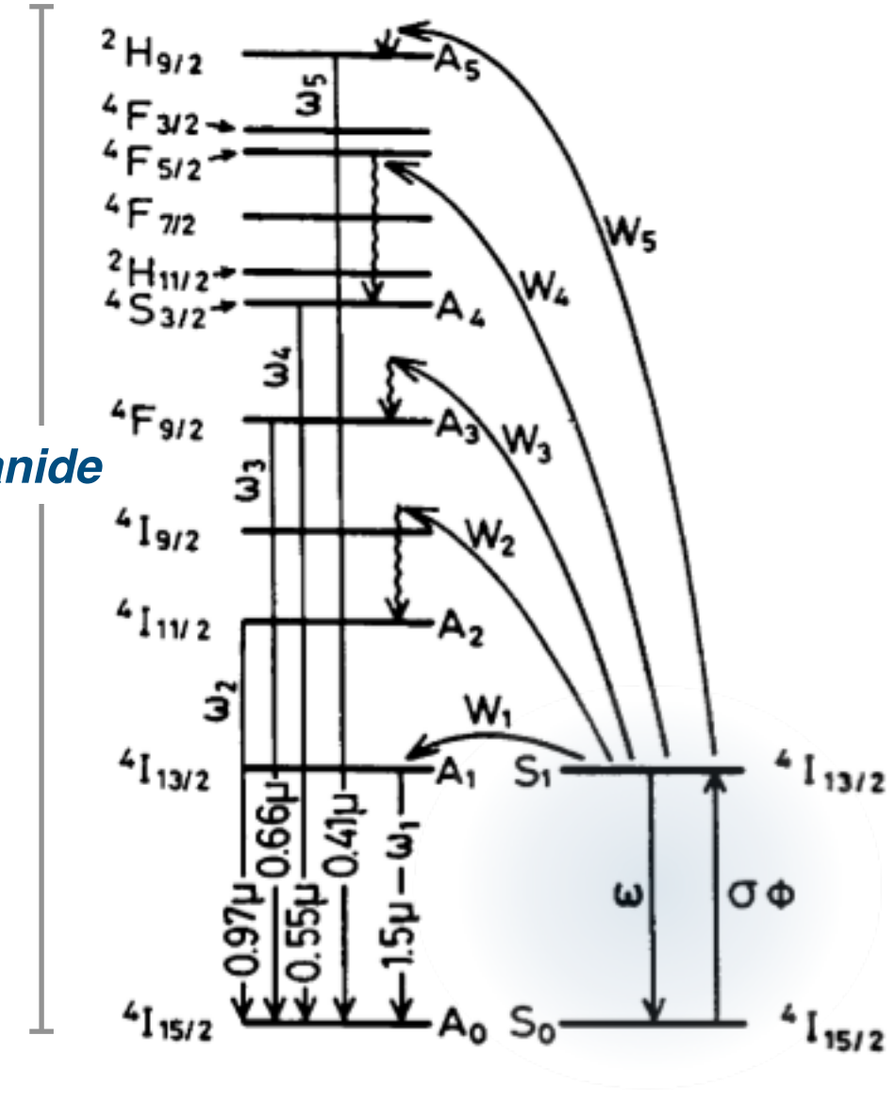
Upconversion in Inorganic Systems

Solid state upconversion

Energy Transfer Upconversion

Lanthanide

Excitation of an excited laser-active ion



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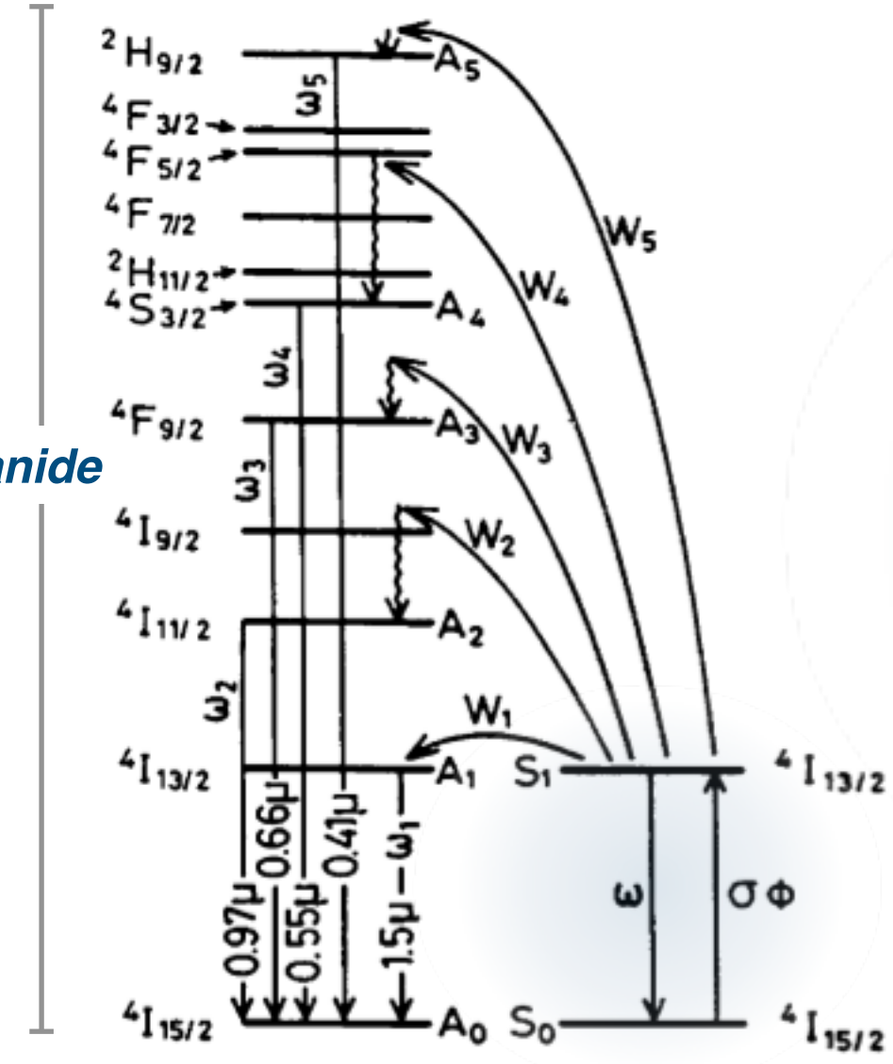

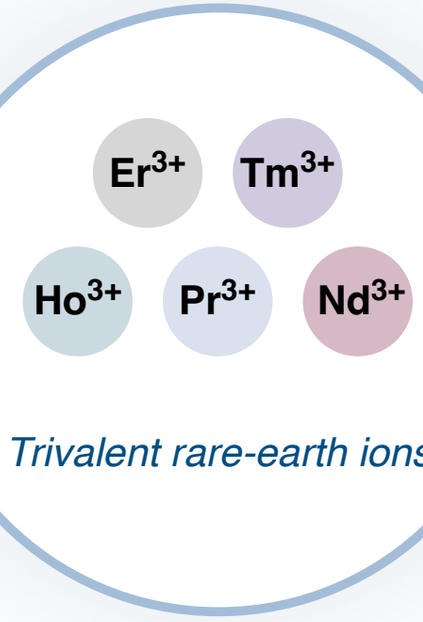

Trivalent rare-earth ions

- *Ground configuration $4f^n$ states*

Upconversion competes with direct radiative decay

Joubert, M-F. *Opt. Mat.* **1999**. *11*, 181–203.

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Upconversion in Inorganic Systems

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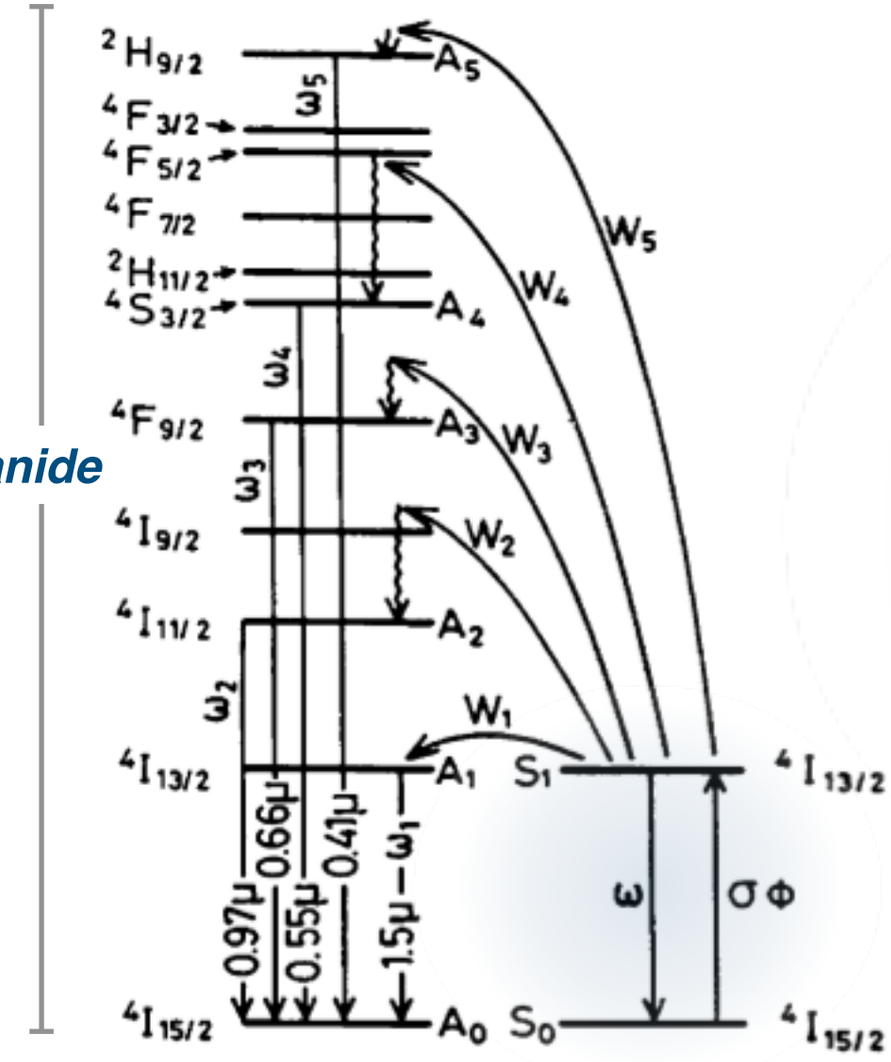

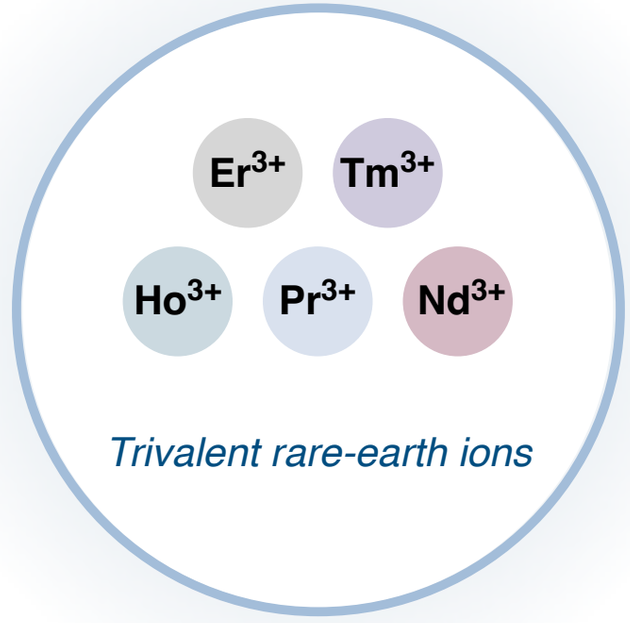

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Upconversion in Inorganic Systems

Solid state upconversion

Energy Transfer Upconversion

(1) Energy Transfer

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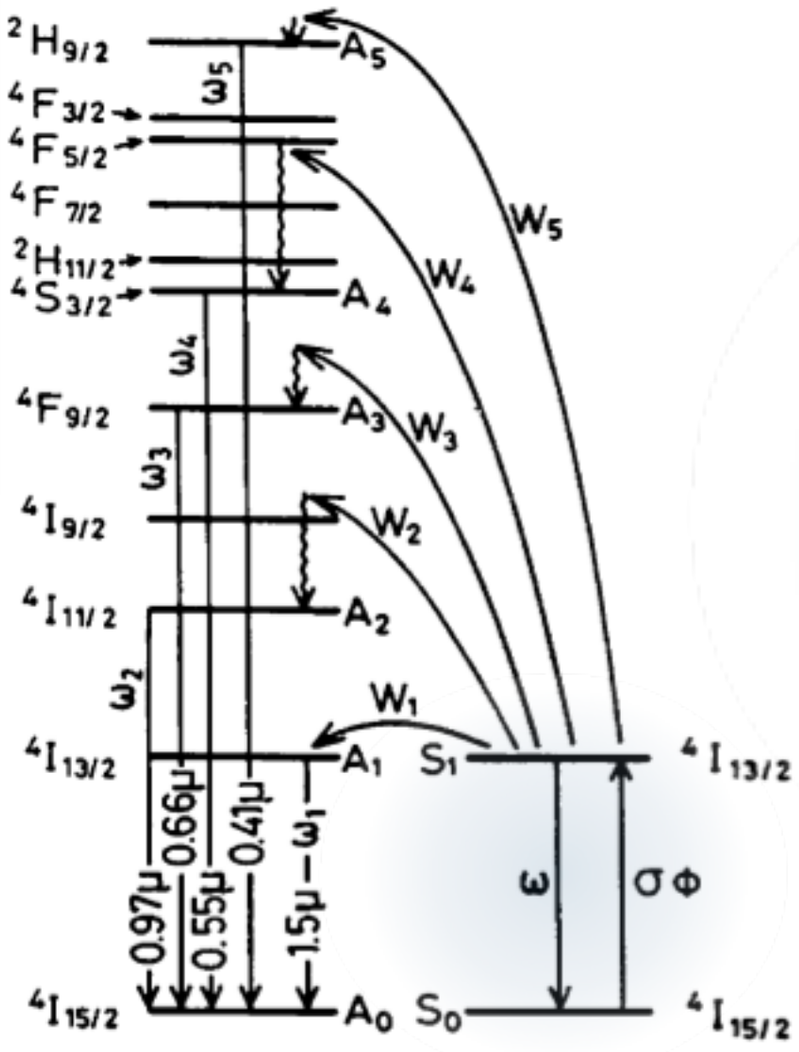

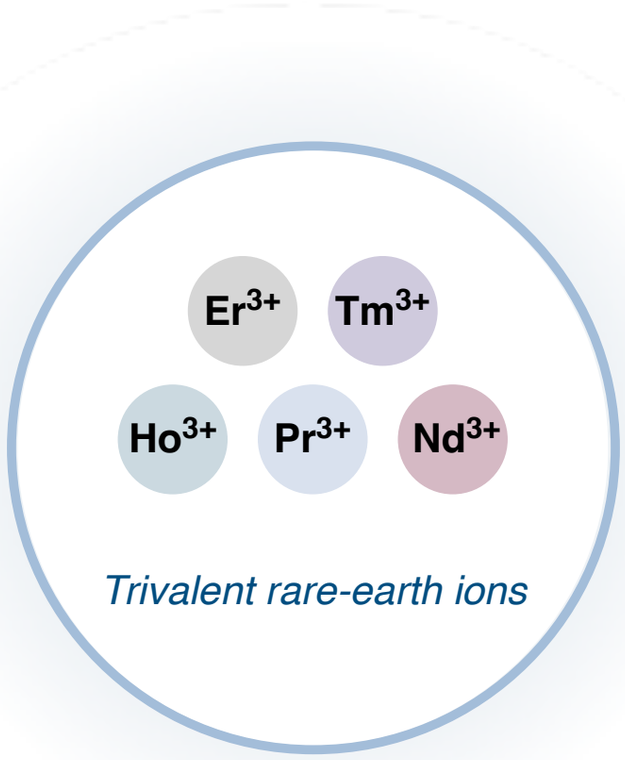

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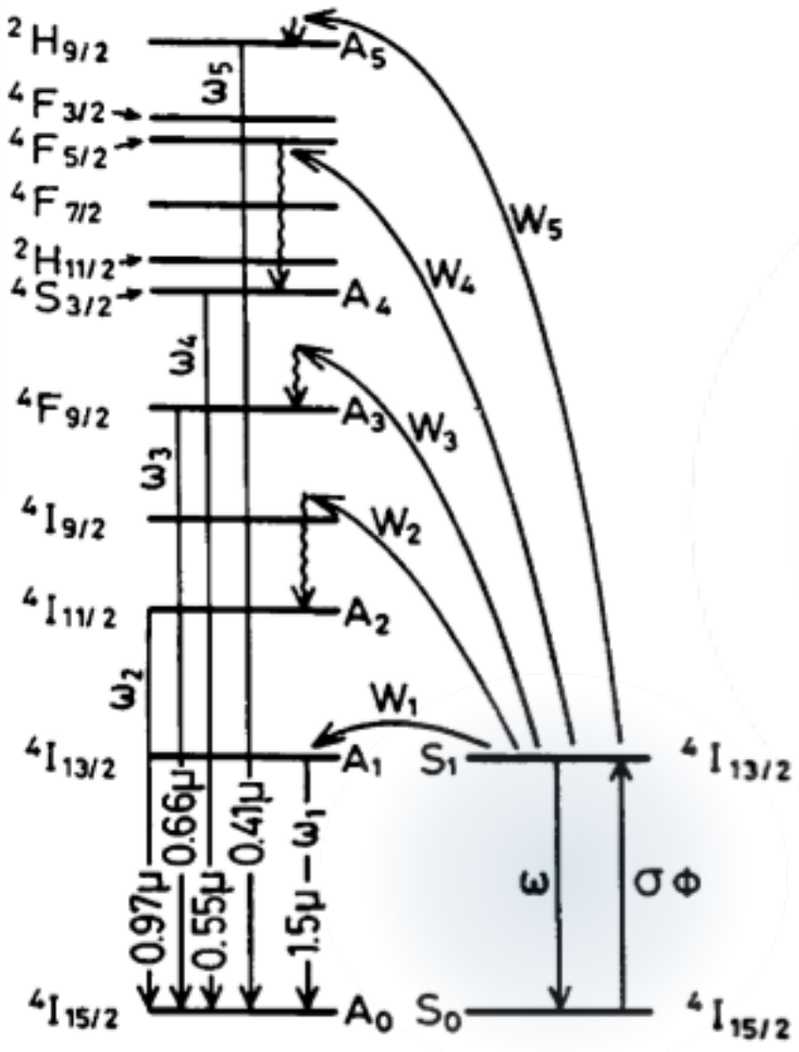

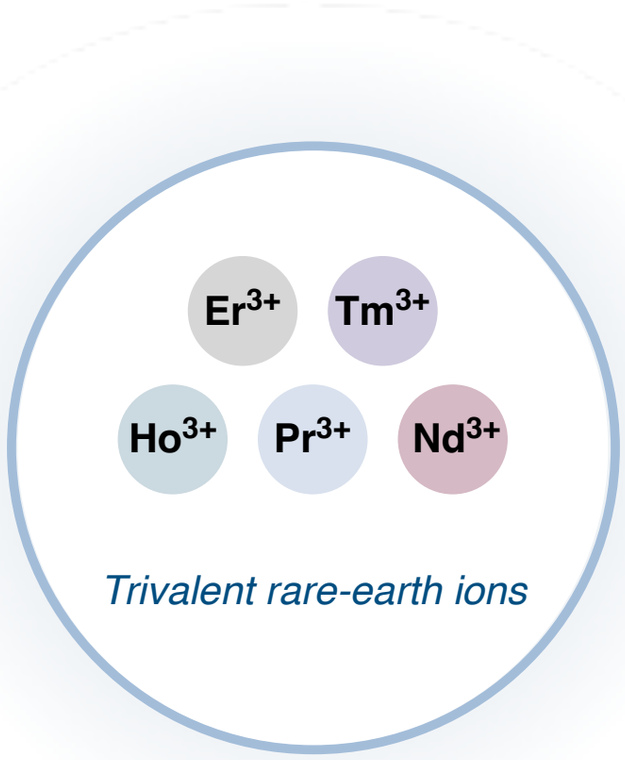

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- ***The most efficient UC systems occur in solid-state materials doped with lanthanide ions***

Haase, M., Schäfer, H. *Angew. Chem. Int. Ed.* **2011**. *50*, 5808–5829.

Upconversion in Inorganic Systems

***Inorganic systems: 5 possible mechanisms** may occur**

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- ***Commonly observed in nanoparticle upconversion***

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**only 4 will be discussed*

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Inorganic systems:* *5 possible mechanisms* *may occur*

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  ($NaY_{0.77}Yb_{0.20}Er_{0.03}F_4$)

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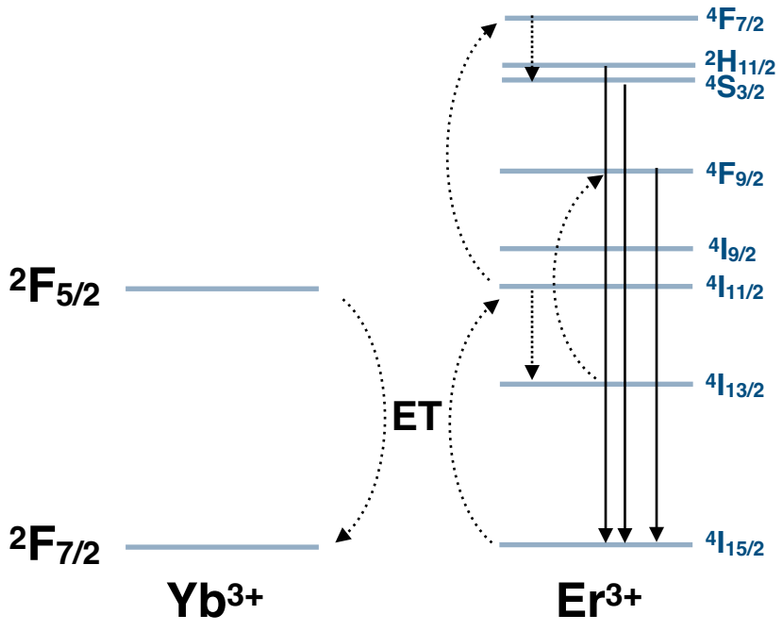

Sensitizer **Acceptor**

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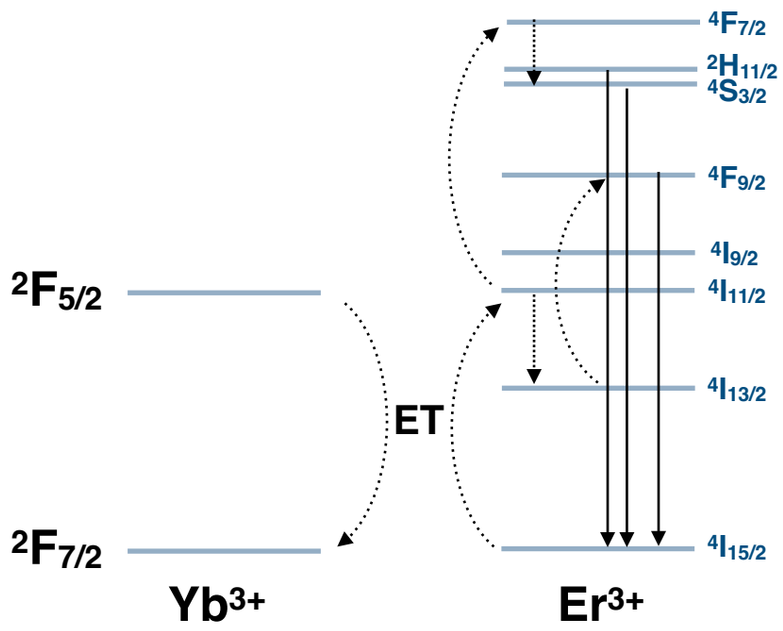

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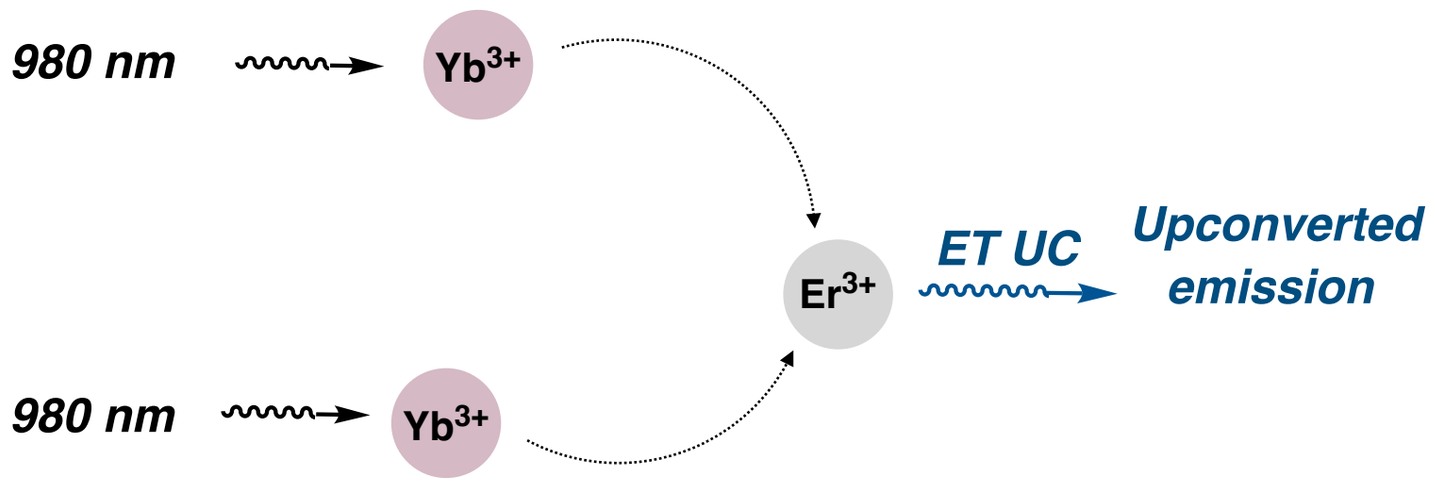

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Photon Upconversion in Inorganic Materials

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- *Inorganic UCs*

**5th mechanism: Cooperative upconversion will <u>not</u> be discussed*

Photon Upconversion in Inorganic Materials

***Inorganic systems: 5 possible mechanisms** may occur**

(1) Energy Transfer

- *Inorganic UCs*

(2) Photon Avalanche

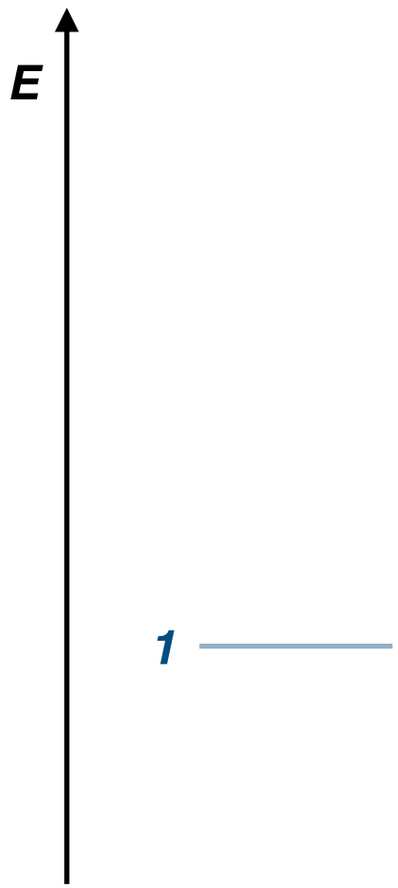
(2) Cross-relaxation Upconversion

(3) Excited-State Absorption

**5th mechanism: Cooperative upconversion will <u>not</u> be discussed*

Inorganic Upconversion: Photon Avalanche

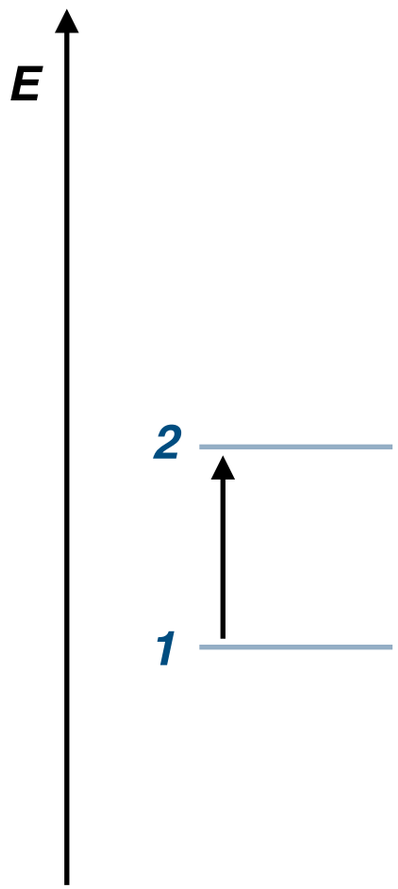
Mechanism of Photon Avalanche



- *Less common mechanism of upconversion*
- *Occurs inside laser cavities*

Inorganic Upconversion: Photon Avalanche

Mechanism of Photon Avalanche



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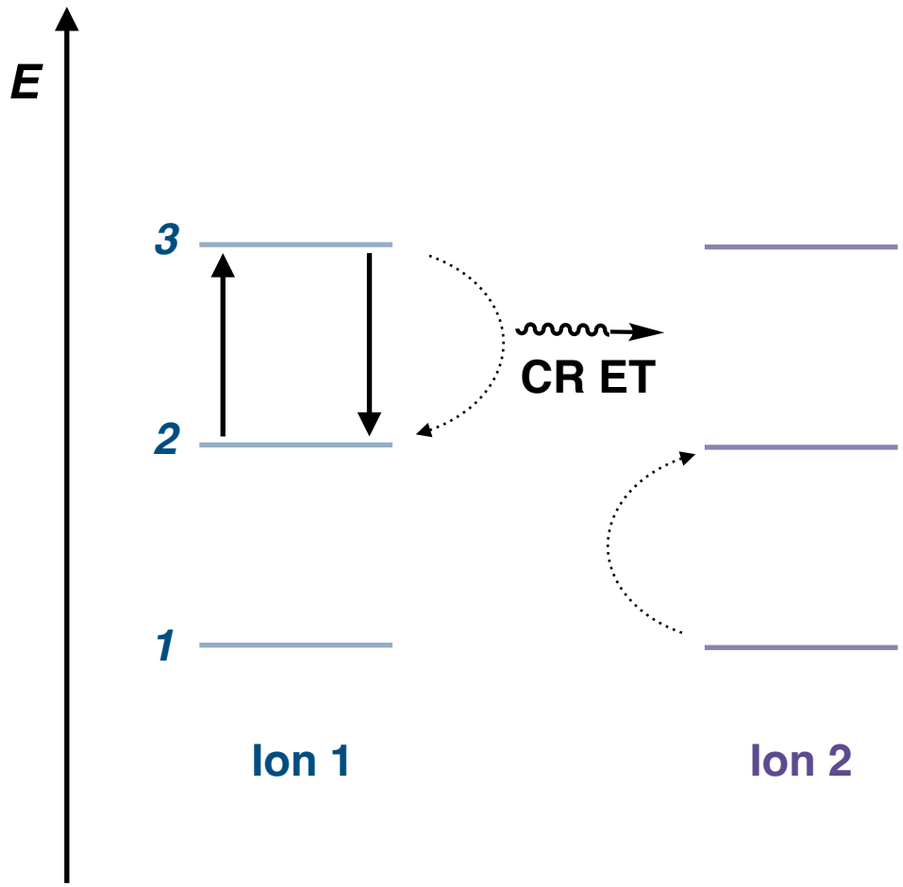
Inorganic Upconversion: Photon Avalanche

Mechanism of Photon Avalanche

Inorganic Upconversion: Photon Avalanche

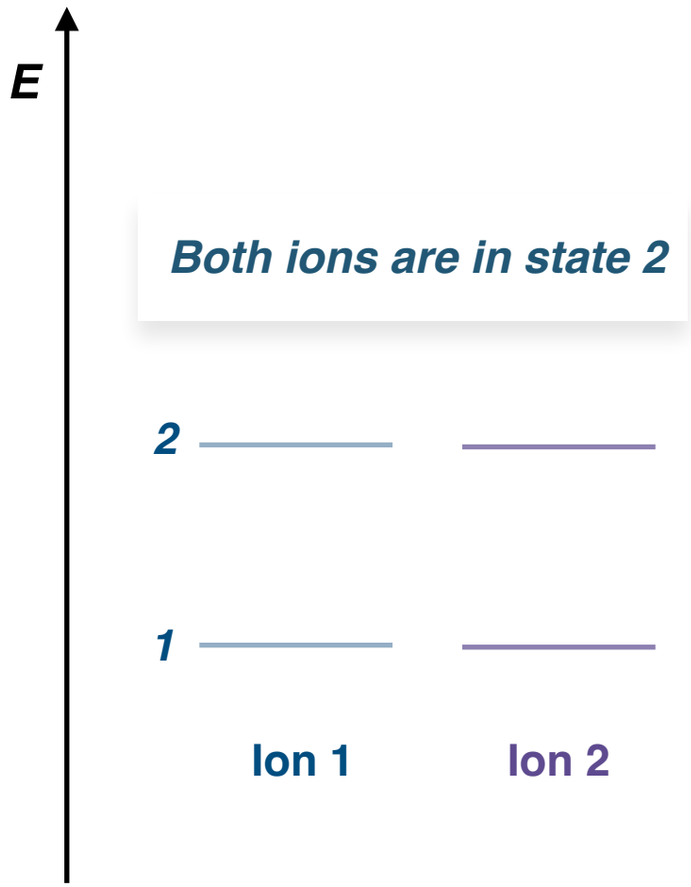
Mechanism of Photon Avalanche



Cross-Relaxation energy transfer (CR ET)

Inorganic Upconversion: Photon Avalanche

Mechanism of Photon Avalanche



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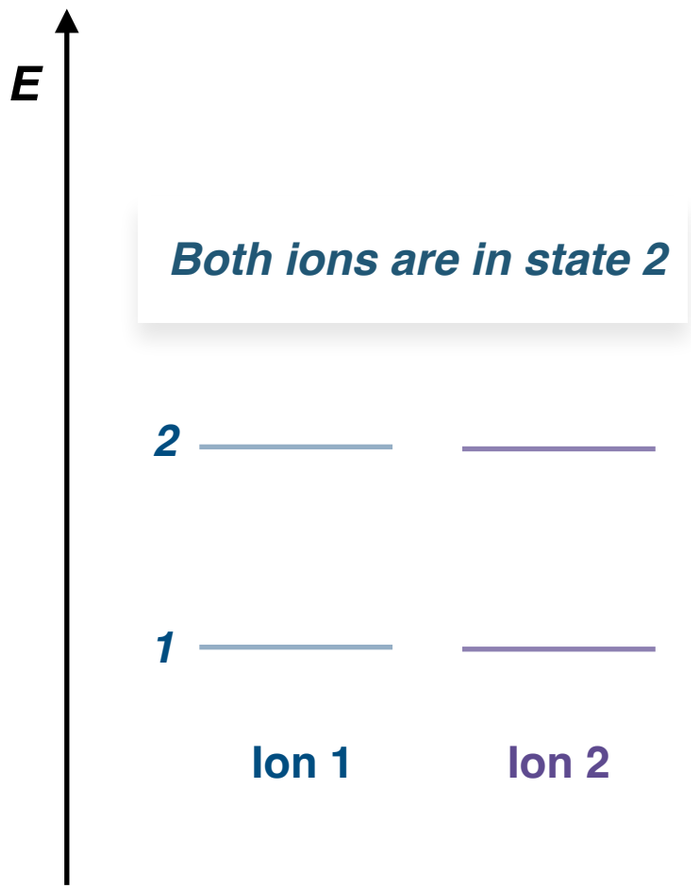
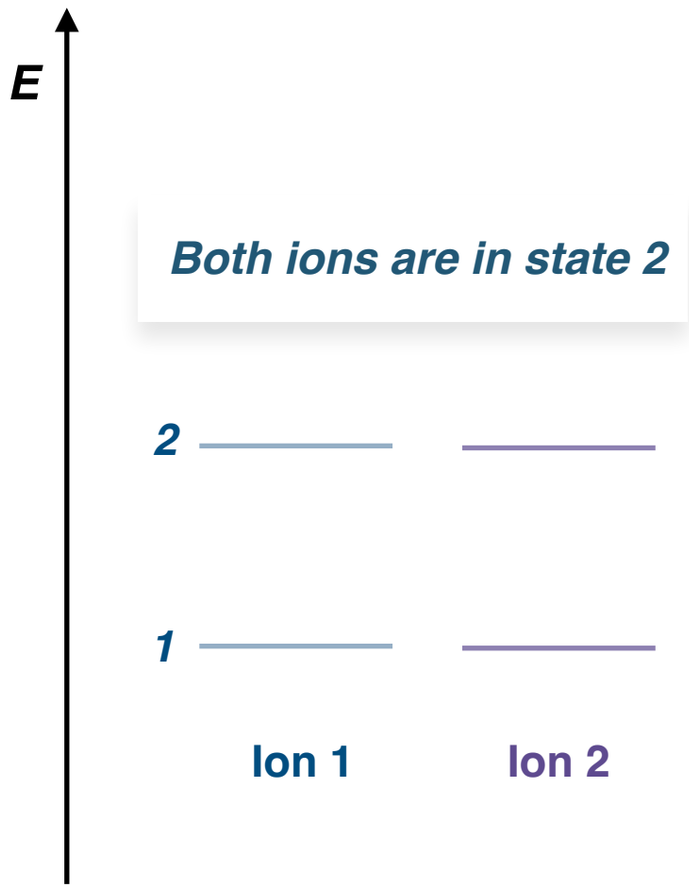


Photon Avalanche Upconversion = ***Excited State Absorption (ESA)*** *then* ***Cross Relaxation ET***

Inorganic Upconversion: Photon Avalanche

Mechanism of Photon Avalanche



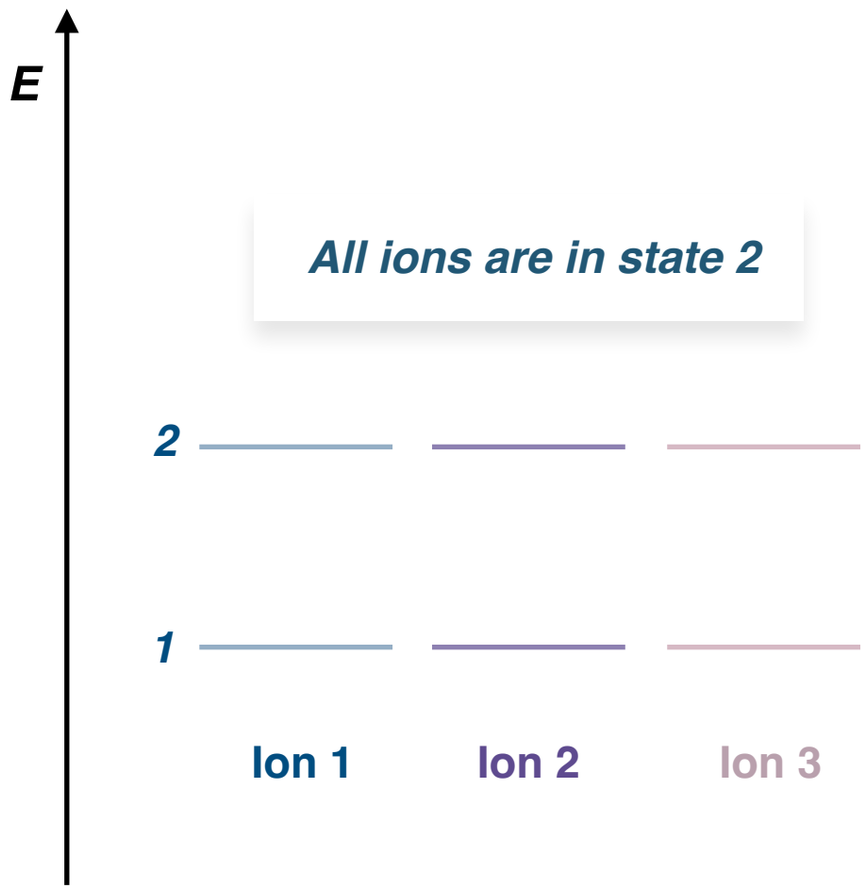
Both ions are in state 2

Process propagates throughout the material

Photon Avalanche Upconversion = ***Excited State Absorption (ESA)*** *then* ***Cross Relaxation ET***

Inorganic Upconversion: Photon Avalanche

Mechanism of Photon Avalanche



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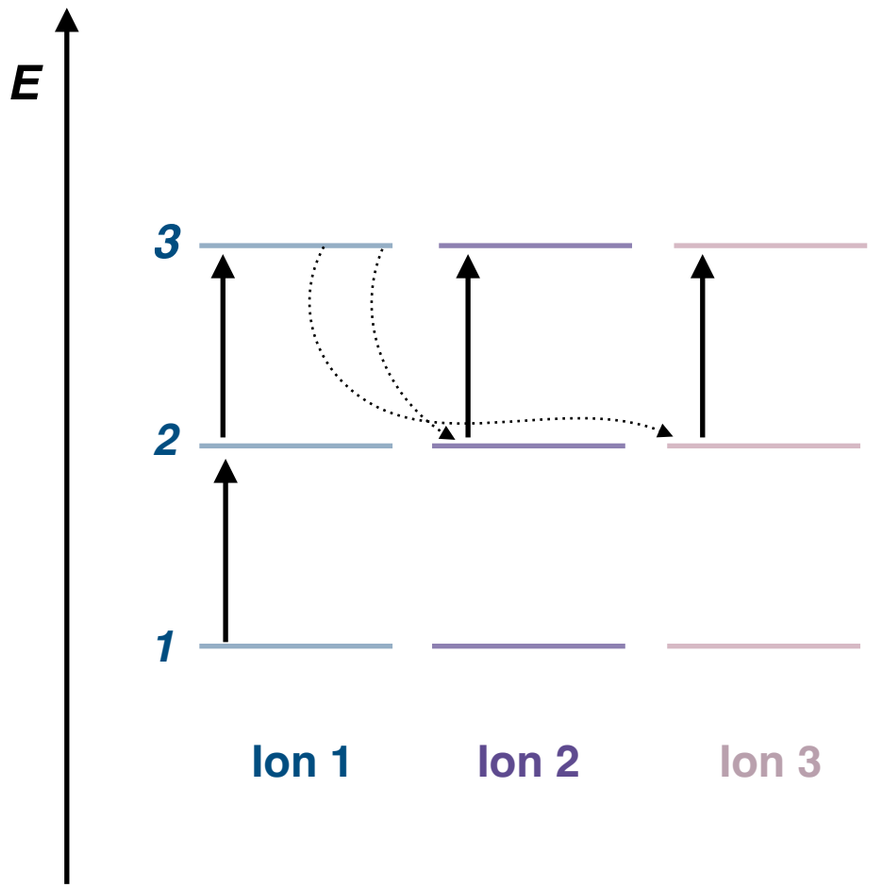
Inorganic Upconversion: Photon Avalanche

Mechanism of Photon Avalanche



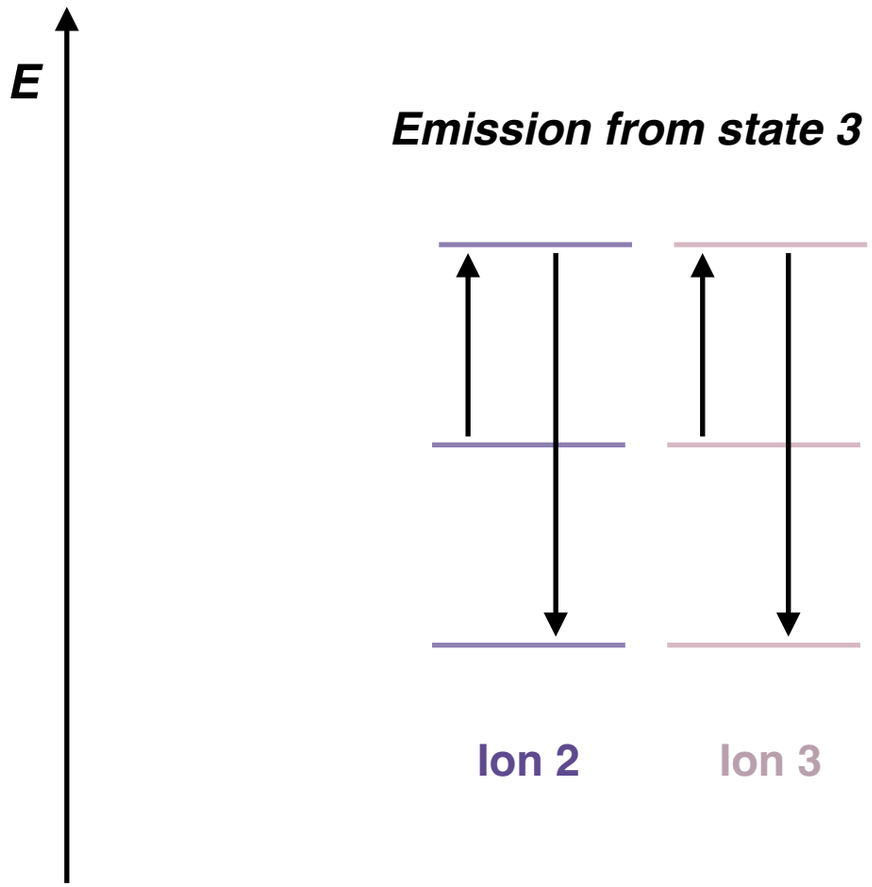
ESA occurs from state 2 to state 3

to induce upconversion

Photon Avalanche Upconversion = ***Excited State Absorption (ESA)*** *then* ***Cross Relaxation ET***

Inorganic Upconversion: Photon Avalanche

Mechanism of Photon Avalanche



ESA occurs from state 2 to state 3

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Photon Avalanche Upconversion = ***Excited State Absorption (ESA)*** *then* ***Cross Relaxation ET***

Upconversion in Inorganic Systems

How is inorganic materials upconversion used towards biological applications?

Upconversion in Inorganic Systems

Applications in a biological context

Immunolabeling and fluorescent imaging

Jethva, P., Momin, M., Khan, T., Omri, A. *Materials.* **2022**. *15*, 2374.

Wang, M., Mi, C., Zhang, Y., Liu, J., Li, F., Mao, C., Xu, S. *J. Phys. Chem.* **2009**. *113*, 19021–19027.

Upconversion in Inorganic Systems

Applications in a biological context

Immunolabeling and fluorescent imaging

Workflow:

1. Amino-functionalization of nanoparticles

Promotes ($NaY_{0.77}Yb_{0.20}Er_{0.03}F_4$) biocompatibility

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Rabbit anti-CEA8

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Upconversion in Inorganic Systems

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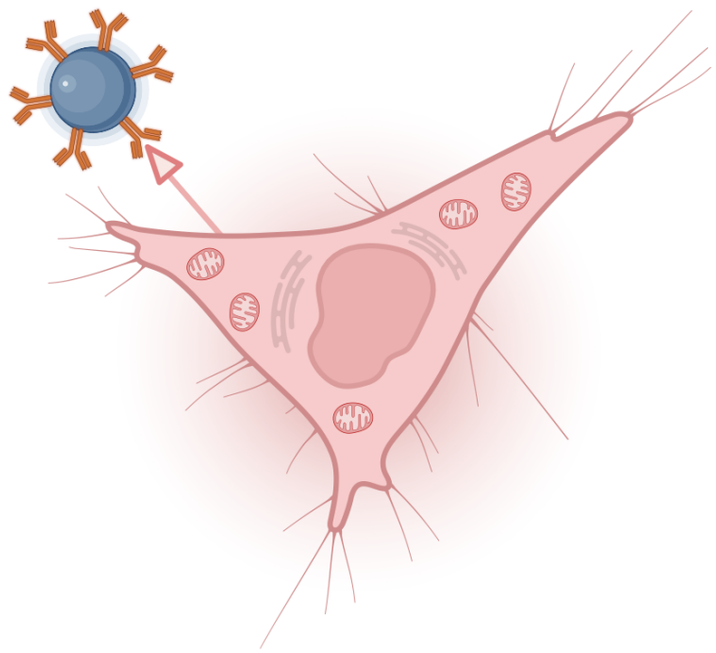
3. Nanoparticle incubation with live HeLa cells



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Upconversion in Inorganic Systems

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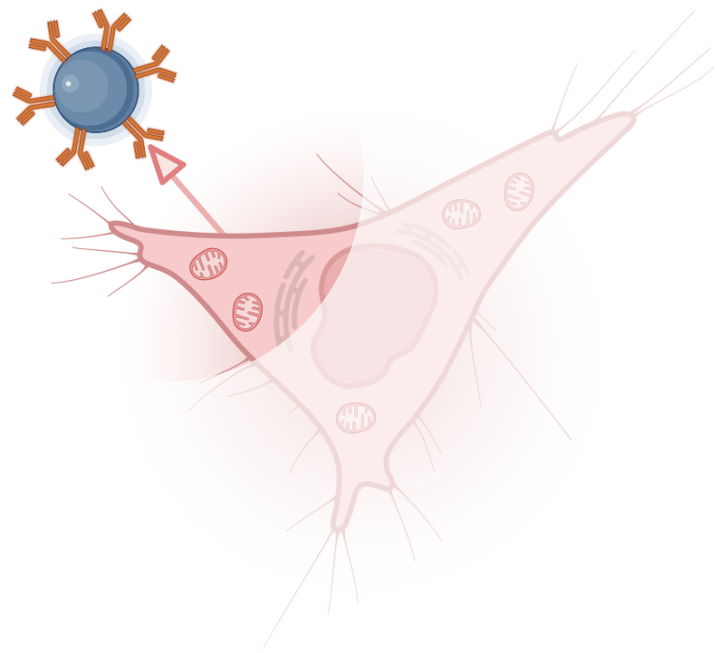

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Upconversion in Inorganic Systems

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Immunolabeling and fluorescent imaging

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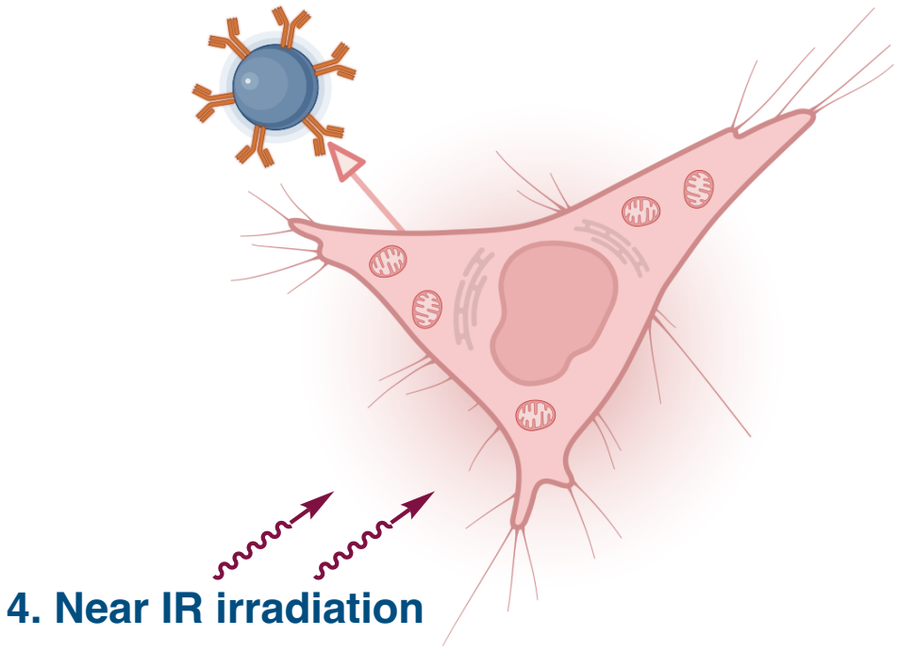

4. Near IR irradiation

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Upconversion in Inorganic Systems

Applications in a biological context

Immunolabeling and fluorescent imaging

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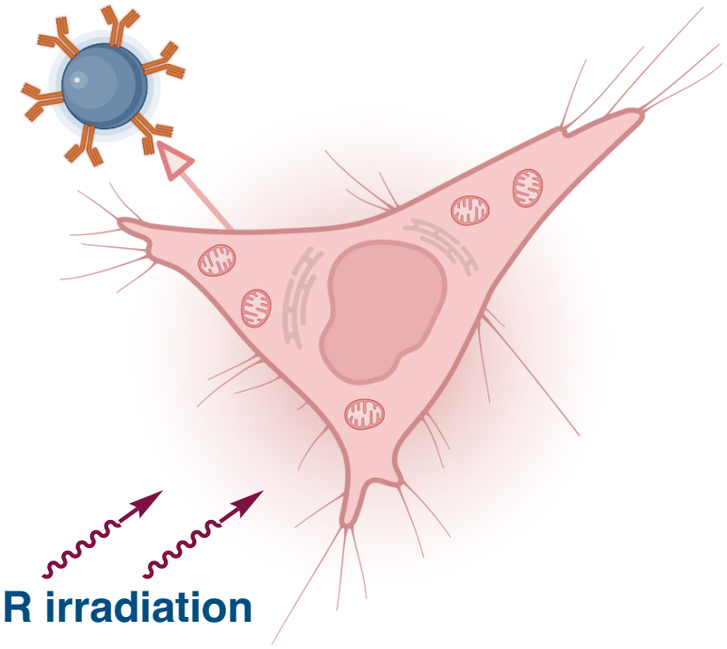
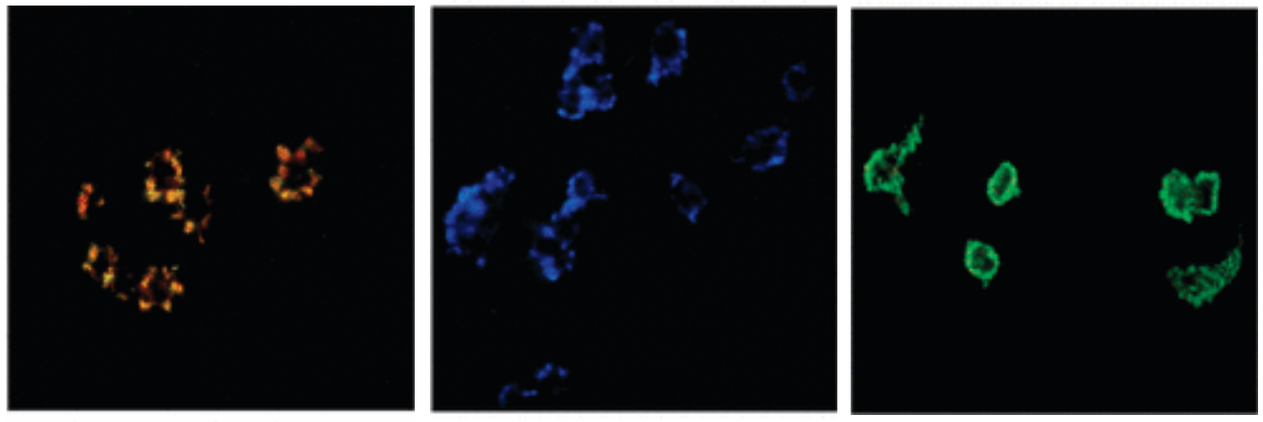


4. Near IR irradiation

5. Inverted fluorescence microscopy



Confirmation of cell membrane NP labelling

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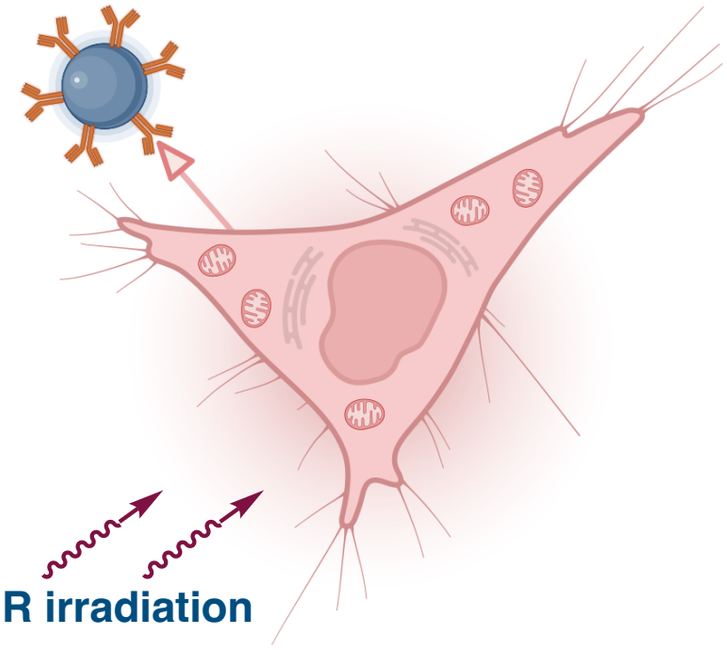

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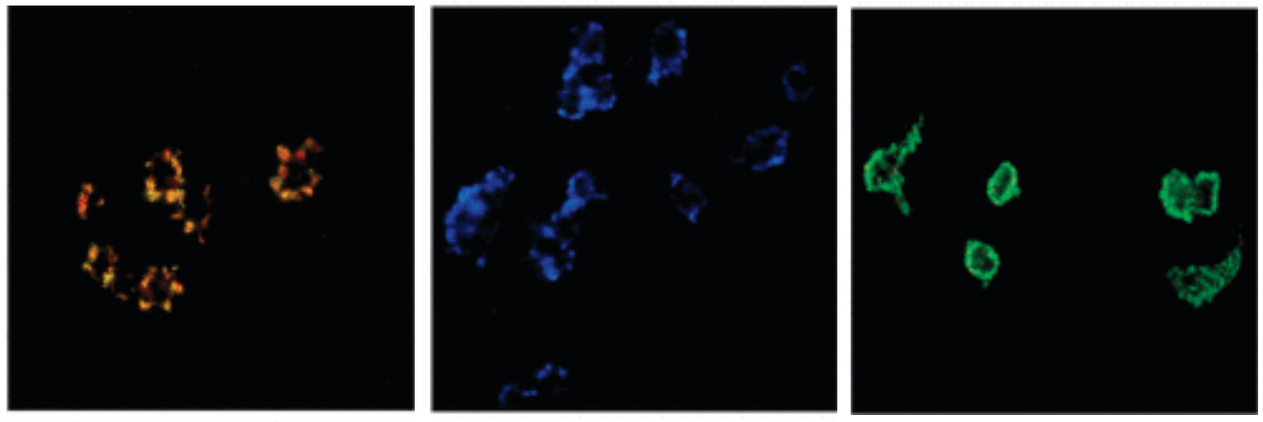

Tune the emission wavelength from same NP

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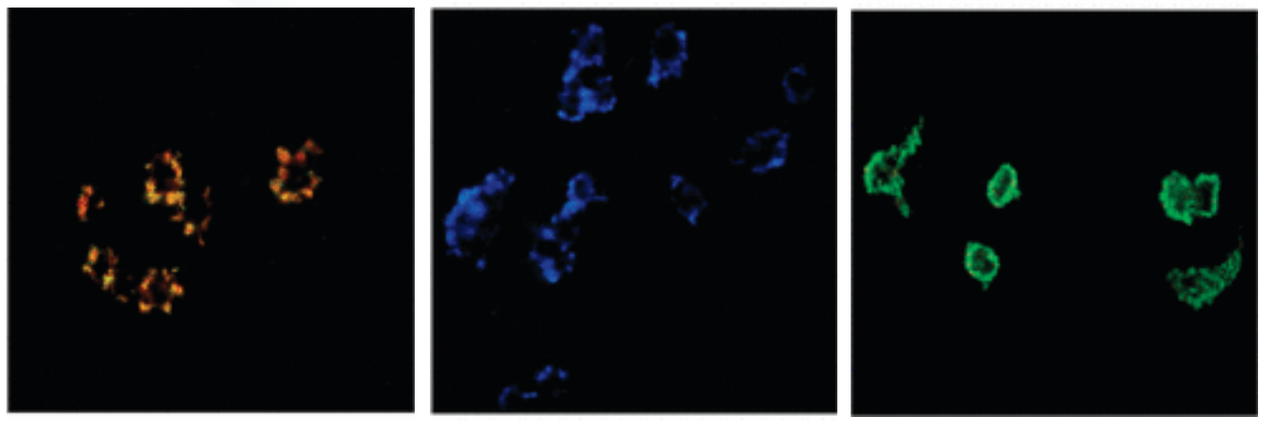
Upconversion in Inorganic Systems

Applications in a biological context

Immunolabeling and fluorescent imaging

- ***Biocompatible interface***
- ***High cell surface targets specificity recognition***
- ***NP UC performs fluorescence for cell imaging***

Inverted fluorescence microscopy



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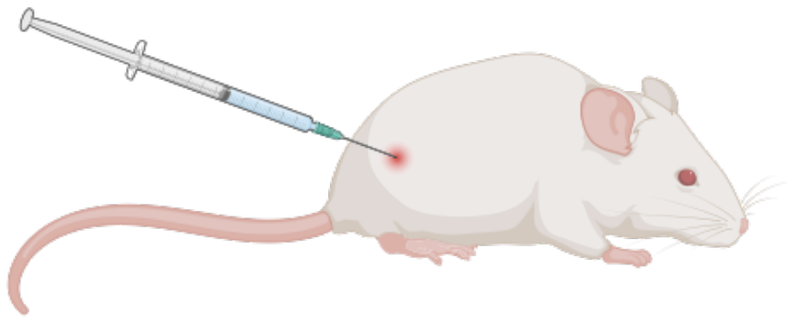
Upconversion in Inorganic Systems

Applications in a biological context

High-Contrast Visualization



Injection with hydrophilic NaLuF4Yb UC nanoparticles

Zheng, X., Zhu, X., Lu, Y., Zhao, J., Feng, W., Jia, G., Wang, F., Li, F., Jin, D. *Anal. Chem.* **2016**. *88*, 3449–3454.

Upconversion in Inorganic Systems

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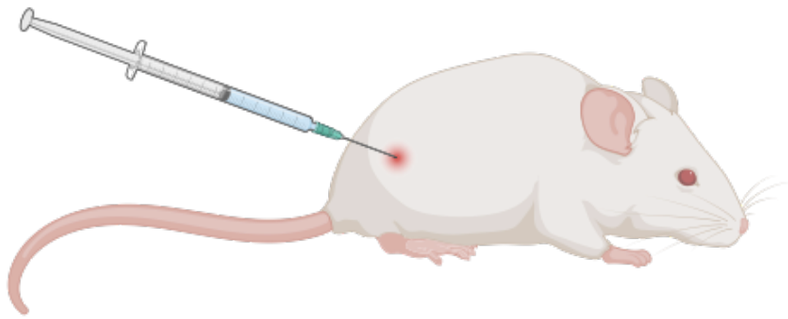

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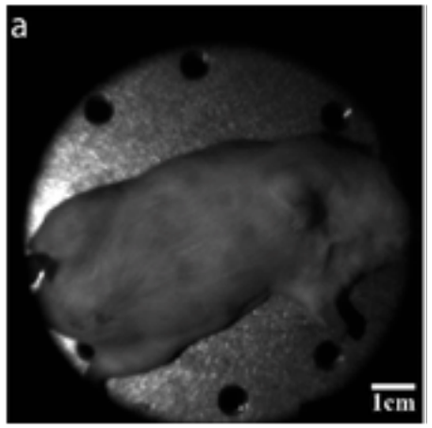

Bright field light

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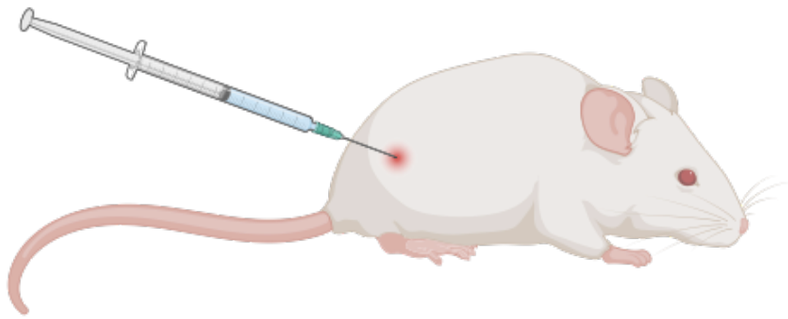

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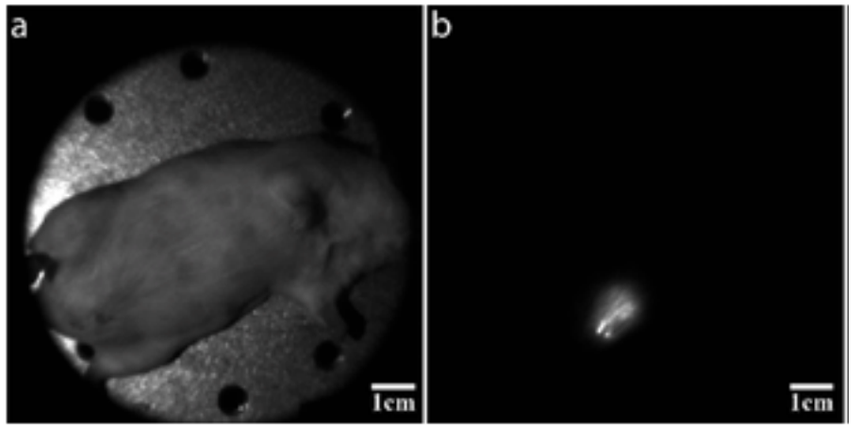

Bright field light

Time-gated luminescence ***(980 nm NIR)***

Zheng, X., Zhu, X., Lu, Y., Zhao, J., Feng, W., Jia, G., Wang, F., Li, F., Jin, D. *Anal. Chem.* **2016**. *88*, 3449–3454.

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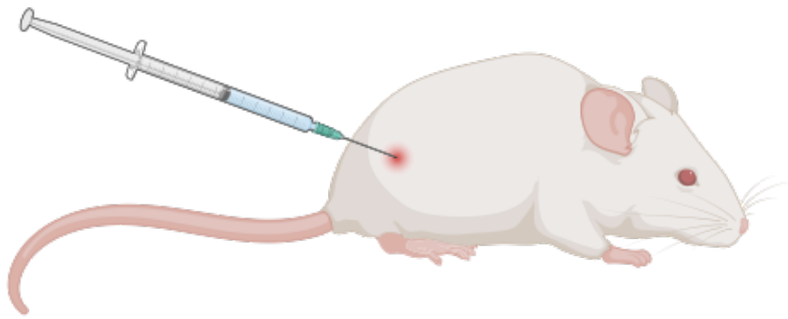

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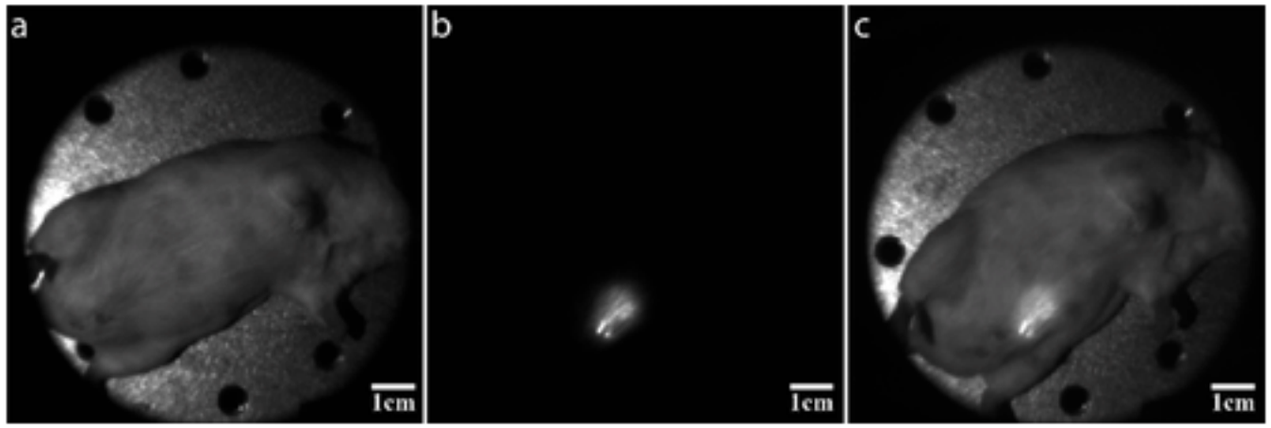

Bright field light

Time-gated luminescence ***(980 nm NIR)***

Bright field light + Time-gated luminescence ***(980 nm NIR)***

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Upconversion in Inorganic Systems

Applications in a biological context

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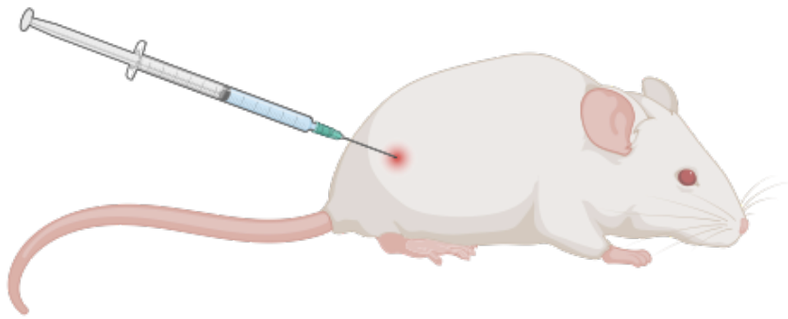
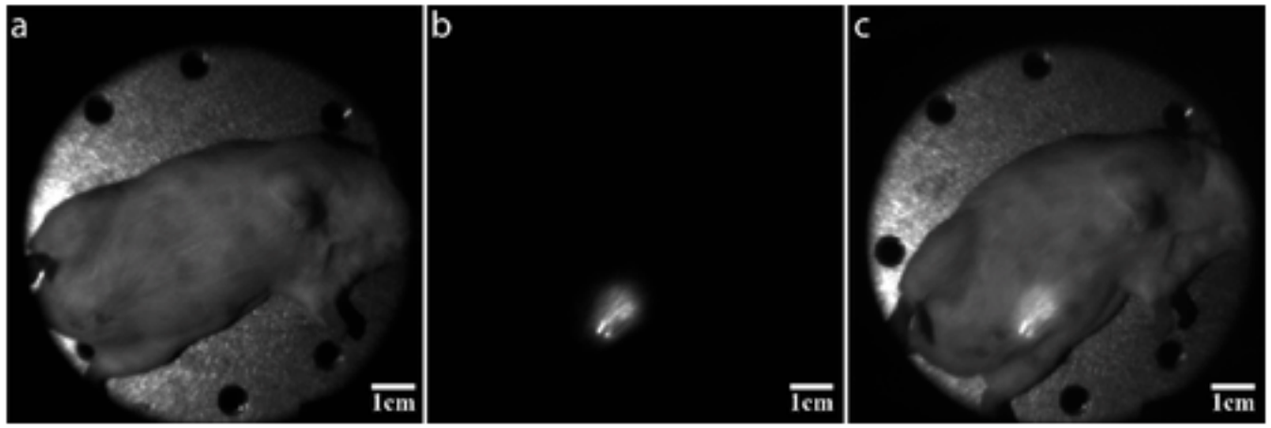


Injection with hydrophilic NaLuF4Yb UC nanoparticles

- ***Lower autofluorescence background signals***

  Enhances signal-to-noise ratio



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Applications in a biological context

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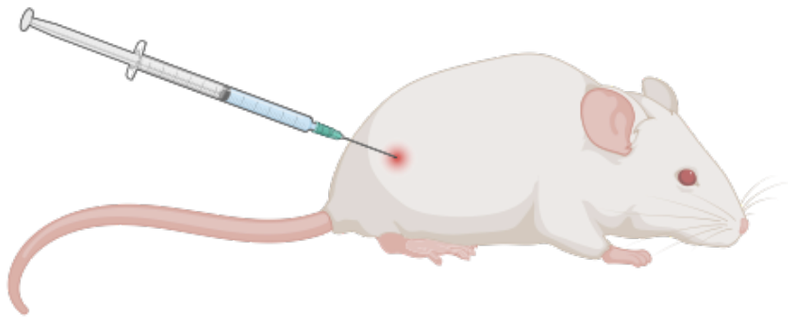
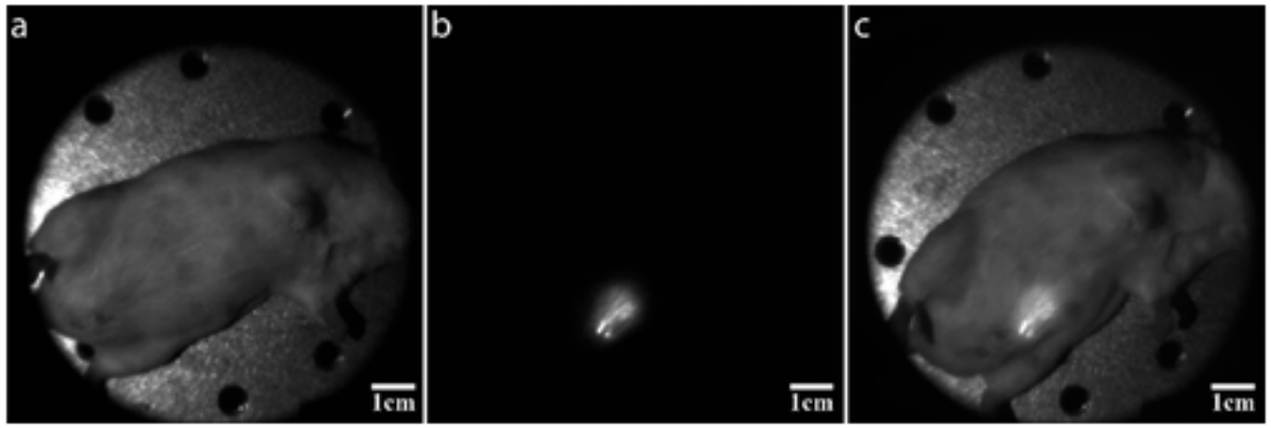


Injection with hydrophilic NaLuF4Yb UC nanoparticles

- ***Lower autofluorescence background signals***

Enhances signal-to-noise ratio

- ***Enables sensitive fluorescence detection***



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Upconversion in Inorganic Systems

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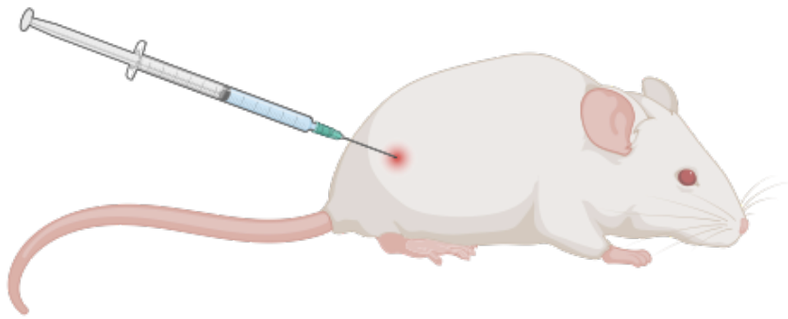
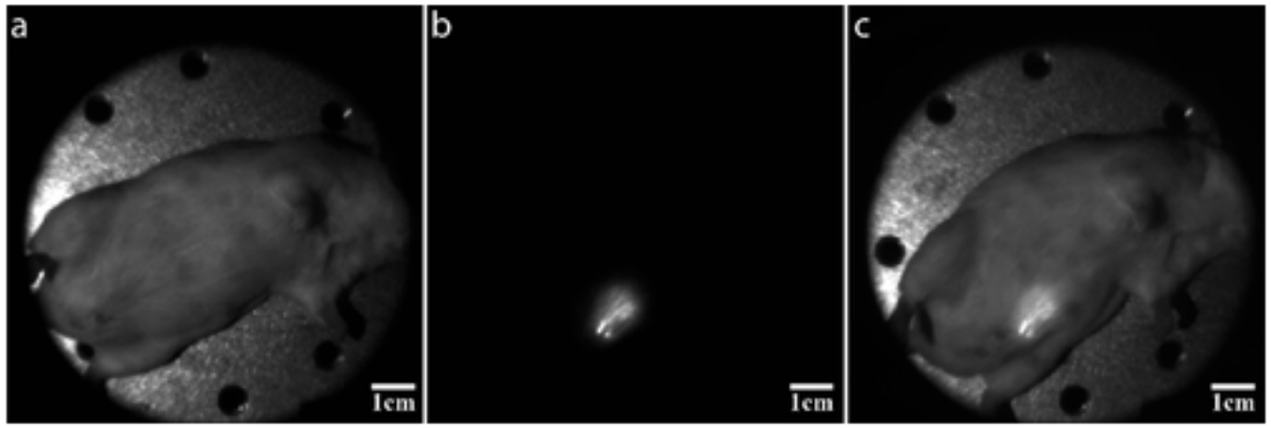


Injection with hydrophilic NaLuF4Yb UC nanoparticles

Deeper tissue penetration opens avenues to more complex settings



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Pharmaceuticals in Medicinal Chemistry

Top 200 Small Molecule Pharmaceuticals by Retail Sales in 2022

1 **Paxlovid** (Ritonavir/Nirmatrelvir) $18.933 Billion Infectious Diseases	2 **Eliquis** (Apixaban) $11.789 Billion Cardiology/Vascular Diseases	3 **Biktarvy** (Bictegravir/Emtricitabine/Tenofovir Alafenamide) $10.390 Billion Infectious Diseases	4 **Revlimid** (Lenalidomide) $10.061 Billion Oncology	5 **Jardiance** (Empagliflozin) $8.388 Billion Diabetes	6 **Imbruvica** (Ibrutinib) $8.352 Billion Oncology	7 **Tivicay** (Dolutegravir) $8.103 Billion Infectious Diseases	8 **Trikafta** (Elexacaftor/Tezacaftor/Ivacaftor) $7.487 Billion Genetic Diseases	9 **Xarelto** (Rivaroxaban) $7.215 Billion Cardiology/Vascular Diseases	10 **Xtandi** (Enzalutamide) $6.236 Billion Oncology	11 **Lagevrio** (Molnupiravir) $5.684 Billion Infectious Diseases	12 **Tagrisso** (Osimertinib) $5.444 Billion Oncology	13 **Ibrance** (Palbociclib) $5.120 Billion Oncology	14 **Farxiga** (Dapagliflozin) $4.781 Billion Diabetes	15 **Entresto** (Sacubitril/Valsartan) $4.644 Billion Cardiology/Vascular Diseases	16 **Invega Sustenna** (Paliperidone Palmitate) $4.140 Billion Neurology	17 **Veklury** (Remdesivir) $3.905 Billion Infectious Diseases	18 **Lynparza** (Olaparib) $3.754 Billion Oncology	19 **Ofev** (Nintedanib) $3.498 Billion Respiratory Diseases	20 **Pomalyst** (Pomalidomide) $3.497 Billion Oncology
21 **Vyvanse** (Lisdexamfetamine) $3.219 Billion Neurology	22 **Rexulti** (Brexpiprazole) $3.121 Billion Neurology	23 **Januvia** (Sitagliptin) $2.813 Billion Diabetes	24 **Lenvima** (Lenvatinib) $2.742 Billion Oncology	25 **Symbicort** (Budesonide and Formoterol) $2.538 Billion Respiratory Diseases	26 **Rinvoq** (Upadacitinib) $2.522 Billion Immunology	27 **Verzenio** (Abemaciclib) $2.483 Billion Oncology	28 **Vyndaqel** (Tafamidis) $2.447 Billion Rare Diseases	29 **Genvoya** (Bictegravir/Cobicistat/Emtricitabine/Tenofovir Alafenamide) $2.404 Billion Infectious Diseases	30 **Otezla** (Apremilast) $2.288 Billion Dermatology	31 **Aubagio** (Teriflunamide) $2.227 Billion Neurology	32 **Triumeq** (Abacavir/Dolutegravir/Lamivudine) $2.217 Billion Infectious Diseases	33 **Sprycel** (Dasatinib) $2.165 Billion Oncology	34 **Trelegy Ellipta** (Fluticasone Furoate/Umeclidinium/Vilanterol Trifenatate) $2.131 Billion Respiratory Diseases	35 **Promacta** (Eltrombopag) $2.068 Billion Hematology	36 **Calquence** (Acalabrutinib) $2.057 Billion Oncology	37 **Vraylar** (Cariprazine) $2.038 Billion Neurology	38 **Spinraza** (Nusinersen) $2.036 Billion Genetic Disease	39 **Gilenya** (Fingolimod) $2.013 Billion Neurology	40 **Venclexta** (Venetoclax) $2.009 Billion Oncology
41 **Abilify Maintena** (Aripiprazole) $1.953 Billion Neurology	42 **Prezista and Prezcobix** (Darunavir/Cobicistat) $1.943 Billion Infectious Diseases	43 **Tasigna** (Nilotinib) $1.929 Billion Hematology	44 **Erleada** (Apalutamide) $1.881 Billion Oncology	45 **Relvar** (Fluticasone Furoate) $1.877 Billion Respiratory Diseases	46 **Descovy** (Emtricitabine/Tenofovir Alafenamide) $1.872 Billion Infectious Diseases	47 **Trajenta** (Linagliptin and Metformin) $1.844 Billion Diabetes	48 **Latuda** (Lurasidone) $1.810 Billion Neurology	49 **Xeljanz** (Tofacitinib) $1.794 Billion Immunology	50 **Opsumit** (Macitentan) $1.783 Billion Cardiology/Vascular Diseases	51 **Zytiga** (Abiraterone Acetate) $1.770 Billion Oncology	52 **Tafinlar** (Dabrafenib/Trametinib) $1.720 Billion Oncology	53 **Jynarque** (Tolvaptan) $1.718 Billion Cardiology/Vascular Diseases	54 **Janumet** (Sitagliptin/Metformin) $1.700 Billion Diabetes	55 **Dovato** (Dolutegravir/Lamivudine) $1.695 Billion Infectious Diseases	56 **Spiriva** (Tiotropium Bromide) $1.691 Billion Respiratory Diseases	57 **Bridion** (Sugammadex) $1.685 Billion Neurology	58 **Alecensa** (Alectinib) $1.653 Billion Oncology	59 **Lipitor** (Atorvastatin) $1.635 Billion Cardiology/Vascular Diseases	60 **Lixiana** (Edoxaban) $1.630 Billion Hematology
61 **Epclusa** (Sofosbuvir/Velpatasvir) $1.570 Billion Infectious Diseases	62 **Jakavi** (Ruxolitinib) $1.561 Billion Hematology	63 **Mavyret** (Glecaprevir/Pibrentasvir) $1.541 Billion Infectious Diseases	64 **Prograf** (Tacrolimus) $1.514 Billion Immunology	65 **Odefsey** (Emtricitabine/Rilpivirine/Tenofovir Alafenamide) $1.469 Billion Infectious Diseases	66 **Tecfidera** (Dimethyl Fumarate) $1.443 Billion Neurology	67 **Betanis** (Mirabegron) $1.437 Billion Nephrology	68 **Lovenox** (Enoxaparin) $1.436 Billion Hematology	69 **Seretide** (Salmeterol/Fluticasone) $1.428 Billion Respiratory Diseases	70 **Juvederm** (Hyaluronic Acid) $1.428 Billion Dermatology	71 **Ingrezza** (Valbenazine) $1.427 Billion Neurology	72 **Trintellix** (Vortioxetine) $1.399 Billion Neurology	73 **Vimpat** (Lacosamide) $1.359 Billion Neurology	74 **Brilinta** (Ticagrelor) $1.358 Billion Cardiology/Vascular Diseases	75 **Mirena** (Levonorgestrel) $1.340 Billion Women's Health	76 **Kyprolis** (Carfilzomib) $1.328 Billion Oncology	77 **Uptravi** (Selexipag) $1.322 Billion Cardiology/Vascular Diseases	78 **Somatuline** (Lanreotide) $1.306 Billion Oncology	79 **Nexium** (Esomeprazole) $1.285 Billion Gastrointestinal Diseases	80 **Sandostatin** (Octreotide) $1.238 Billion Oncology
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181 **Zetia** (Ezetimibe) $357 Million Cardiology/Vascular Diseases	182 **Mayzent** (Siponimod) $357 Million Neurology	183 **Radicava** (Edaravone) $349 Million Neurology	184 **Sutent** (Sunitinib Malate) $347 Million Oncology	185 **Alphagan** (Brimonidine Tartrate/Timolol Maleate) $346 Million Ophthalmology	186 **Lorbrena** (Lorlatinib) $343 Million Oncology	187 **Adempas** (Riociguat/Vericiguat) $341 Million Cardiology/Vascular Diseases	188 **Cipralex** (Escitalopram) $339 Million Neurology	189 **Inomax** (Nitric Oxide) $339 Million Respiratory Diseases	190 **Pantoloc** (Pantoprazole) $339 Million Gastrointestinal Diseases	191 **Celebrex** (Celecoxib) $338 Million Musculoskeletal	192 **Zyprexa** (Olanzapine) $336 Million Neurology	193 **Voltaren** (Diclofenac) $334 Million Neurology	194 **Faslodex** (Fulvestrant) $334 Million Oncology	195 **Zithromax** (Azithromycin) $331 Million Infectious Diseases	196 **Cymbalta** (Duloxetine) $331 Million Neurology	197 **Medrol** (Methylprednisolone) $308 Million Immunology	198 **Neupro** (Rotigotine) $305 Million Neurology	199 **Orenitram** (Treprostinil Diolamine) $305 Million Cardiology/Vascular Diseases	200 **Exjade** (Deferasirox) $323 Million Hematology

McGrath, N. A.; Brichacek, M.; Njardarson, J. T., *J. Chem. Educ.* **2010**, *87*, 1348.

Pharmaceuticals in Medicinal Chemistry

Top 200 Small Molecule Pharmaceuticals by Retail Sales in 2022

1 **Paxlovid** (Ritonavir/Nirmatrelvir) $18.933 Billion Infectious Diseases	2 **Eliquis** (Apixaban) $11.789 Billion Cardiology/Vascular Diseases	3 **Biktarvy** (Bictegravir/Emtricitabine/Tenofovir Alafenamide) $10.390 Billion Infectious Diseases	4 **Revlimid** (Lenalidomide) $10.061 Billion Oncology	5 **Jardiance** (Empagliflozin) $8.388 Billion Diabetes	6 **Imbruvica** (Ibrutinib) $8.352 Billion Oncology	7 **Tivicay** (Dolutegravir) $8.103 Billion Infectious Diseases	8 **Trikafta** (Elexacaftor/Tezacaftor/Ivacaftor) $7.487 Billion Genetic Diseases	9 **Xarelto** (Rivaroxaban) $7.215 Billion Cardiology/Vascular Diseases	10 **Xtandi** (Enzalutamide) $6.236 Billion Oncology	11 **Lagevrio** (Molnupiravir) $5.684 Billion Infectious Diseases	12 **Tagrisso** (Osimertinib) $5.444 Billion Oncology	13 **Ibrance** (Palbociclib) $5.120 Billion Oncology	14 **Farxiga** (Dapagliflozin) $4.781 Billion Diabetes	15 **Entresto** (Sacubitril/Valsartan) $4.644 Billion Cardiology/Vascular Diseases	16 **Invega Sustenna** (Paliperidone Palmitate) $4.140 Billion Neurology	17 **Veklury** (Remdesivir) $3.905 Billion Infectious Diseases	18 **Lynparza** (Olaparib) $3.754 Billion Oncology	19 **Ofev** (Nintedanib) $3.498 Billion Respiratory Diseases	20 **Pomalyst** (Pomalidomide) $3.497 Billion Oncology
21 **Vyvanse** (Lisdexamfetamine) $3.219 Billion Neurology	22 **Rexulti** (Brexpiprazole) $3.121 Billion Neurology	23 **Januvia** (Sitagliptin) $2.813 Billion Diabetes	24 **Lenvima** (Lenvatinib) $2.742 Billion Oncology	25 **Symbicort** (Budesonide and Formoterol) $2.538 Billion Respiratory Diseases	26 **Rinvoq** (Upadacitinib) $2.522 Billion Immunology	27 **Verzenio** (Abemaciclib) $2.483 Billion Oncology	28 **Vyndaqel** (Tafamidis) $2.447 Billion Rare Diseases	29 **Genvoya** (Bictegravir/Cobicistat/Emtricitabine/Tenofovir Alafenamide) $2.404 Billion Infectious Diseases	30 **Otezla** (Apremilast) $2.288 Billion Dermatology	31 **Aubagio** (Teriflunamide) $2.227 Billion Neurology	32 **Triumeq** (Abacavir/Dolutegravir/Lamivudine) $2.217 Billion Infectious Diseases	33 **Sprycel** (Dasatinib) $2.165 Billion Oncology	34 **Trelegy Ellipta** (Fluticasone Furoate/Umeclidinium/Vilanterol Trifenatate) $2.131 Billion Respiratory Diseases	35 **Promacta** (Eltrombopag) $2.068 Billion Hematology	36 **Calquence** (Acalabrutinib) $2.057 Billion Oncology	37 **Vraylar** (Cariprazine) $2.038 Billion Neurology	38 **Spinraza** (Nusinersen) $2.036 Billion Genetic Disease	39 **Gilenya** (Fingolimod) $2.013 Billion Neurology	40 **Venclexta** (Venetoclax) $2.009 Billion Oncology
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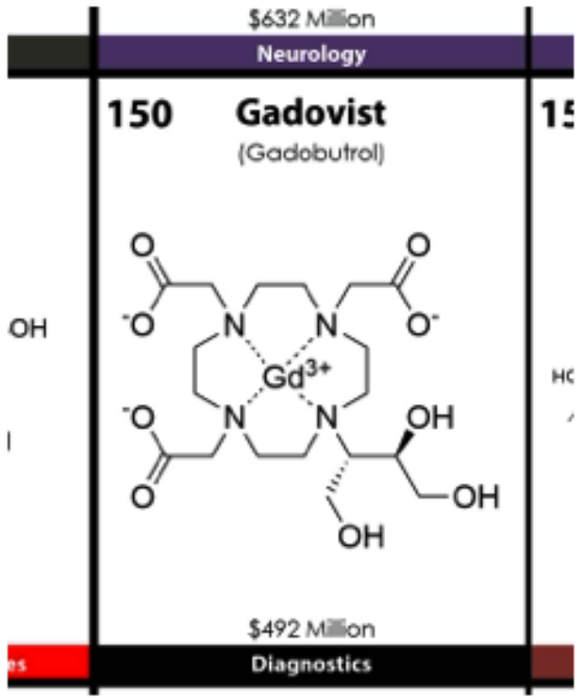
181 **Zetia** (Ezetimibe) $357 Million Cardiology/Vascular Diseases	182 **Mayzent** (Siponimod) $357 Million Neurology	183 **Radicava** (Edaravone) $349 Million Neurology	184 **Sutent** (Sunitinib Malate) $347 Million Oncology	185 **Alphagan** (Brimonidine Tartrate/Timolol Maleate) $346 Million Ophthalmology	186 **Lorbrena** (Lorlatinib) $343 Million Oncology	187 **Adempas** (Riociguat/Vericiguat) $341 Million Cardiology/Vascular Diseases	188 **Cipralex** (Escitalopram) $339 Million Neurology	189 **Inomax** (Nitric Oxide) $339 Million Respiratory Diseases	190 **Pantoloc** (Pantoprazole) $339 Million Gastrointestinal Diseases	191 **Celebrex** (Celecoxib) $338 Million Musculoskeletal	192 **Zyprexa** (Olanzapine) $336 Million Neurology	193 **Voltaren** (Diclofenac) $334 Million Neurology	194 **Faslodex** (Fulvestrant) $334 Million Oncology	195 **Zithromax** (Azithromycin) $331 Million Infectious Diseases	196 **Cymbalta** (Duloxetine) $331 Million Neurology	197 **Medrol** (Methylprednisolone) $308 Million Immunology	198 **Neupro** (Rotigotine) $305 Million Neurology	199 **Orenitram** (Treprostinil Diolamine) $305 Million Cardiology/Vascular Diseases	200 **Exjade** (Deferasirox) $323 Million Hematology

McGrath, N. A.; Brichacek, M.; Njardarson, J. T., *J. Chem. Educ.* **2010**, *87*, 1348.

Incorporation of Inorganic Systems

Applications to bioimaging

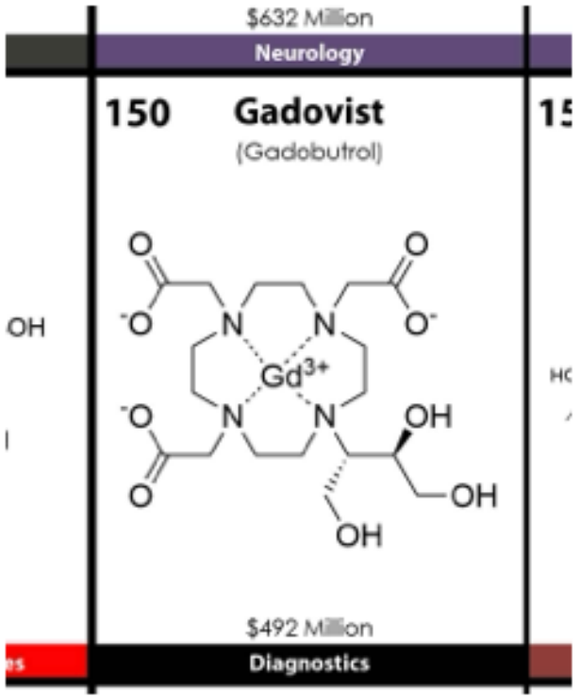


Gadovist®

Gadobutrol, Bayer

Incorporation of Inorganic Systems

Applications to bioimaging



Paramagnetic contrast reagent

Gadovist®

Gadobutrol, Bayer

Upconversion in Inorganic Systems

Applications to bioimaging

Upconversion in MRI

Gd^{3+}

Gadolinium dopant

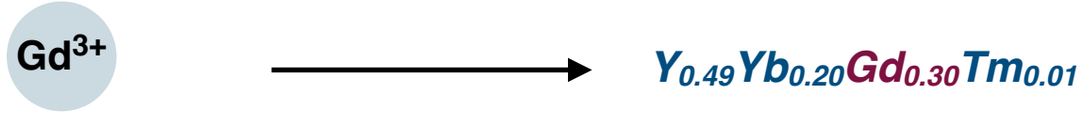
4f orbitals

Wang, X., Chen, J-T., Zhu, H., Chen, X., Yan, X-P. *Anal. Chem.* **2013**. *85*, 10225–10231.

Upconversion in Inorganic Systems

Applications to bioimaging

Upconversion in MRI



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Upconversion nanoparticles

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Upconversion in Inorganic Systems

Applications to bioimaging

Upconversion in MRI

Gd^{3+}

Gadolinium dopant

4f orbitals

→

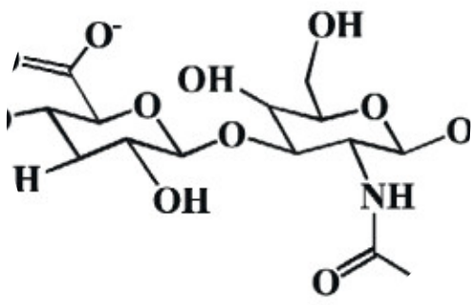
$Y_{0.49}Yb_{0.20}Gd_{0.30}Tm_{0.01}$

Upconversion nanoparticles

→

HA- $Y_{0.49}Yb_{0.20}Gd_{0.30}Tm_{0.01}$

HA-tagged Upconversion nanoparticles



Hyaluronic acid

Wang, X., Chen, J-T., Zhu, H., Chen, X., Yan, X-P.. *Anal. Chem.* **2013**. *85*, 10225–10231.

Upconversion in Inorganic Systems

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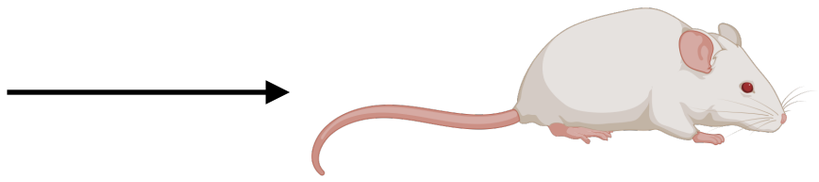
HA-tagged Upconversion nanoparticles



MDA-MB-231 tumor mice

Wang, X., Chen, J-T., Zhu, H., Chen, X., Yan, X-P.. *Anal. Chem.* **2013**. *85*, 10225–10231.

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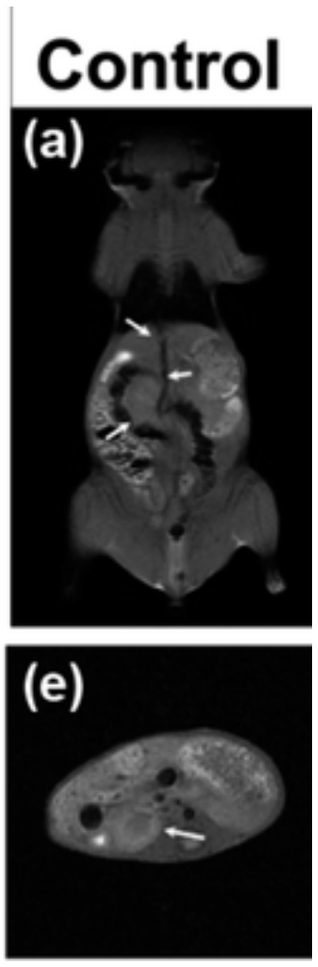

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Upconversion in Inorganic Systems

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HA-tagged Upconversion nanoparticles

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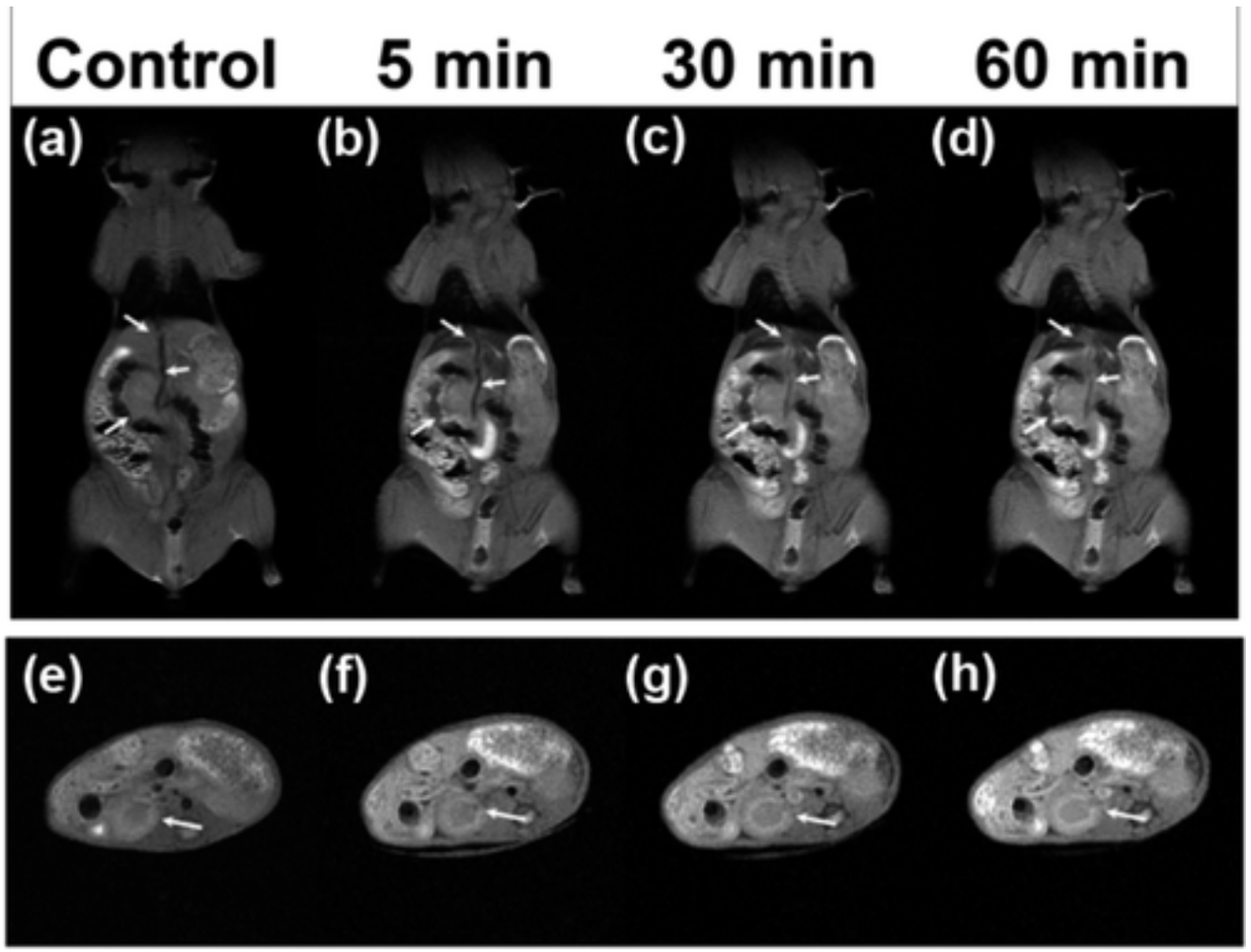
MDA-MB-231 tumor mice



- ***Contrast enhancement towards tumor visualization***

Wang, X., Chen, J-T., Zhu, H., Chen, X., Yan, X-P.. *Anal. Chem.* **2013**. *85*, 10225–10231.

Upconversion in Inorganic Systems

Applications to bioimaging

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HA-tagged Upconversion nanoparticles

Normal nude mice

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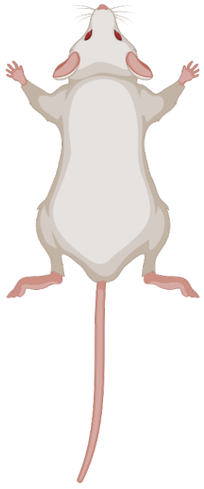
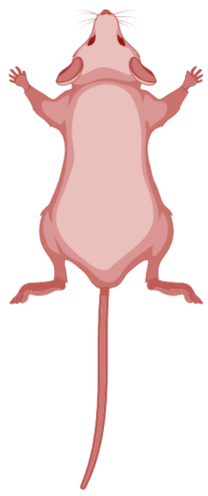


Normal nude mice



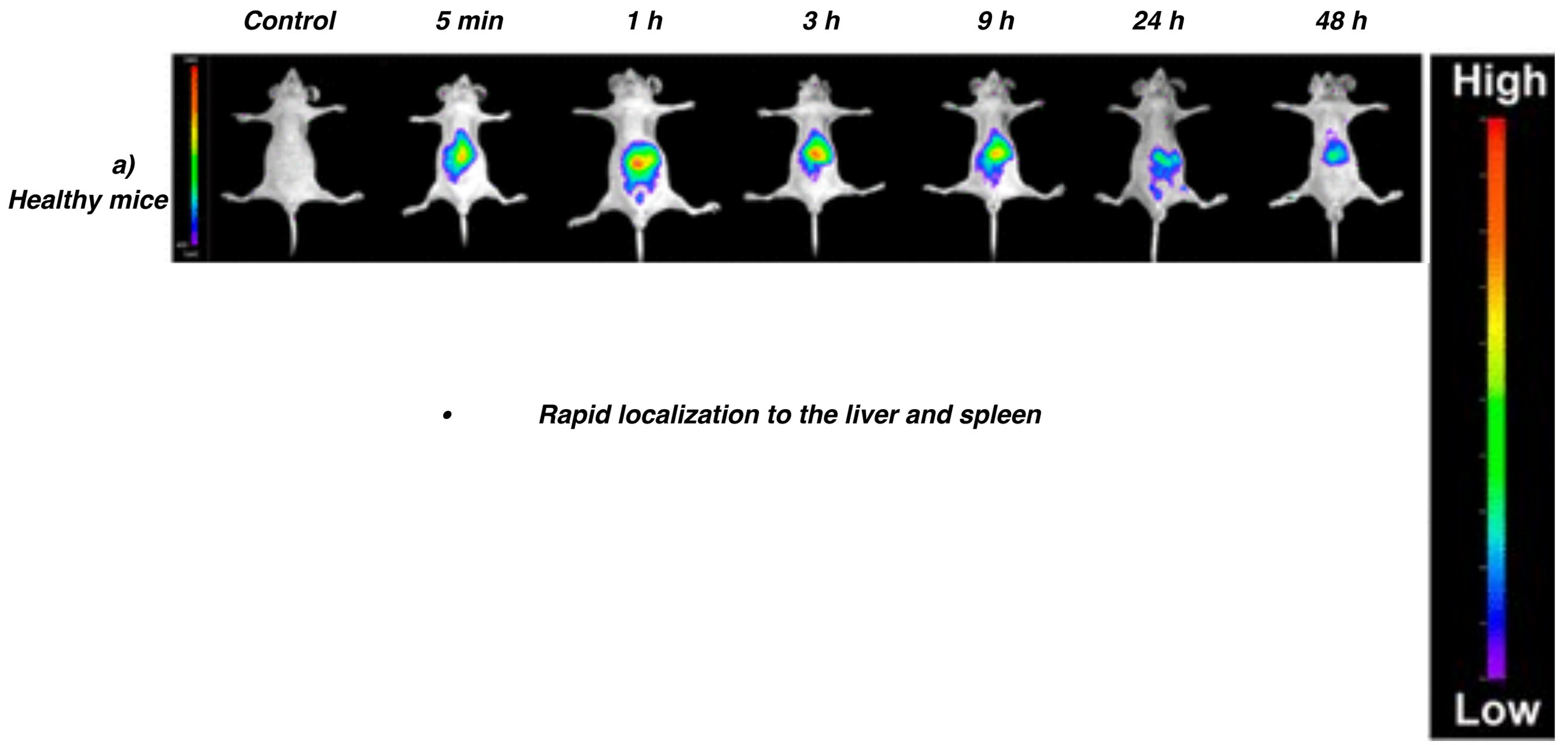
MDA-MB-231 tumor mice

- ***late-stage breast cancer model***

Wang, X., Chen, J-T., Zhu, H., Chen, X., Yan, X-P.. *Anal. Chem.* **2013**. *85*, 10225–10231.

Upconversion in Inorganic Systems

Applications to bioimaging



- ***Rapid localization to the liver and spleen***

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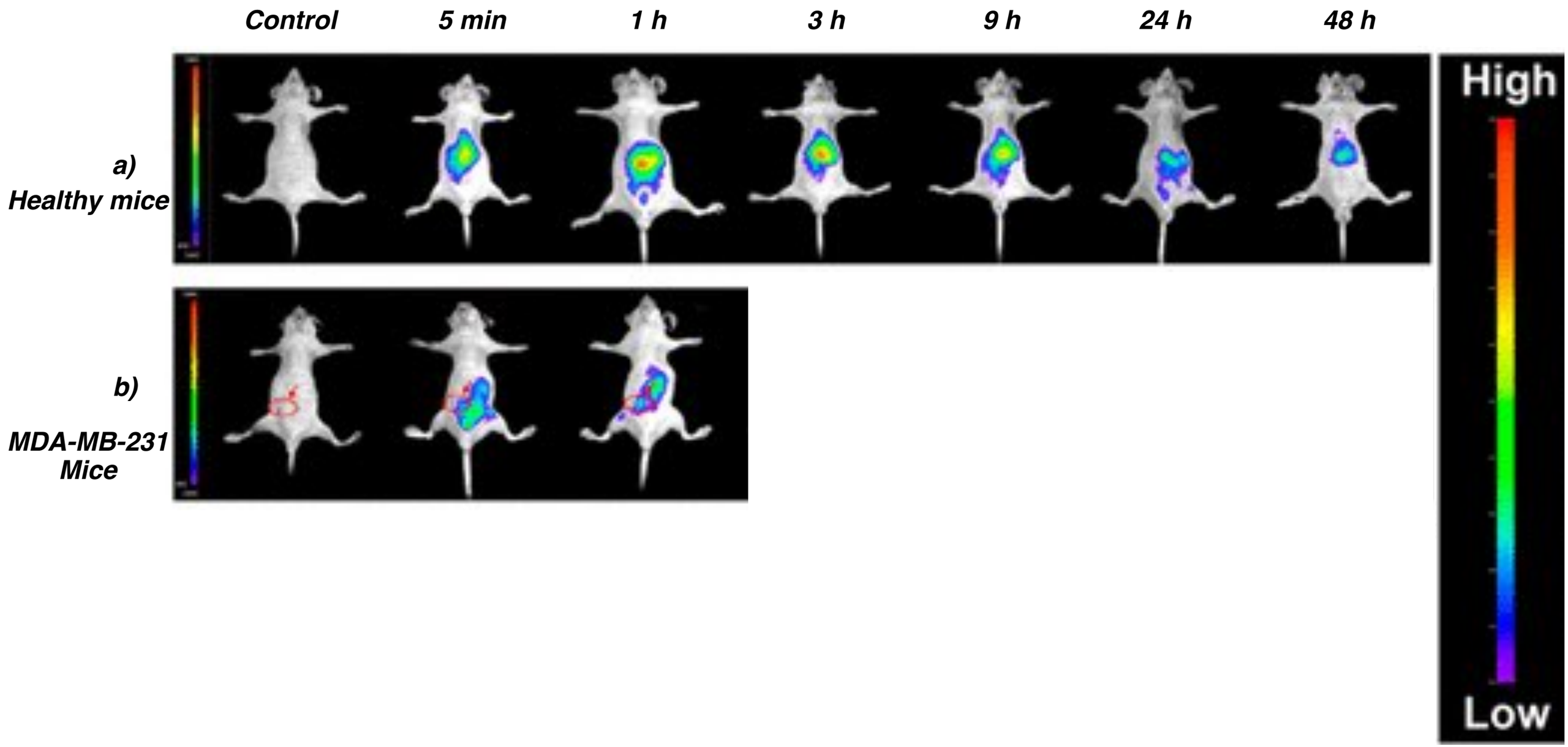
Upconversion in Inorganic Systems

Applications to bioimaging



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Upconversion in Inorganic Systems

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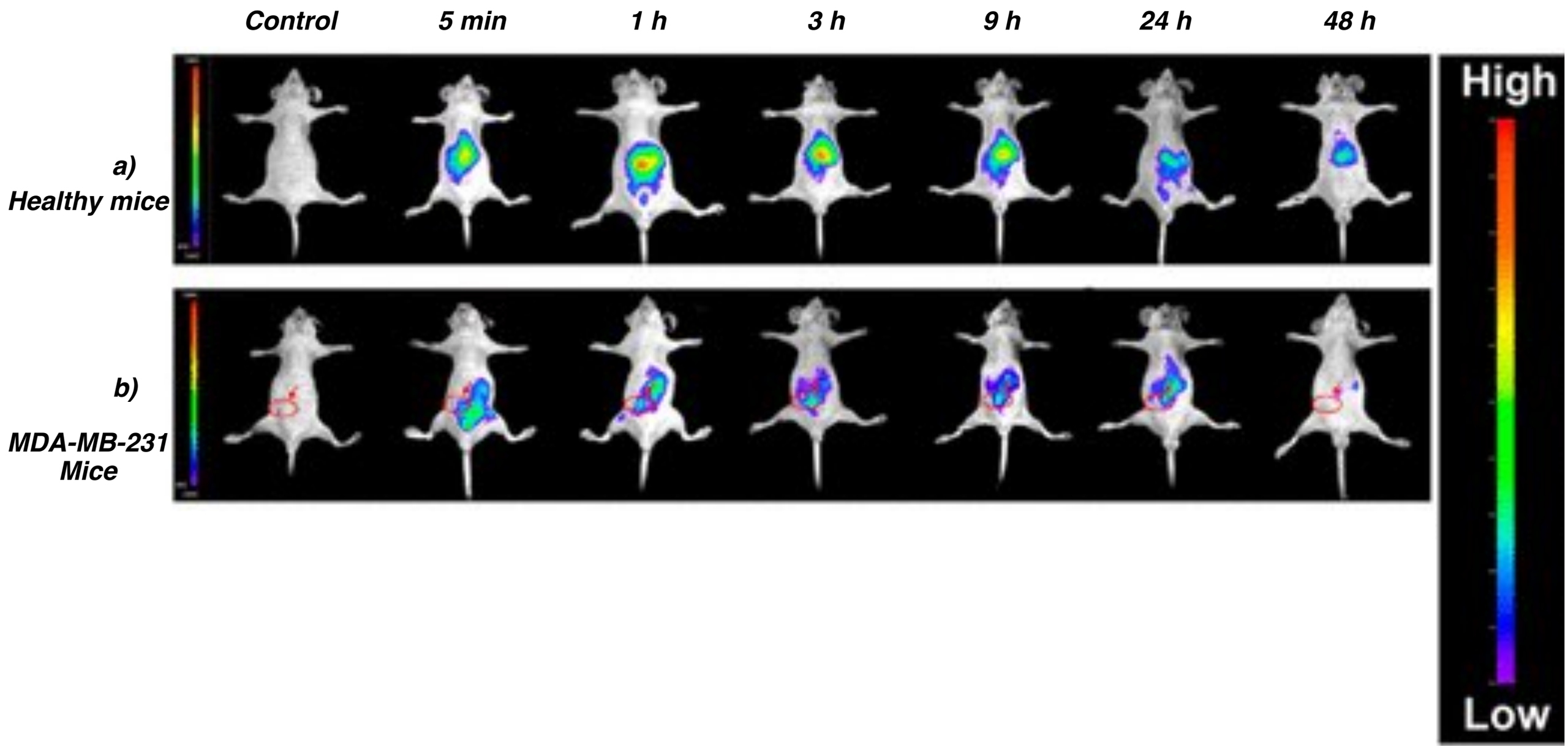

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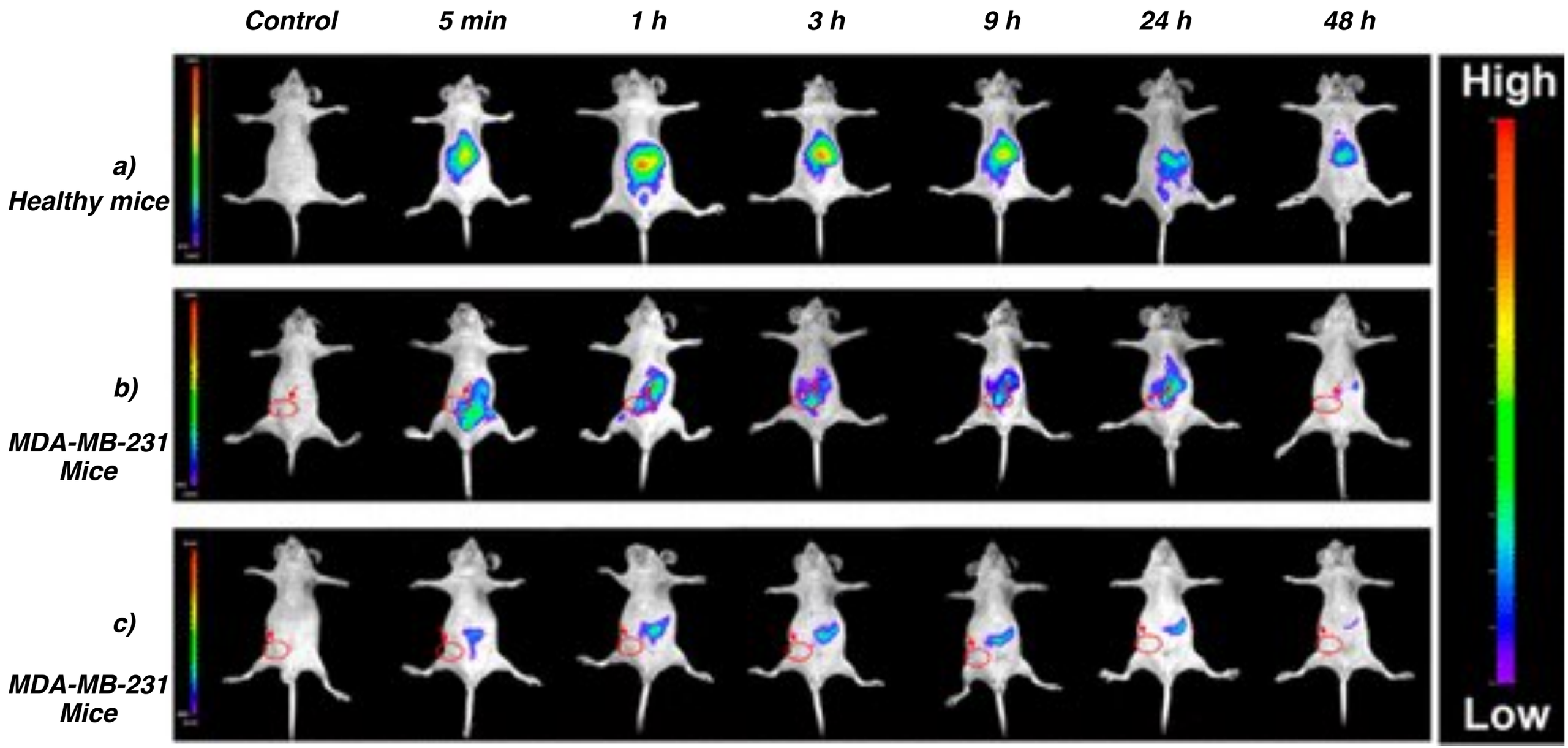


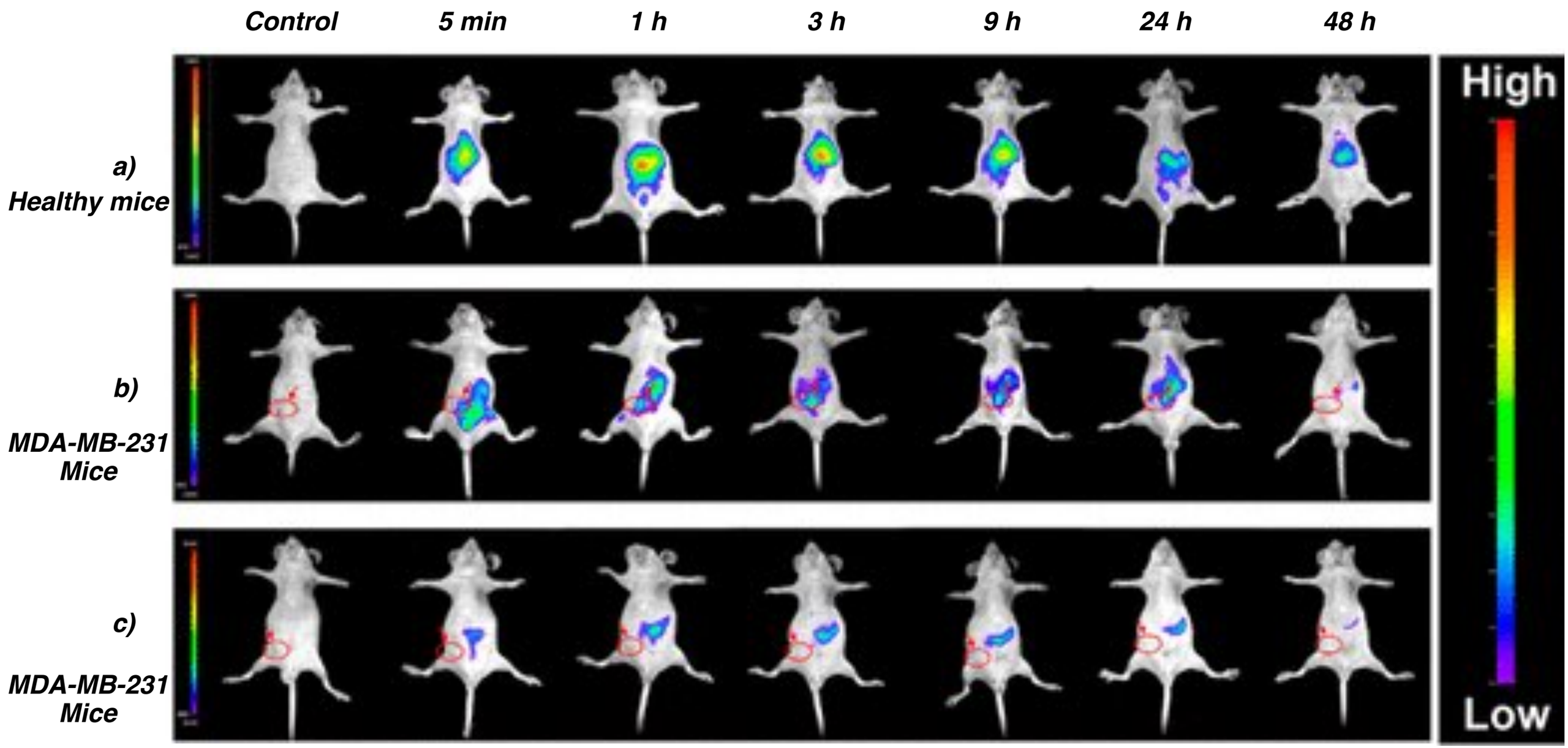
DEG-UCNP control nanoparticles

- ***No HA tag***

Wang, X., Chen, J-T., Zhu, H., Chen, X., Yan, X-P. *Anal. Chem.* **2013**. *85*, 10225–10231.

Upconversion in Inorganic Systems

- *Upconversion luminescence nanoparticles underwent highly specific binding*



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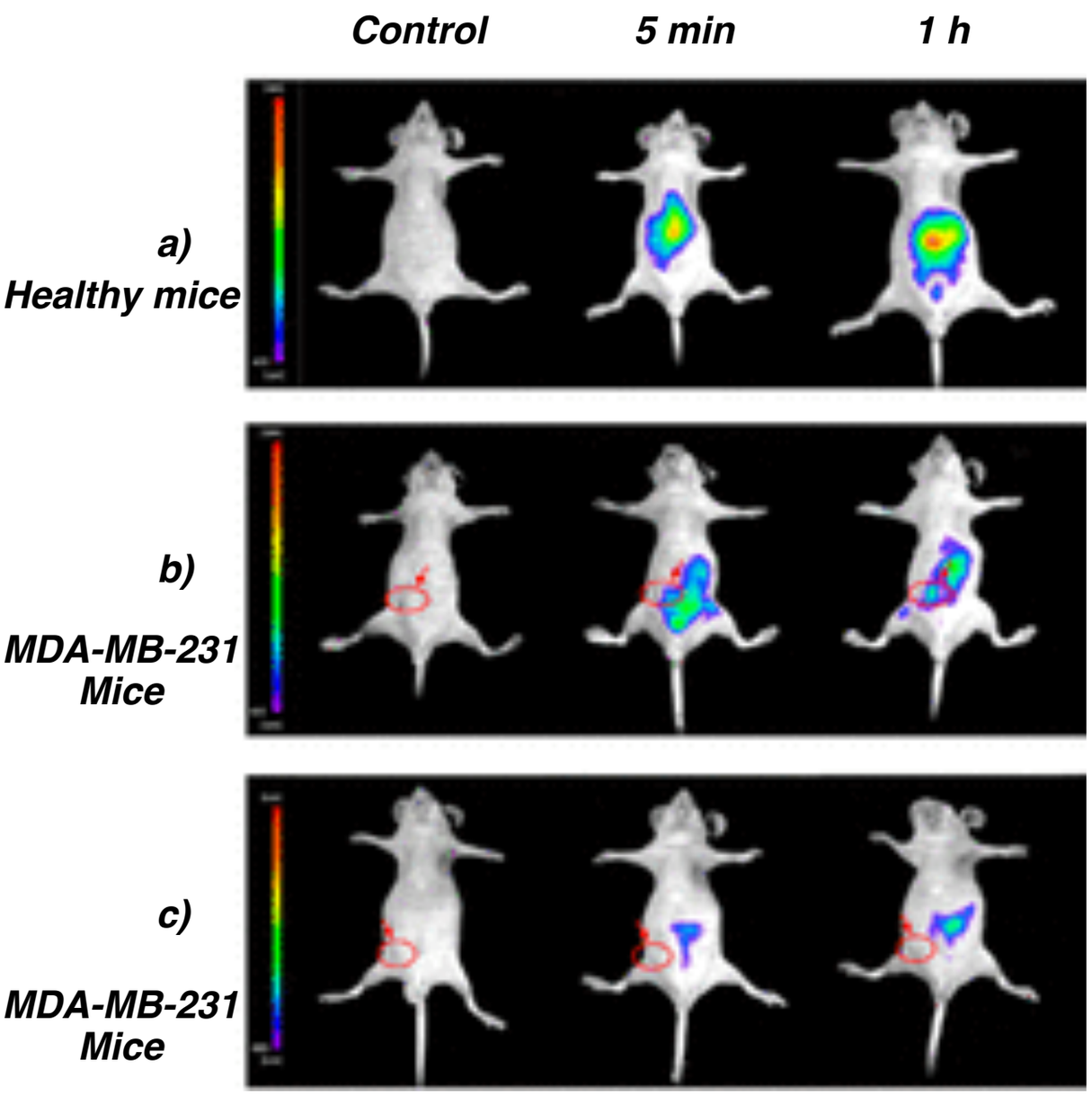


DEG-UCNP control nanoparticles

- ***No HA tag***

- ***high HA-UCNP affinity*** *to CD44-positive MDA-MB-231 tumor in vivo models*

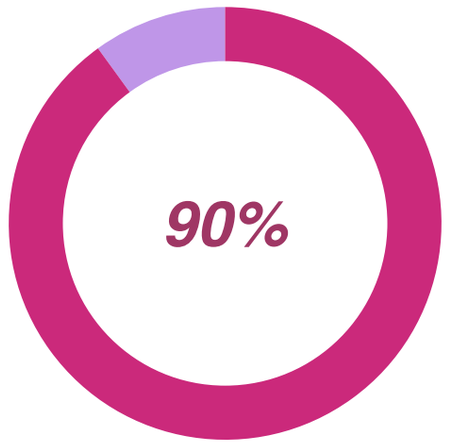
Wang, X., Chen, J-T., Zhu, H., Chen, X., Yan, X-P. *Anal. Chem.* **2013**. *85*, 10225–10231.

How is upconversion applied to challenging drug delivery?

A major challenge of small molecule drug development is poor water solubility

Vargarson, A. M., Anselmo, A. C., Mitragotri, S. *Nat. Biomed. Engin.* **2021**. *5*, 951–967.

A major challenge of small molecule drug development is poor water solubility



Discovery pipeline candidates exhibit high lipophilicity metrics

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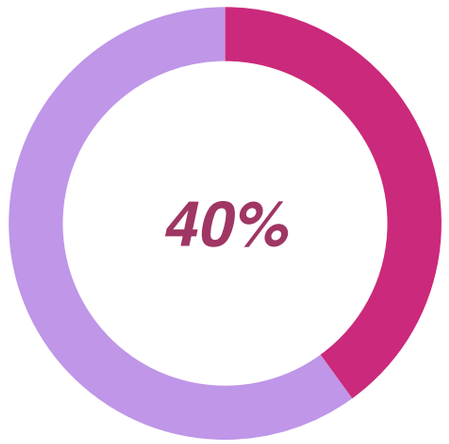

***Market-approved** compounds exhibit high lipophilicity metrics*

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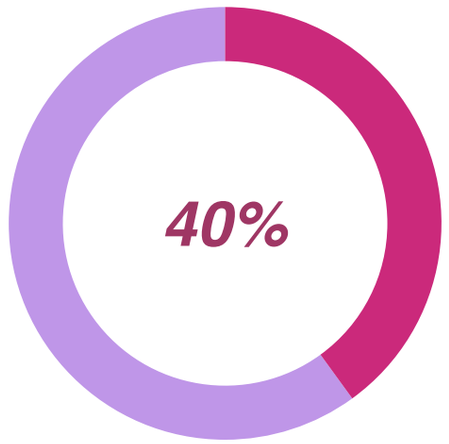
A major challenge of small molecule drug development is poor water solubility



***Market-approved** compounds exhibit high lipophilicity metrics*

*Can **upconverting** nanosystems be used to overcome **drug-delivery** hurdles?*

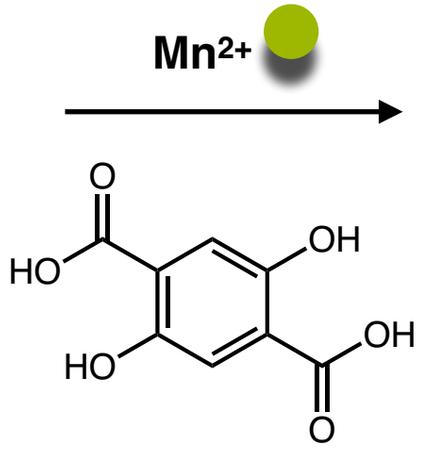
Vargarson, A. M., Anselmo, A. C., Mitragotri, S. *Nat. Biomed. Engin.* **2021**. *5*, 951–967.

Upconversion in Inorganic Materials

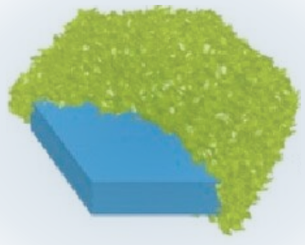
Upconverting nanoparticles for water-insoluble drug delivery

Overview of assembly process:

Lanthanide-doped nanoparticles



2,5-dihydroxyterephthalic acid



Upconverting nanoparticle decorated Mn-MOFs

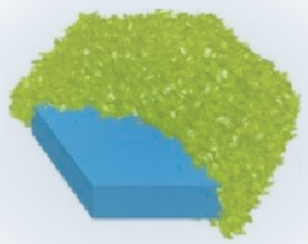
- ***Microporous structure***
- ***Greater sites for drug loading***

Zhao, X., He, S., Li, B., Liu, B., Shi, Y., Cong, W., Gao, F., Li, J., Wang, F., Liu, K., Sheng, C., Su, J., Hu, H-G. *Nano. Lett.* **2023**, *23*, 863–871.

Upconversion in Inorganic Materials

Upconverting nanoparticles for water-insoluble drug delivery

Overview of assembly process:



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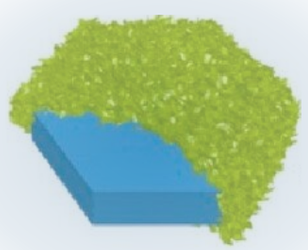

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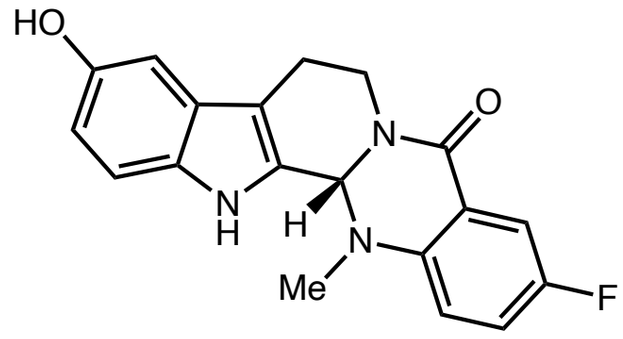

3-F-10-OH-Evodiamine (FOE)

- *Anticancer*

Dong, G., Wang, S., Miao, Z., Yao, J., Zhang, Y., Gun, Z., Zhang, W., Sheng, C. *J. Med. Chem.* **2012**, *55*, 7593–7613.

Zhao, X., He, S., Li, B., Liu, B., Shi, Y., Cong, W., Gao, F., Li, J., Wang, F., Liu, K., Sheng, C., Su, J., Hu, H-G. *Nano. Lett.* **2023**, *23*, 863–871.

Upconversion in Inorganic Materials

Upconverting nanoparticles for water-insoluble drug delivery

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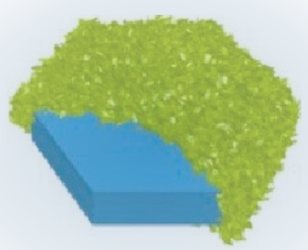

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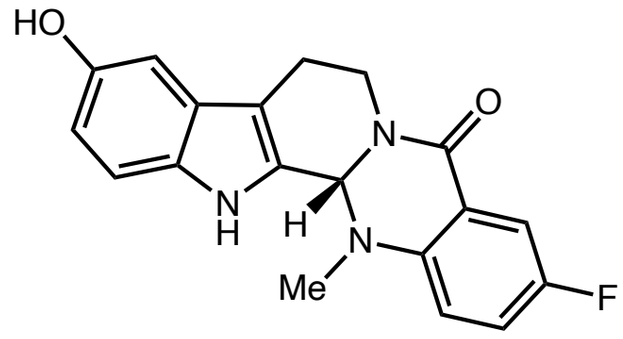

3-F-10-OH-Evodiamine (FOE)

- *Anticancer*
- *Highly water-**in**soluble*

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Upconversion in Inorganic Materials

Upconverting nanoparticles for water-insoluble drug delivery

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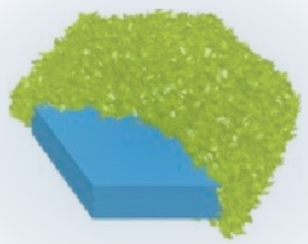
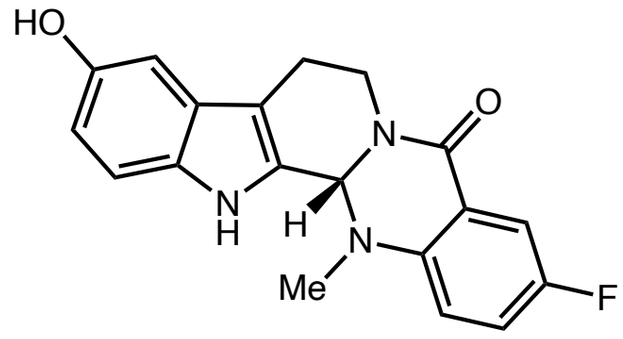


Upconverting nanoparticle decorated Mn-MOFs



3-F-10-OH-Evodiamine (FOE)

- *Anticancer*
- *Highly water-**in**soluble*
- *Synthetic functionalization unproductive*

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Upconversion in Inorganic Materials

Upconverting nanoparticles for water-insoluble drug delivery

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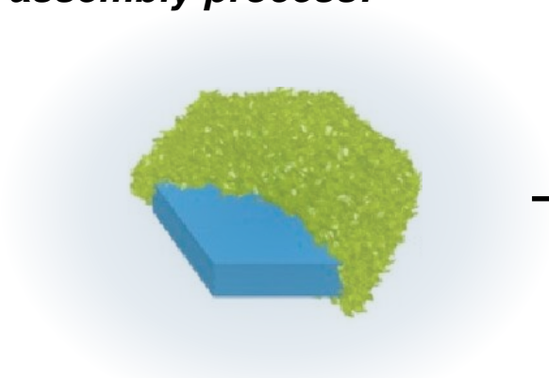

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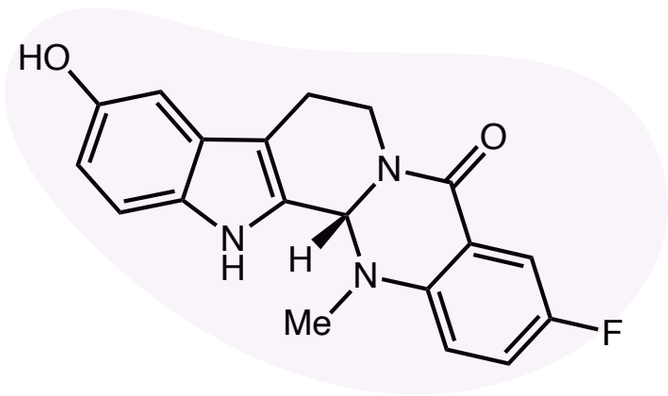
FOE



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Upconversion in Inorganic Materials

Upconverting nanoparticles for water-insoluble drug delivery

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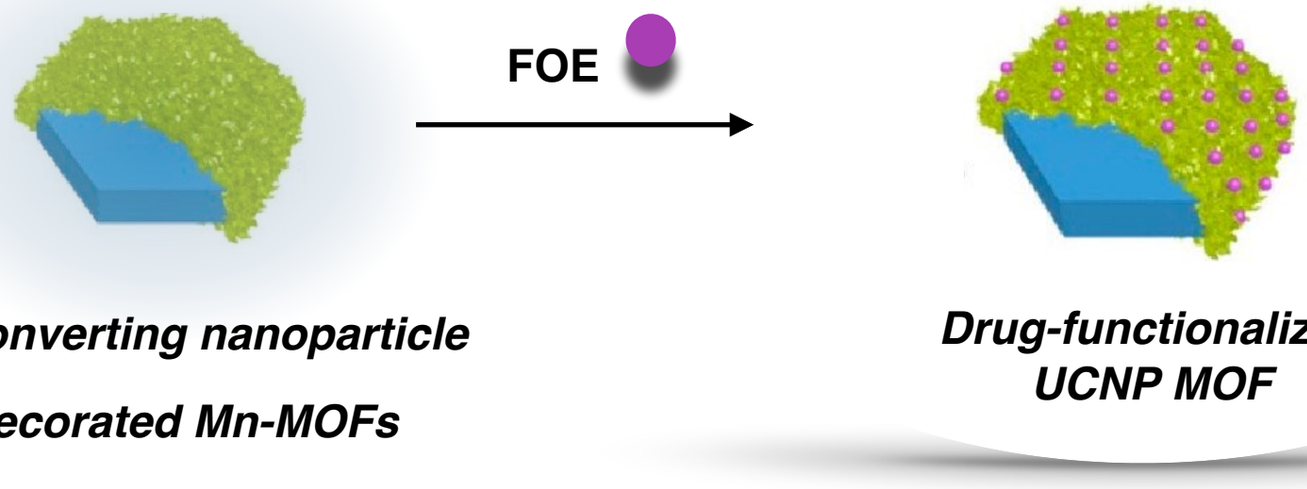

Upconverting nanoparticle decorated Mn-MOFs

Drug-functionalized UCNP MOF

multi-functionalized drug-delivery platform

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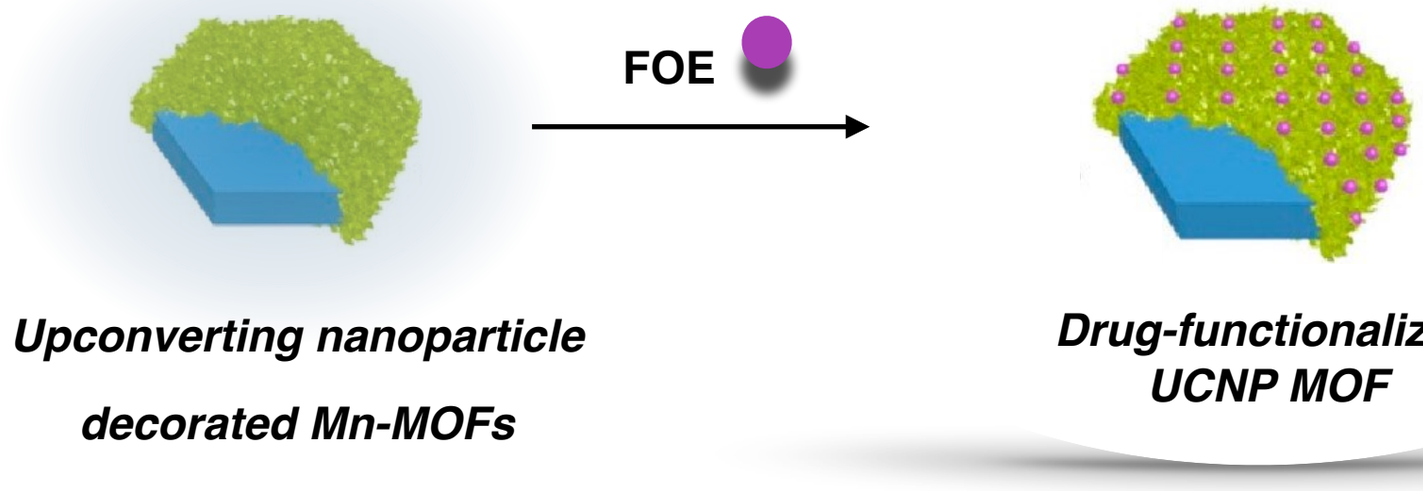
Upconversion in Inorganic Materials

Upconverting nanoparticles for water-insoluble drug delivery

Overview of assembly process:



Upconverting nanoparticle decorated Mn-MOFs

Drug-functionalized UCNP MOF

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4T1 model

Breast cancer model

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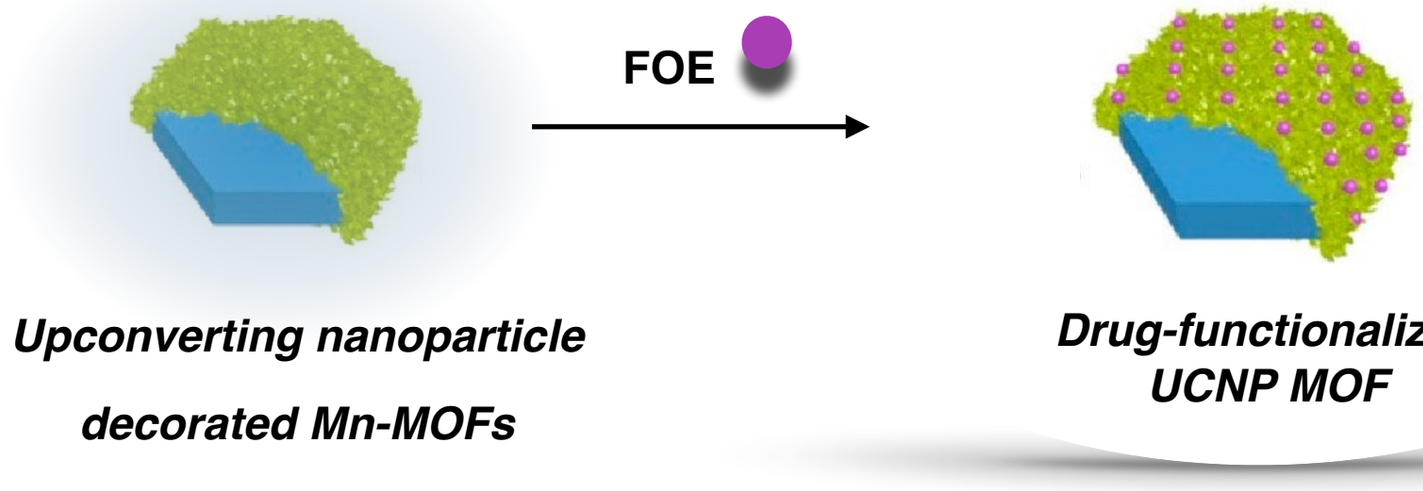

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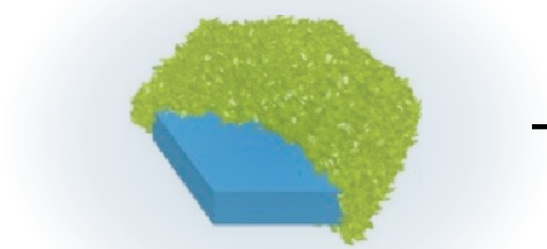
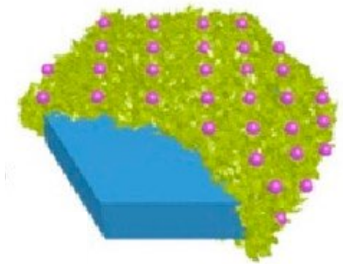


Upconverting nanoparticle decorated Mn-MOFs

FOE



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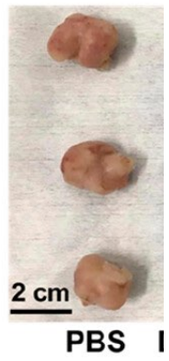

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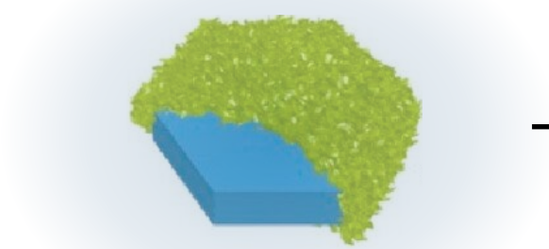

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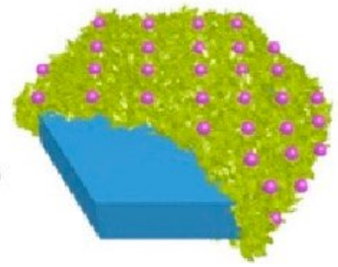

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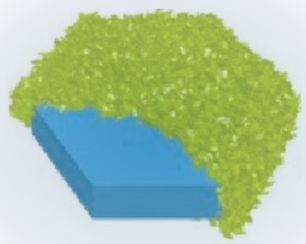

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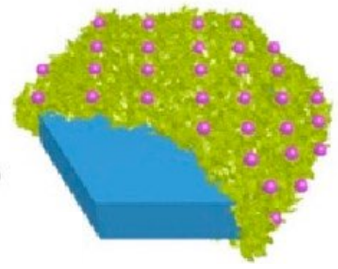

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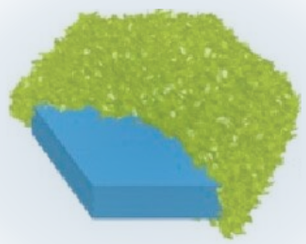

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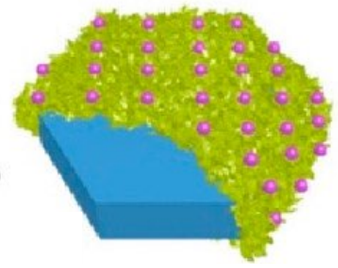

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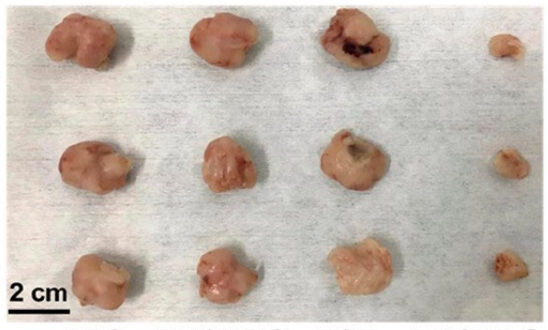

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Upconversion in Inorganic Materials

Upconversion applied to nanoparticle therapeutics → ***Photoactive*** *sensor activation*

Upconversion-induced nanoparticle drug delivery

Chen, G., Giu, H., Prasad, P. N., Chen, X. *Chem. Rev.* **2014**, *114*, 5161–5214.

Upconversion in Inorganic Materials

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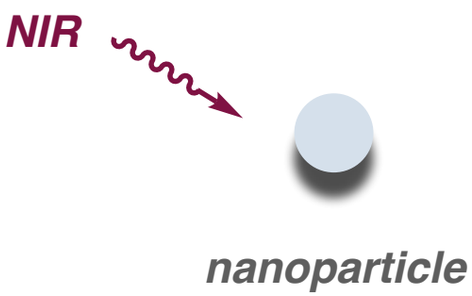

Low light intensity *minimizes overheating and photodamage in biological specimens*

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Upconversion in Inorganic Materials

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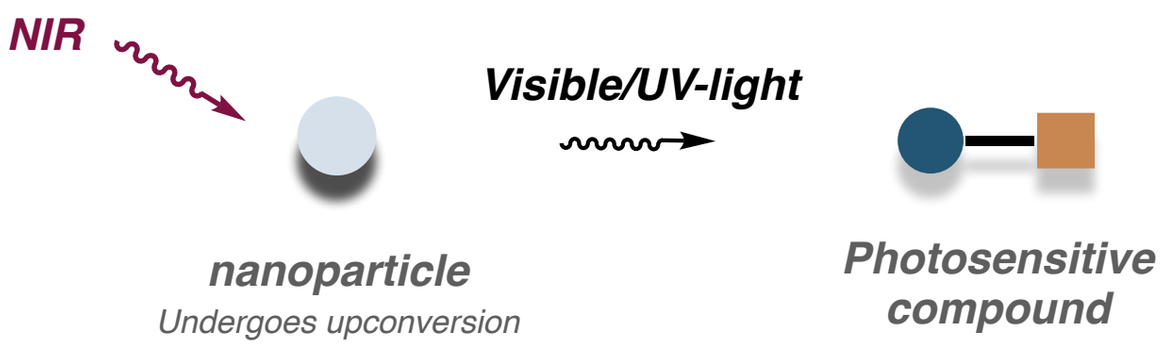

NIR absorbing *lanthanide-doped* ***nanoparticles*** *are capable visible/UV light emission*

Haase, M., Schäfer, H. *Angew. Chem. Int. Ed.* **2011**. *50*, 5808–5829.

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Upconversion in Inorganic Materials

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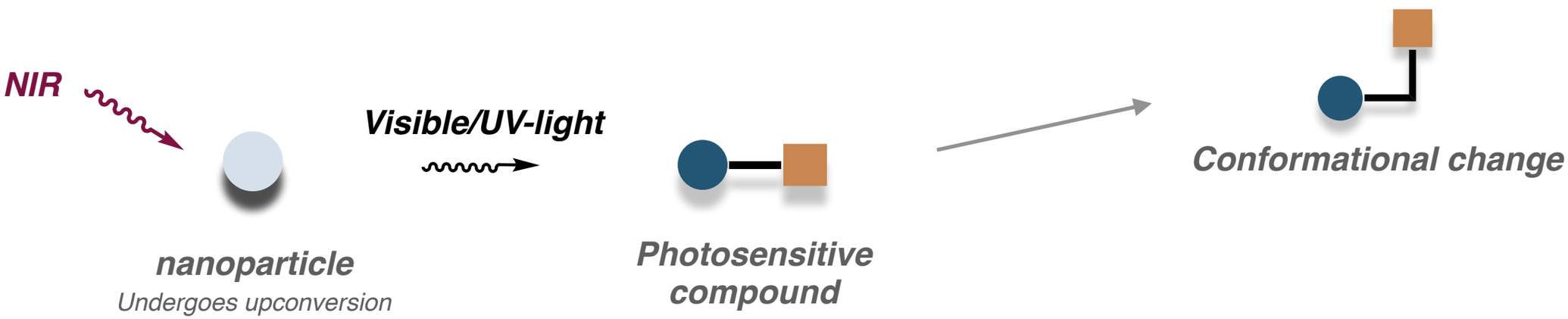

Upconversion-induced conformational changes are used in biosensor development

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Upconversion in Inorganic Materials

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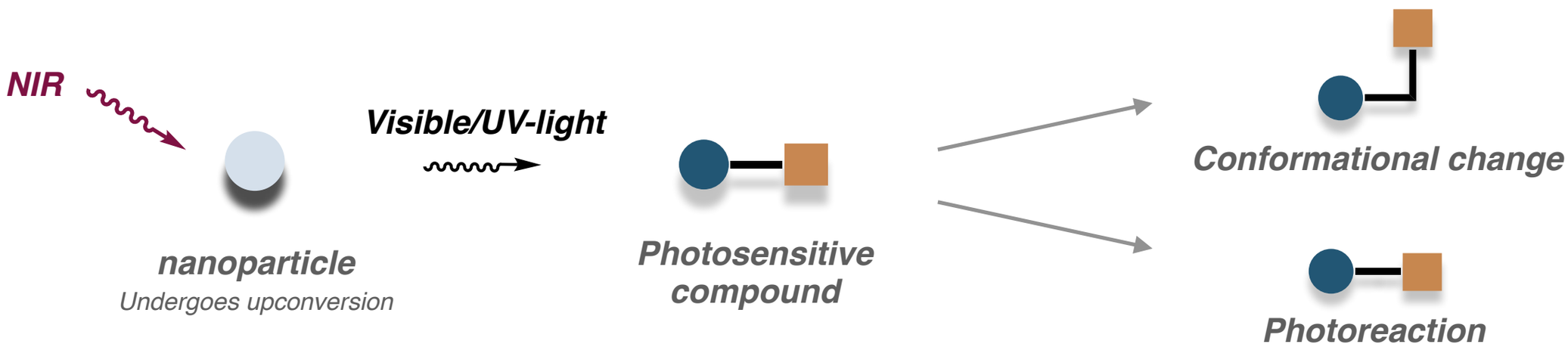

Nanoparticles *emit visible/UV light to induce photoreactivity*

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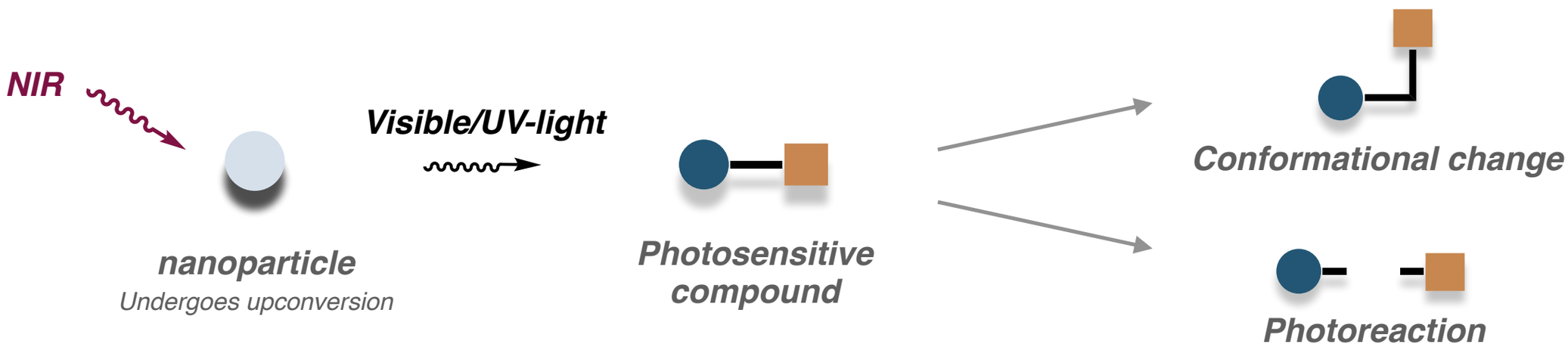

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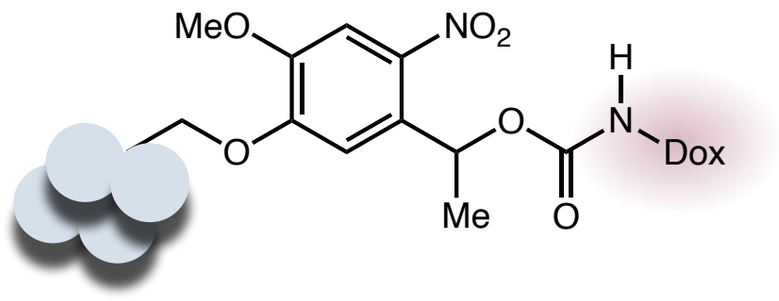
Upconversion in Inorganic Materials

Upconversion enabled photocleavable linker for drug delivery



LiYF4:Tm^{3+}/Yb^{3+} nanoparticles

Dcona, M. M., Yu, Q., Capobianco, J. A., Hartman, M. C.T. *Chem. Commun. (Camb).* **2015**, *51*, 8477–8479.

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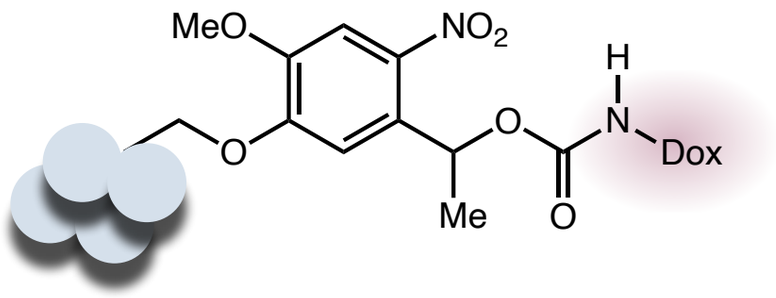

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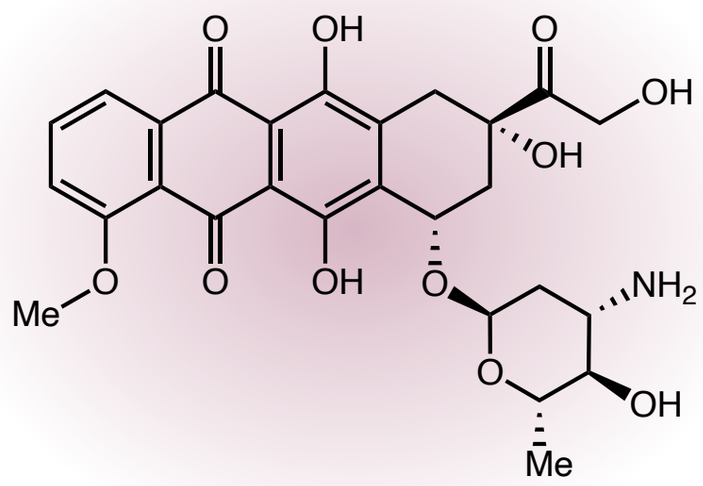

Doxorubicin

Side effects:

- *Cardiomyopathy*
- *Congestive heart failure*

Single, P. K., Iliskovic, N. *N. Engl. J. Med.* **1998**, *339*, 900–905.

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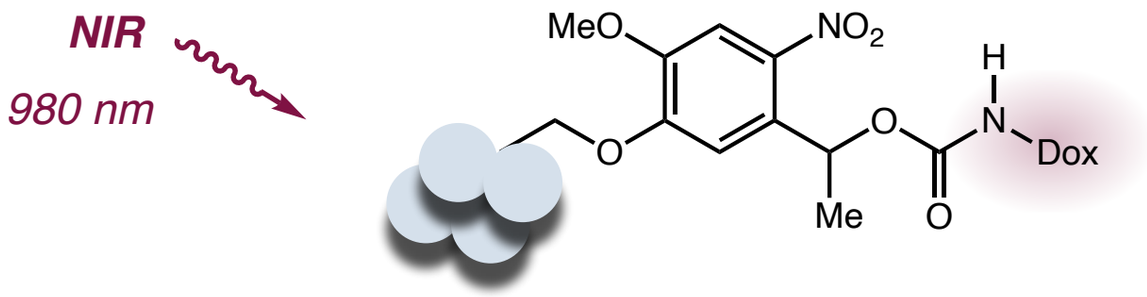

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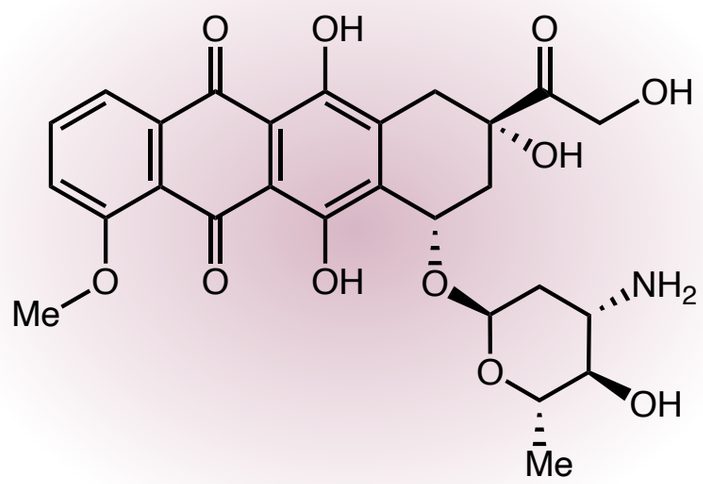

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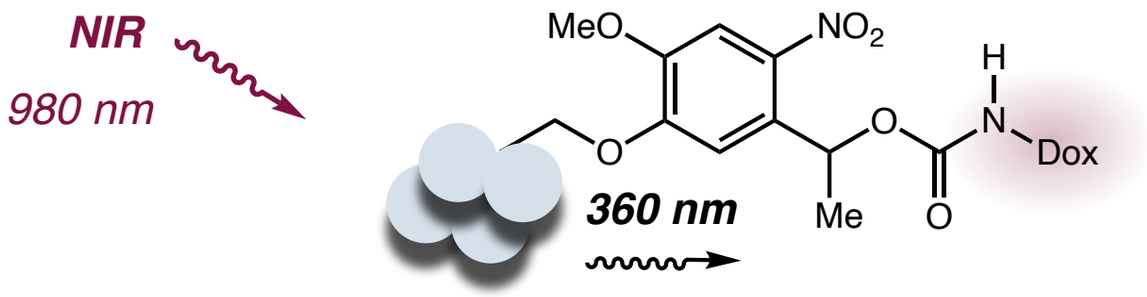

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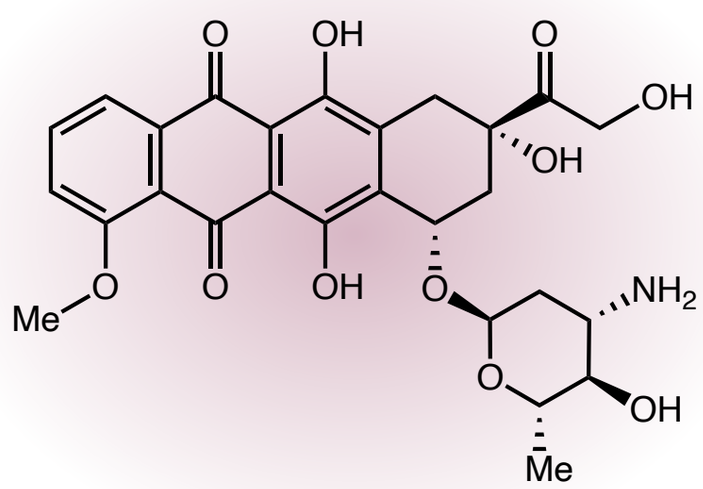

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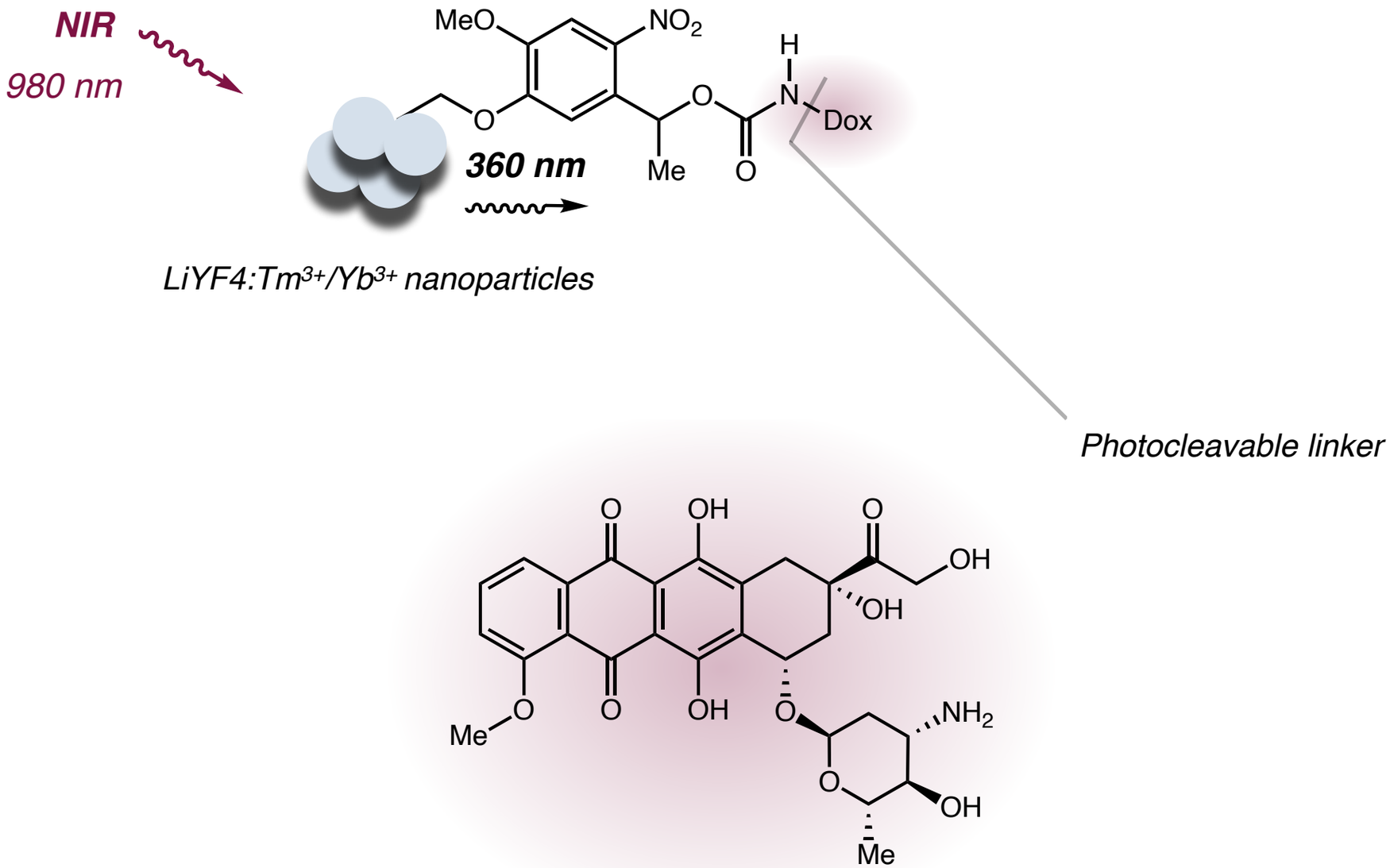

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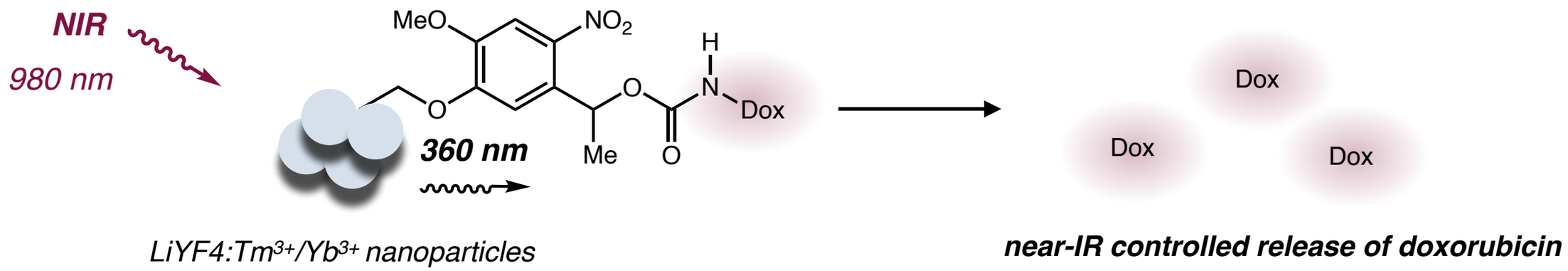
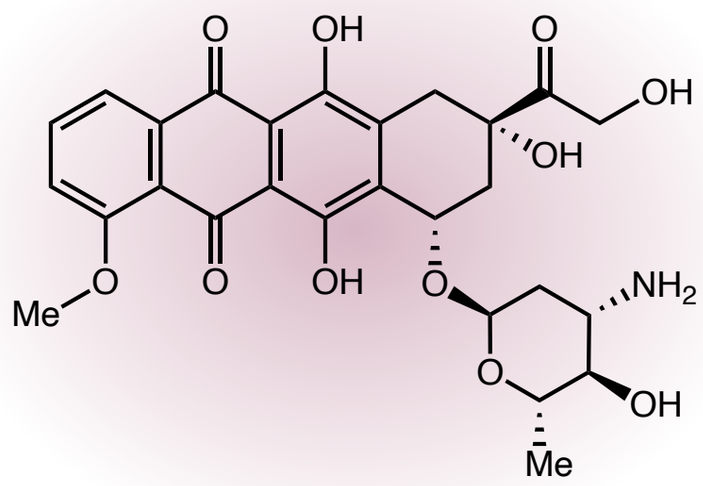


$LiYF4:Tm^{3+}/Yb^{3+}$ nanoparticles

near-IR controlled release of doxorubicin



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Upconversion in Inorganic Materials

Upconversion in

drug delivery

AuNPs

Gold nanoparticles

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Upconversion in Inorganic Materials

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- *Effective intracellular delivery*
- *High biocompatibility*
- ***Absorb 550 nm***

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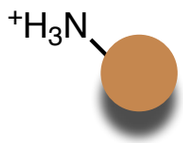
DOPA-PEI coating

functionalization



Positively charged AuNPs

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NaYYbErF$_4$-PEG-CO$_2$H ***Pos-AuNPs***

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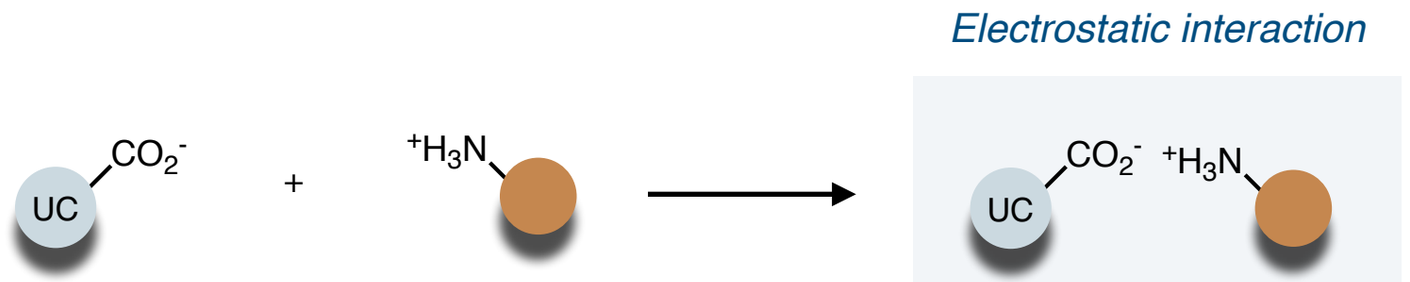

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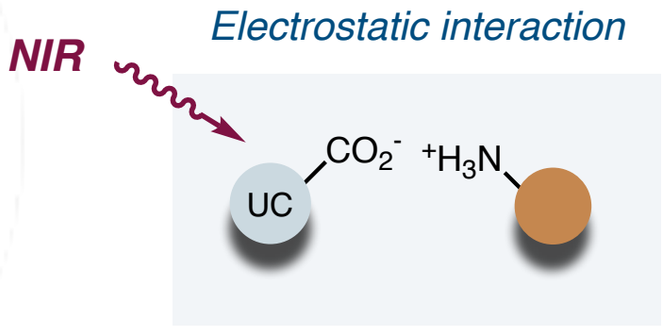

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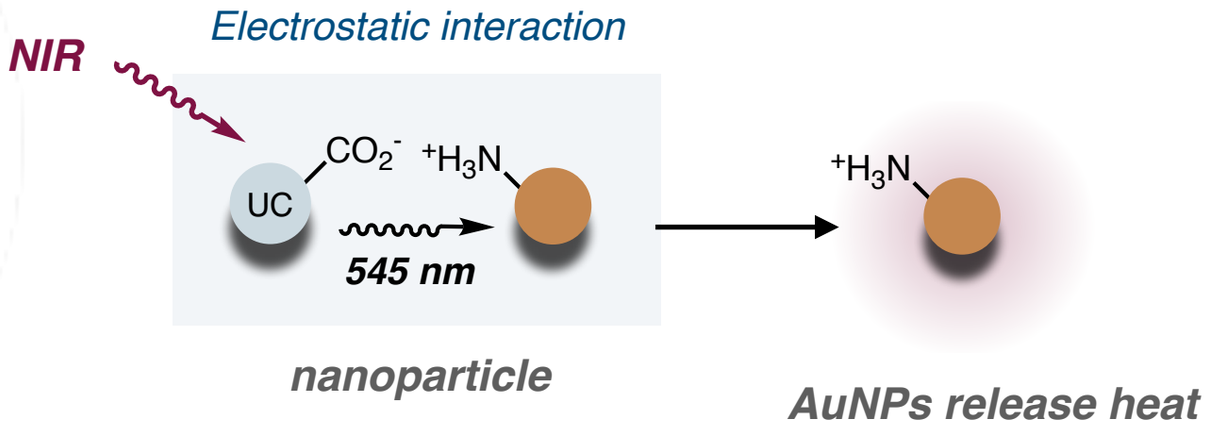

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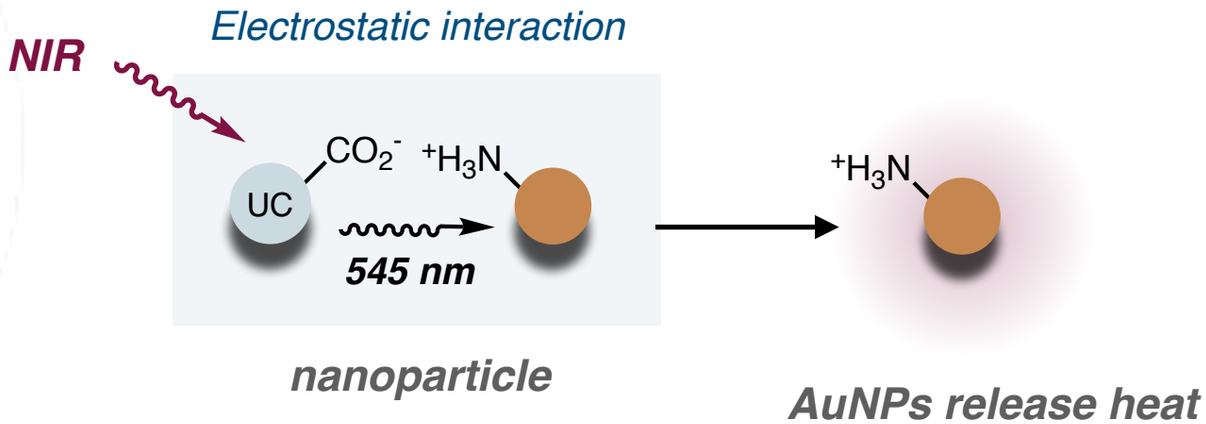

- ***Photoporation-based drug delivery***

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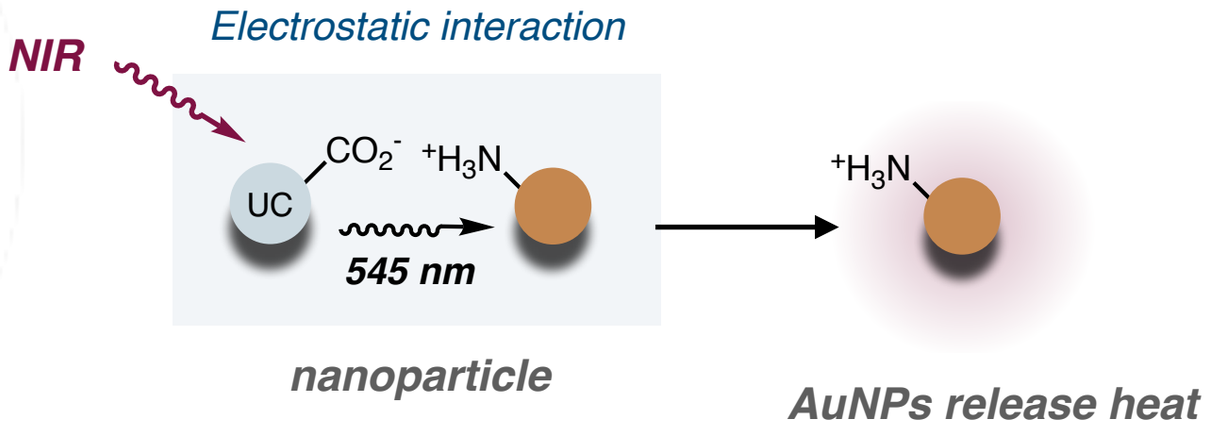
Upconversion in

drug delivery



- ***Photoporation-based drug delivery***

- ***Upconverting nanoparticle composite more effectively delivered BRN into cells***

  As evidenced by IL-6 expression levels

Kim, H. J., Cho, H. B., Kim, H-R., Lee, S., Park, J., Park, K-H. *Nano. Converg.* **2024**, *11*, 1–16.

Chen, G., Giu, H., Prasad, P. N., Chen, X. *Chem. Rev.* **2014**, *114*, 5161–5214.

Upconversion in chiral self-assembled nanomaterials

Upconversion in chiral self-assembled nanomaterials

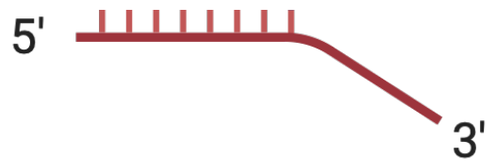
↓

Intracellular miRNA detection

Intracellular miRNA detection

Understanding the role of microRNA

miRNA

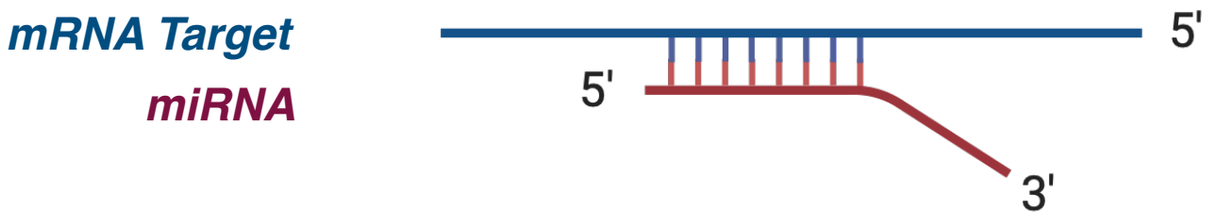


- ***single-stranded non-coding RNA molecules***
- ***standard length: 21-23 nucleotides***

Chen, Y., Gao, D-Y., Huang, L. *Adv. Drug. Deliv. Rev.* **2015**, *81*, 128–141.

Intracellular miRNA detection

Understanding the role of miRNA

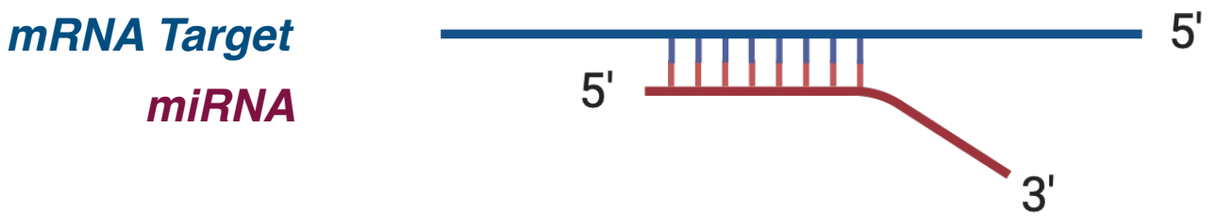


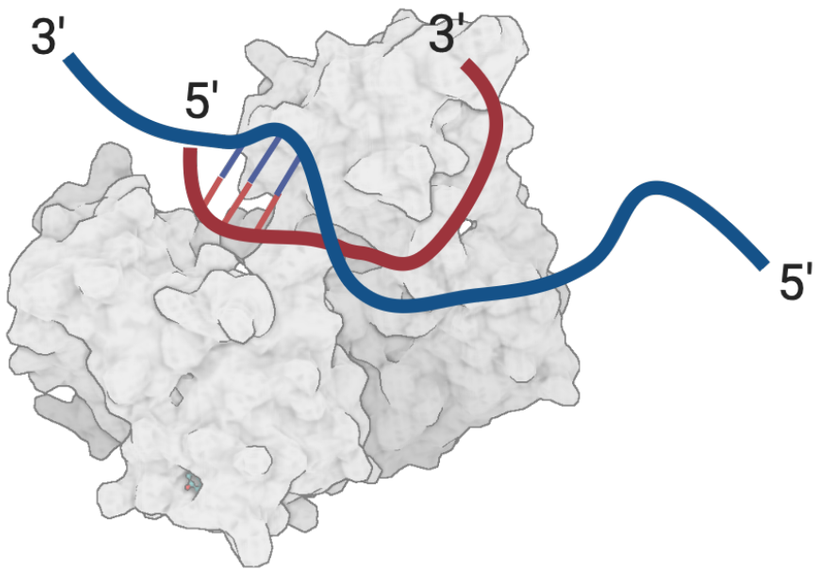
- **miRNA participates in RNA silencing**

Chen, Y., Gao, D-Y., Huang, L. *Adv. Drug. Deliv. Rev.* **2015**, *81*, 128–141.

Intracellular miRNA detection

Understanding the role of miRNA





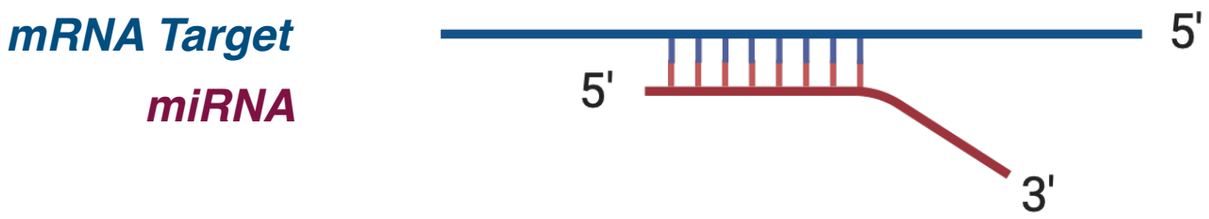
- **miRNA participates in RNA silencing**

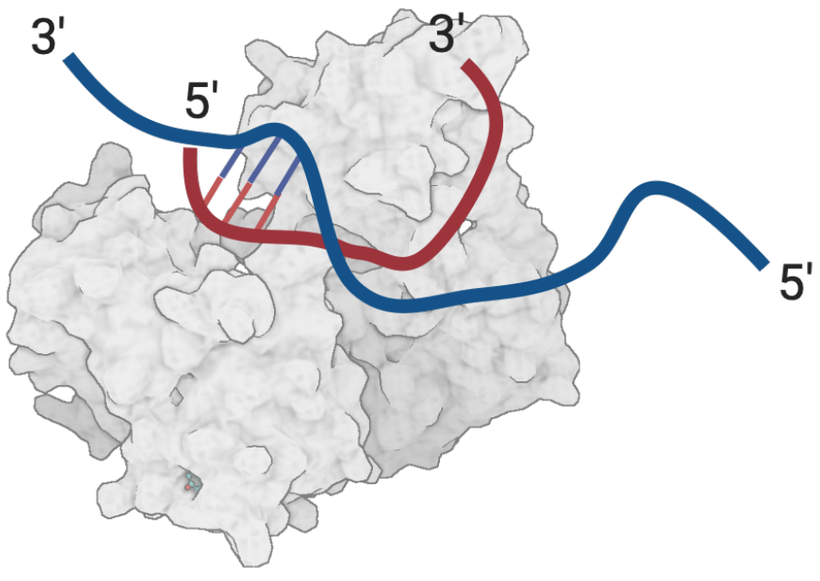
Regulatory processes

Chen, Y., Gao, D-Y., Huang, L. *Adv. Drug. Deliv. Rev.* **2015**, *81*, 128–141.

Intracellular miRNA detection

Understanding the role of miRNA





- **miRNA participates in RNA silencing**

Tumor suppressor genes

Cell cycle regulation

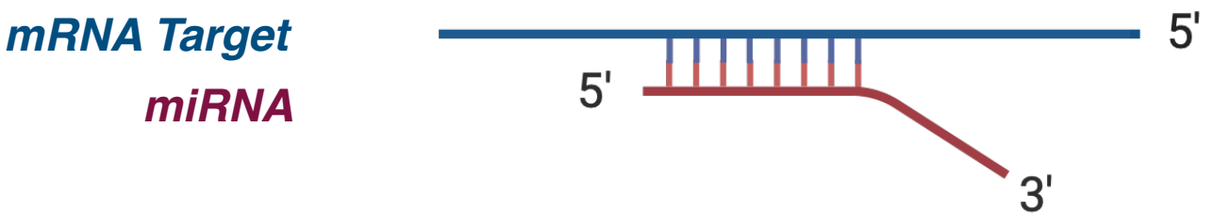
Metabolism

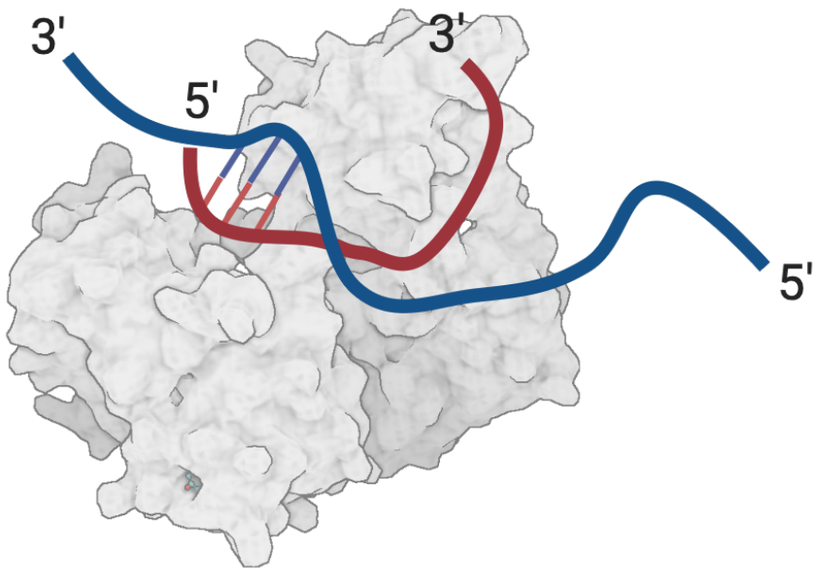
Metastasis

Chen, Y., Gao, D-Y., Huang, L. *Adv. Drug. Deliv. Rev.* **2015**, *81*, 128–141.

Intracellular miRNA detection

Understanding the role of miRNA





miRNAs can act as disease markers

- *Low abundance*
- *Degradation*
- *Sequence similarity*

Git, A., Dvinge, H., Salmon-Divon, M., Osborne, M., Kutter, C., Hadfield, J., Bertone, P., Caldas, C. *RNA.* **2010**, *16*, 991–1006.

Intracellular miRNA detection

Understanding the role of miRNA

miRNAs can act as disease markers

- ***challenging detection***
- ***require sensitive quantification***

Chen, Y., Gao, D-Y., Huang, L. *Adv. Drug. Deliv. Rev.* **2015**, *81*, 128–141.

Intracellular miRNA detection

Understanding the role of miRNA

- ***Used to quantify miRNA expression***

Quantitative RT-PCR

miRNAs can act as disease markers

Chen, Y., Gao, D-Y., Huang, L. *Adv. Drug. Deliv. Rev.* **2015**, *81*, 128–141.

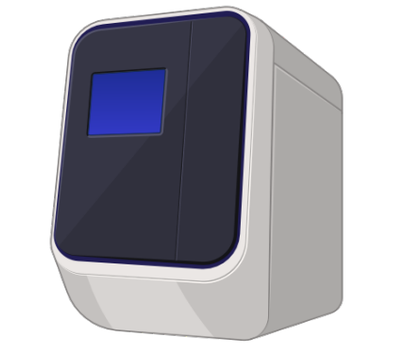
Intracellular miRNA detection

Understanding the role of miRNA

- ***Used to quantify miRNA expression***

Quantitative RT-PCR

Retrotranscription



miRNAs can act as disease markers

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Intracellular miRNA detection

Understanding the role of miRNA

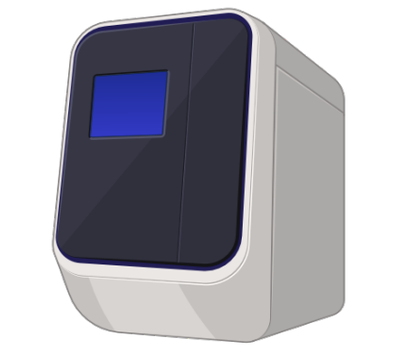
- ***Used to quantify miRNA expression***

Quantitative RT-PCR

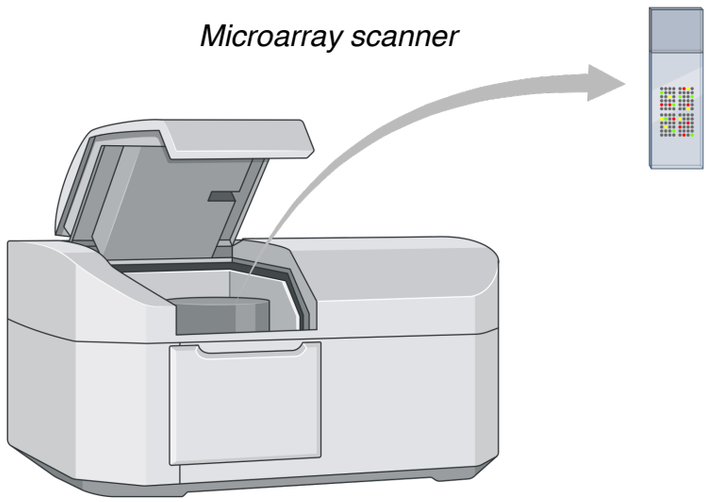
Microarray hybridization

miRNAs can act as disease markers

Retrotranscription



Microarray scanner



Chen, Y., Gao, D-Y., Huang, L. *Adv. Drug. Deliv. Rev.* **2015**, *81*, 128–141.

Intracellular miRNA detection

Understanding the role of miRNA

- ***Used to quantify miRNA expression***

Quantitative RT-PCR

Microarray hybridization

miRNAs can act as disease markers

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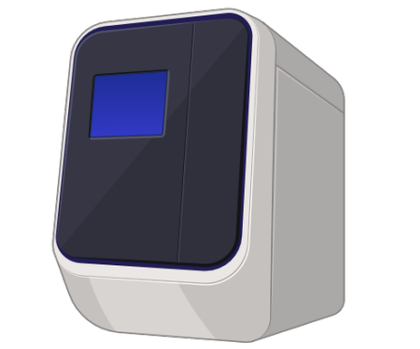
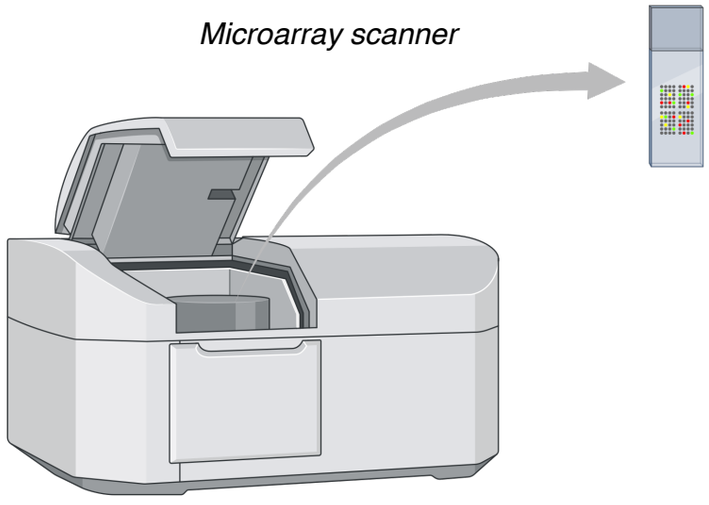


Microarray scanner



- ***High sensitivity and throughput***

Chen, Y., Gao, D-Y., Huang, L. *Adv. Drug. Deliv. Rev.* **2015**, *81*, 128–141.

Intracellular miRNA detection

Understanding the role of miRNA

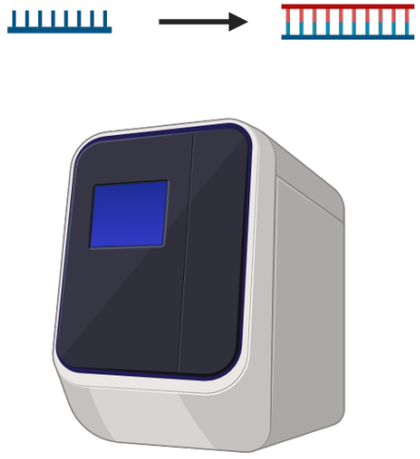
- ***Used to quantify miRNA expression***

Quantitative RT-PCR

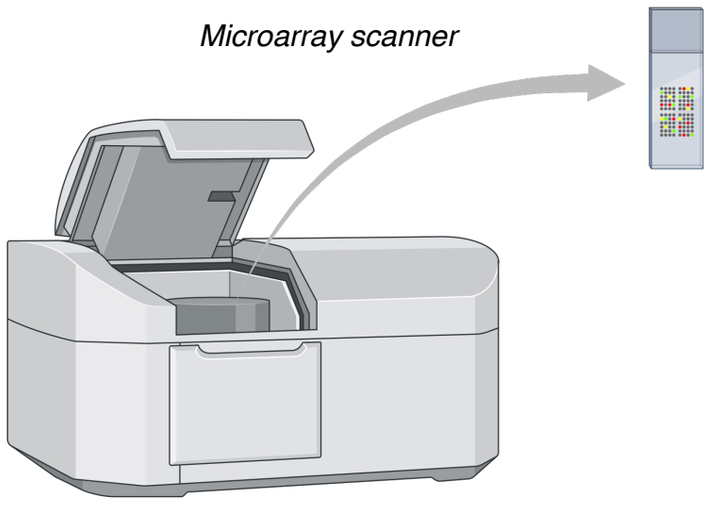
Microarray hybridization

miRNAs can act as disease markers

Retrotranscription



Microarray scanner



- ***High sensitivity and throughput***
- ***Expensive, operationally complex***

Chen, Y., Gao, D-Y., Huang, L. *Adv. Drug. Deliv. Rev.* **2015**, *81*, 128–141.

Intracellular miRNA detection

Understanding the role of miRNA

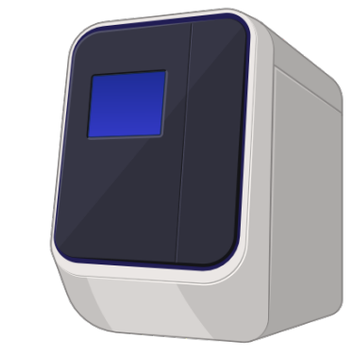
- ***Used to quantify miRNA expression***

Quantitative RT-PCR

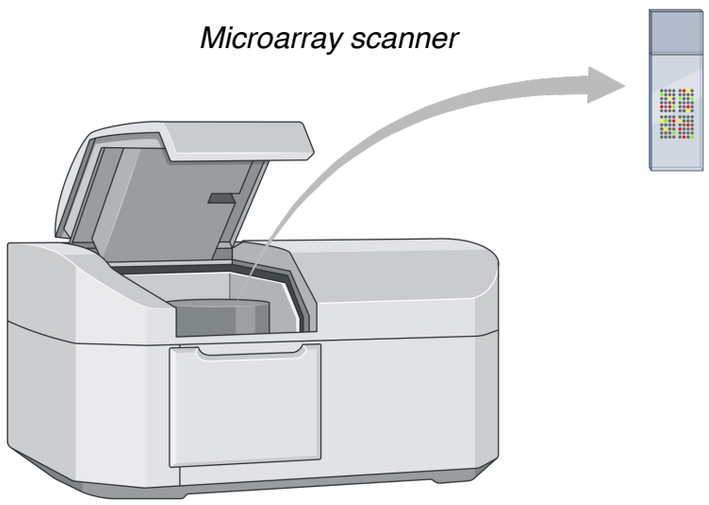
Microarray hybridization

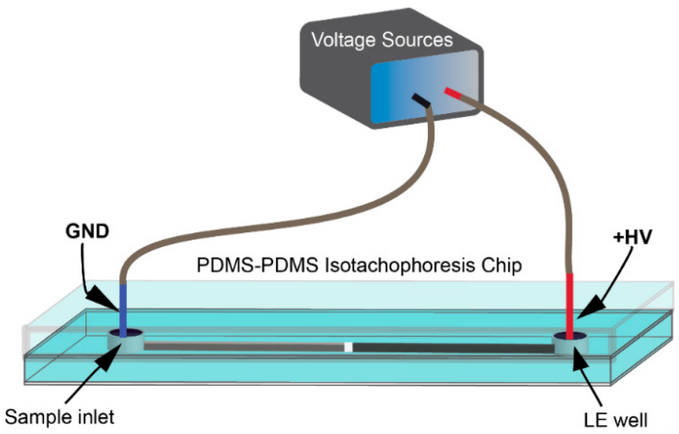
2-stage Isotachophoresis

Retrotranscription



Microarray scanner





Jin, Z., Geissler, D., Qui, X., Wenger, D. K., Hildebrandt, N. *Angew. Chem. Int. Ed.* **2015**, *54*, 10024–10029.

Intracellular miRNA detection

Understanding the role of miRNA

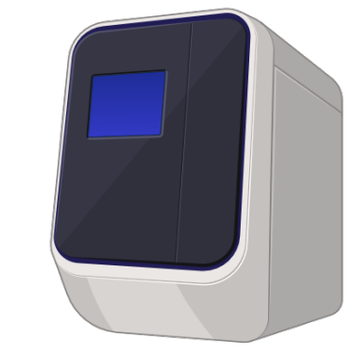
- ***Used to quantify miRNA expression***

Quantitative RT-PCR

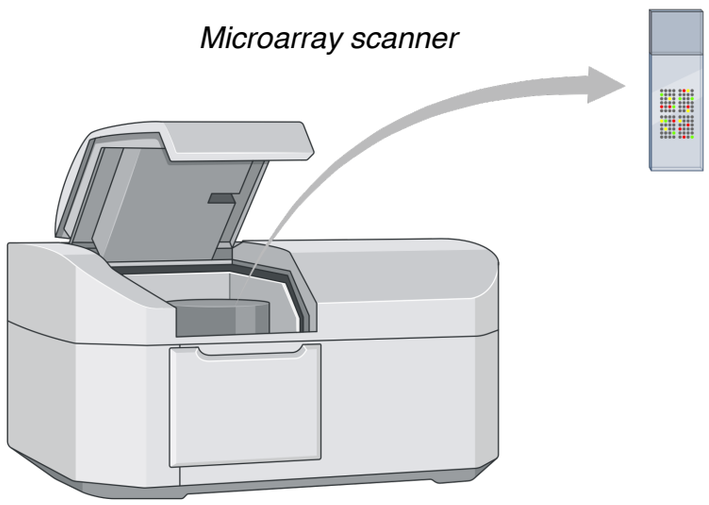
Microarray hybridization

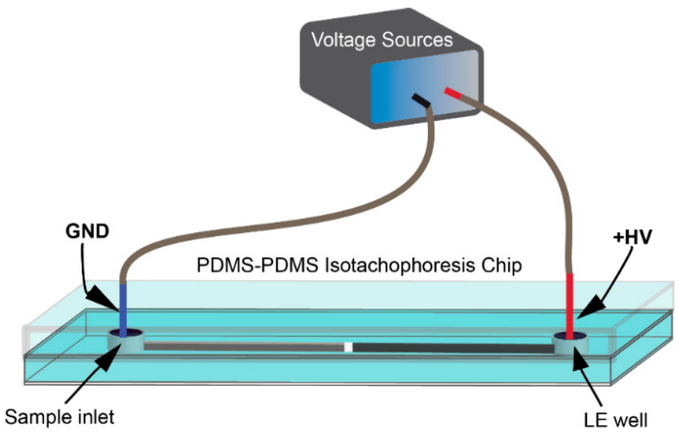
2-stage Isotachophoresis

Retrotranscription



Microarray scanner





- ***Require miRNA to be extracted from the cell prior to analysis***

Jin, Z., Geissler, D., Qui, X., Wenger, D. K., Hildebrandt, N. *Angew. Chem. Int. Ed.* **2015**, *54*, 10024–10029.

Intracellular miRNA detection

Upconversion towards intracellular miRNA detection

How can you detect miRNA formation in real time?

Intracellular miRNA detection

Upconversion towards intracellular miRNA detection

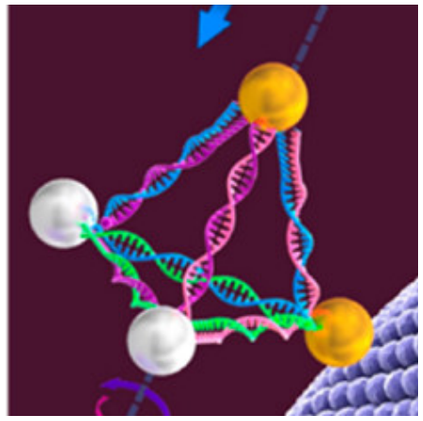
How can you detect miRNA formation in real time?

Goal: assay miRNA in live cells

Intracellular miRNA detection

Upconversion towards intracellular miRNA detection

DNA-driven self-assembled pyramids



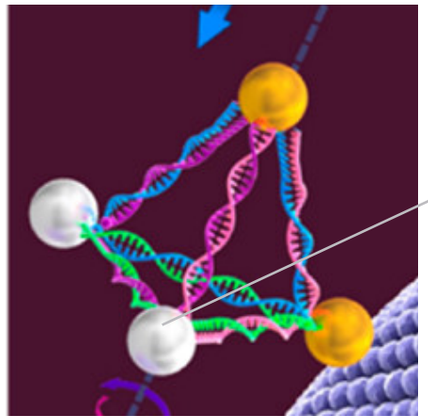
Au-UCNP pyramids

Li, S., Xu, L., Ma, W., Wu, X., Sun, M., Huang, H., Wang, L., Kotov, N. A., Xu, C. *J. Am. Chem. Soc.* **2016**, *138*, 306–312.

Intracellular miRNA detection

Upconversion towards intracellular miRNA detection

DNA-driven self-assembled pyramids



Au-UCNP pyramids

UCNP: $NaGdF_4:Yb^{3+}, Er^{3+}$

- *Superior photostability*
- *High signal-to-noise ratio*

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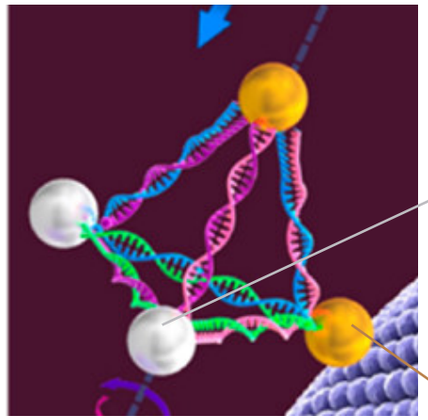
Intracellular miRNA detection

Upconversion towards intracellular miRNA detection

DNA-driven self-assembled pyramids



Au-UCNP pyramids

UCNP: $NaGdF_4:Yb^{3+}, Er^{3+}$

- *Superior photostability*
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Au NP

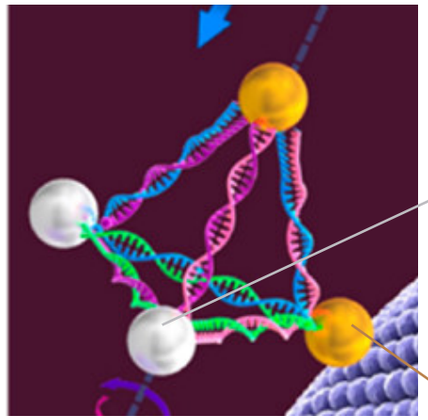
- *Prolate geometry*

Li, S., Xu, L., Ma, W., Wu, X., Sun, M., Huang, H., Wang, L., Kotov, N. A., Xu, C. *J. Am. Chem. Soc.* **2016**, *138*, 306–312.

Intracellular miRNA detection

Upconversion towards intracellular miRNA detection

DNA-driven self-assembled pyramids



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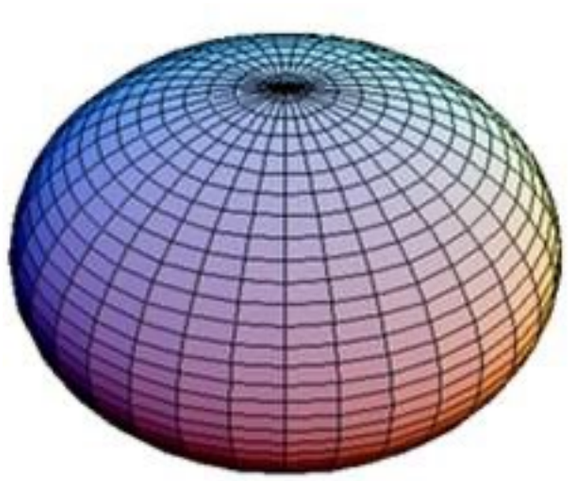
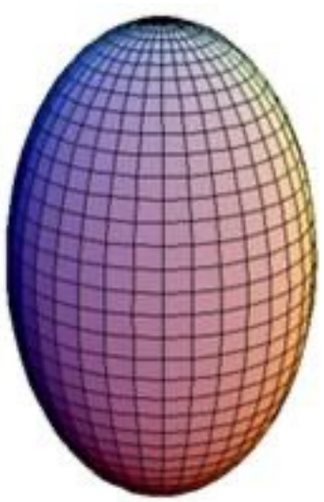


Oblate spheroid



Prolate spheroid

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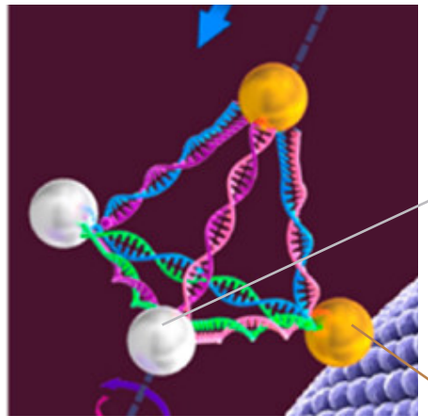
Intracellular miRNA detection

Upconversion towards intracellular miRNA detection

DNA-driven self-assembled pyramids



Au-UCNP pyramids

UCNP: $NaGdF_4:Yb^{3+}, Er^{3+}$

- *Superior photostability*
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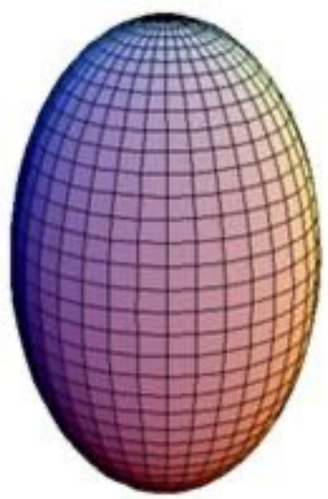
Au NP

- *Prolate geometry*
- *Target pyramids exhibit **chiroptical** activities*



Prolate spheroid

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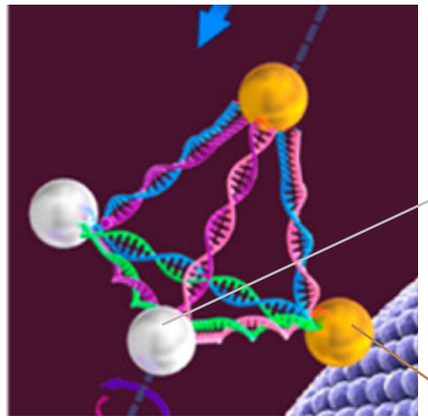
Intracellular miRNA detection

Upconversion towards intracellular miRNA detection

DNA-driven self-assembled pyramids



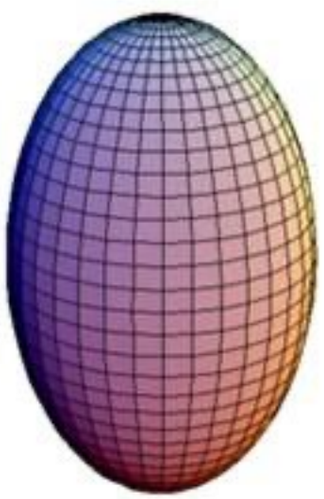
Au-UCNP pyramids

UCNP: $NaGdF_4:Yb^{3+}, Er^{3+}$

- *Superior photostability*
- *High signal-to-noise ratio*
- ***Does <u>not</u> exhibit dichroism signal***

Au NP

- *Prolate geometry*
- *Target pyramids exhibit **chiroptical** activities*
- ***Emits circular dichroism signal***



Prolate spheroid

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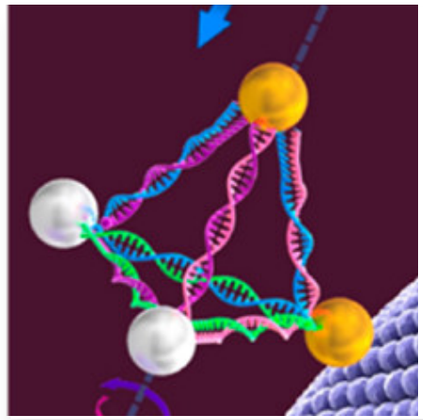
Intracellular miRNA detection

Upconversion towards intracellular miRNA detection

DNA-driven self-assembled pyramids



Au-UCNP pyramids

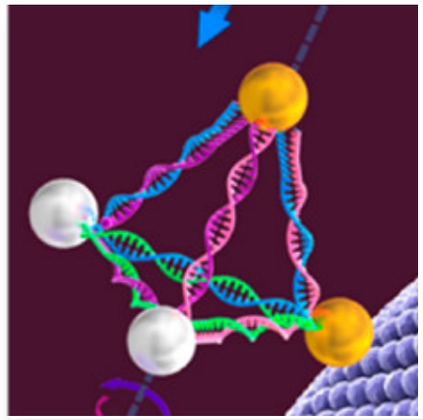
DNA: distance tether

Li, S., Xu, L., Ma, W., Wu, X., Sun, M., Huang, H., Wang, L., Kotov, N. A., Xu, C. *J. Am. Chem. Soc.* **2016**, *138*, 306–312.

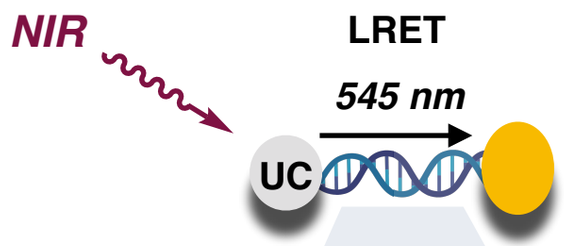
Intracellular miRNA detection

Upconversion towards intracellular miRNA detection

DNA-driven self-assembled pyramids



Au-UCNP pyramids



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Intracellular miRNA detection

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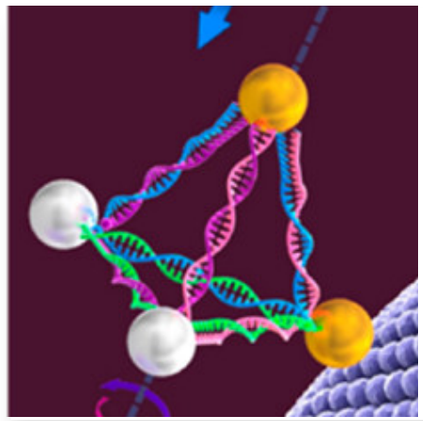

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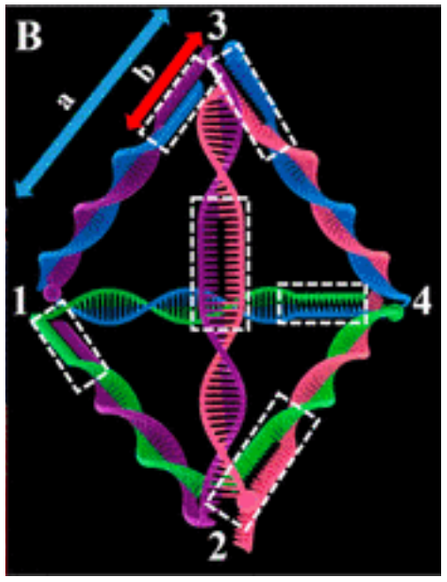
Intracellular miRNA detection

Upconversion towards intracellular miRNA detection

- ***Inside the cell:***

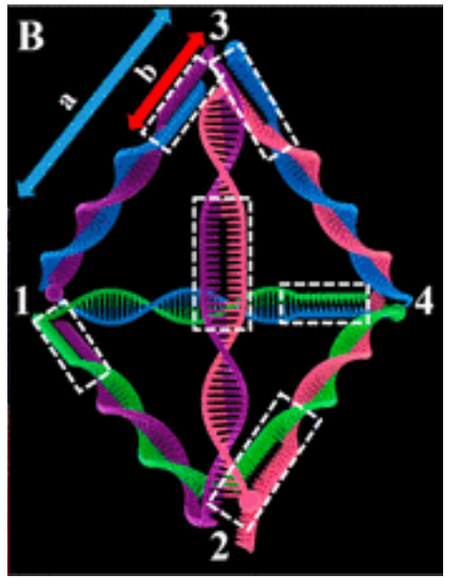


Li, S., Xu, L., Ma, W., Wu, X., Sun, M., Huang, H., Wang, L., Kotov, N. A., Xu, C. *J. Am. Chem. Soc.* **2016**, *138*, 306–312.

Intracellular miRNA detection

Upconversion towards intracellular miRNA detection

- ***Inside the cell:***



DNA-Py1	*TTTTCAACATCAGTCTGATAAGCTACTGTTCTTTCCCTCAACATCAG*
	TCTGATAAGCTACGGTTTTCAACATCAGTCTGATAAGCTACTTGAC
DNA-Py2	*TTTCCGTAGCTTATCAGTTAAGCTAGGGTTTCATTAATCAACATCAG*
	TTCGATAAGCTATTTTCAACATCAGTCTGATAAGCTACAACTT
DNA-Py3	*TTTACTAAGCGATTACTGATGTTGATTAATGTTTACAACATCAGTCTG*
	ATAAGCTAACTGATTTTGAACAGTAGCTTATCAGGACTCGTGGTC
DNA-Py4	*TTTAAGTTGTAGCTTATCAGCTGACTACATTTTTGTCAAGTAGCTTAT*
	CAGTTACAGCTCGCTTTATCAGTTAGCTTATCAGAGATCGTAGCT

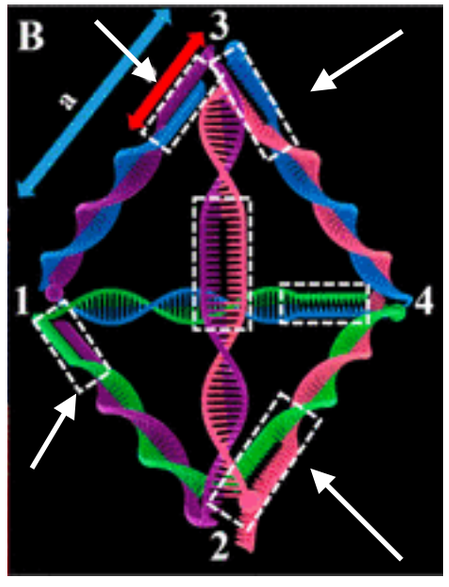
Sequences complementary to target miRNA

Li, S., Xu, L., Ma, W., Wu, X., Sun, M., Huang, H., Wang, L., Kotov, N. A., Xu, C. *J. Am. Chem. Soc.* **2016**, *138*, 306–312.

Intracellular miRNA detection

Upconversion towards intracellular miRNA detection

- ***Inside the cell:***



DNA-Py1	*TTTTCAACATCAGTCTGATAAGCTACTGTTCTTTCCCTCAACATCAG*
	TCTGATAAGCTACGGTTTTCAACATCAGTCTGATAAGCTACTTGAC
DNA-Py2	*TTTCCGTAGCTTATCAGTTAAGCTAGGGTTTCATTAATCAACATCAG*
	TTCGATAAGCTATTTTCAACATCAGTCTGATAAGCTACAACTT
DNA-Py3	*TTTACTAAGCGATTACTGATGTTGATTAATGTTTACAACATCAGTCTG*
	ATAAGCTAACTGATTTTGAACAGTAGCTTATCAGGACTCGTGGTC
DNA-Py4	*TTTAAGTTGTAGCTTATCAGCTGACTACATTTTTGTCAAGTAGCTTAT*
	CAGTTACAGCTCGCTTTATCAGTTAGCTTATCAGAGATCGTAGCT

Non-complemented DNA base pairs

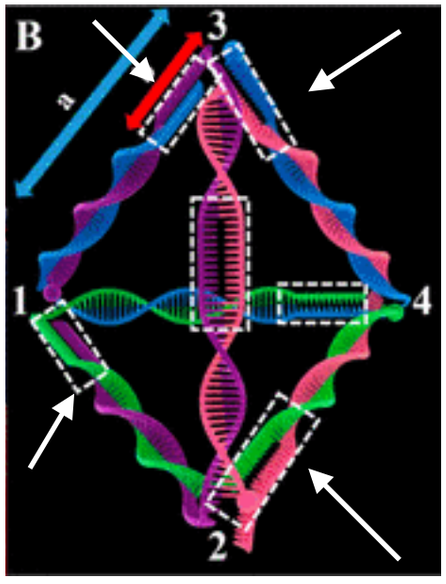
Sequences complementary to target miRNA

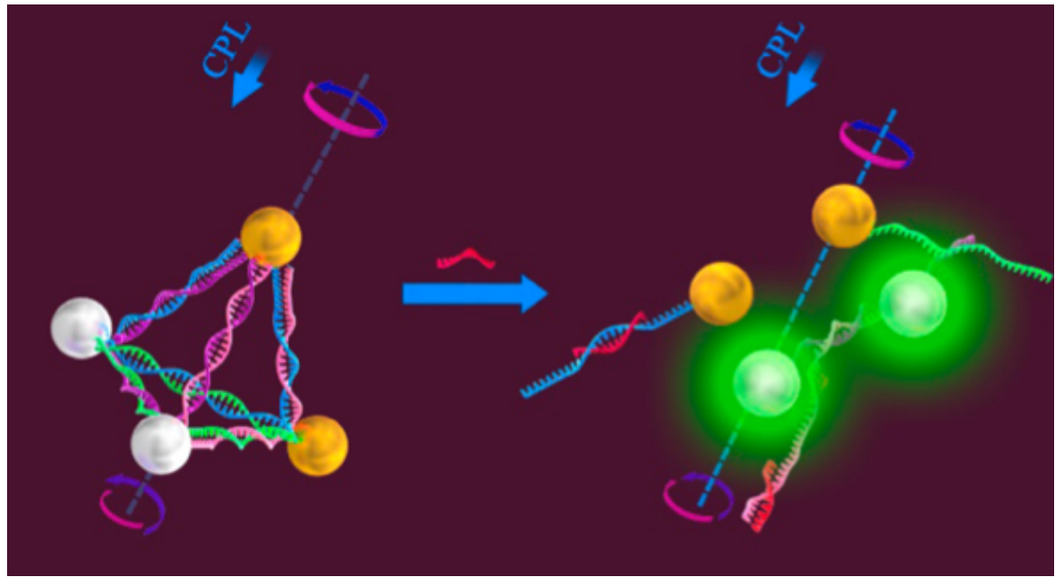
Li, S., Xu, L., Ma, W., Wu, X., Sun, M., Huang, H., Wang, L., Kotov, N. A., Xu, C. *J. Am. Chem. Soc.* **2016**, *138*, 306–312.

Intracellular miRNA detection

Upconversion towards intracellular miRNA detection

- ***Inside the cell:***





target miRNA binding

induces disassembly

Non-complemented

DNA base pairs

Sequences complementary to target miRNA

Li, S., Xu, L., Ma, W., Wu, X., Sun, M., Huang, H., Wang, L., Kotov, N. A., Xu, C. *J. Am. Chem. Soc.* **2016**, *138*, 306–312.

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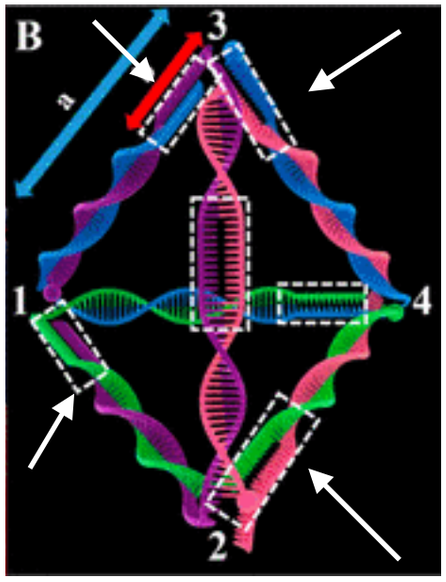

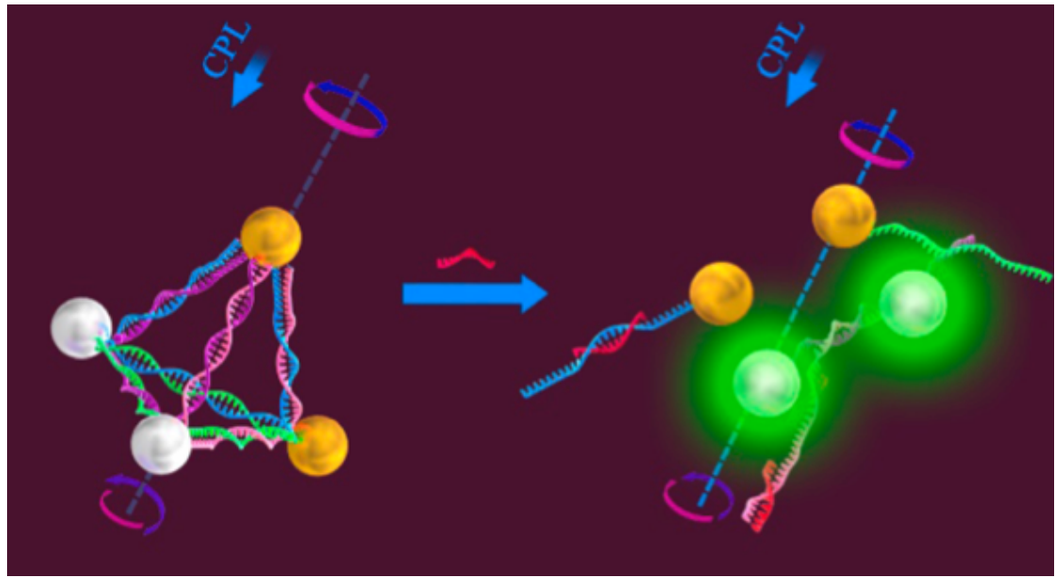

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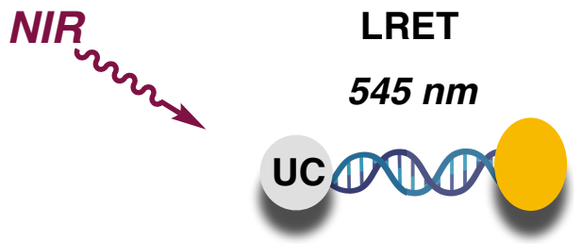

Non-complemented

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Intracellular miRNA detection

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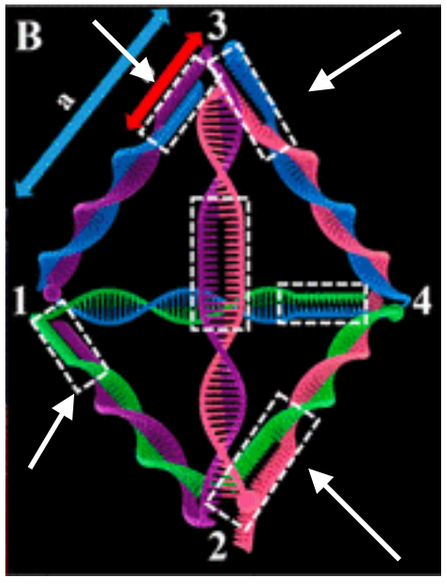
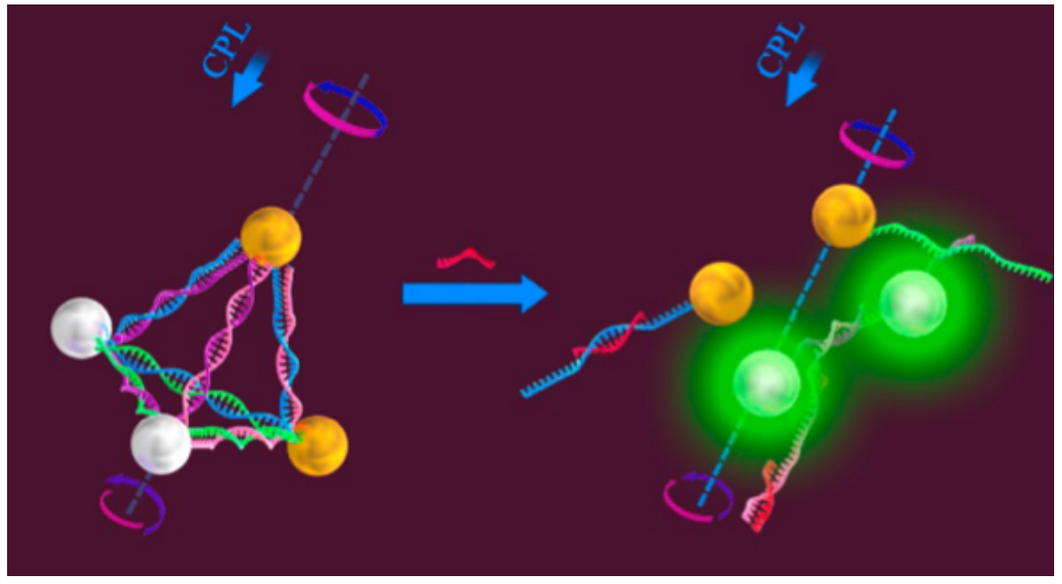
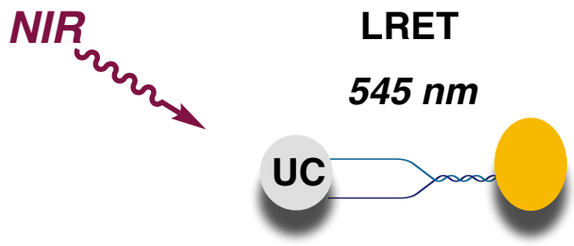




target miRNA binding

induces disassembly



Non-complemented

DNA base pairs

Sequences complementary to target miRNA

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Intracellular miRNA detection

Upconversion towards intracellular miRNA detection

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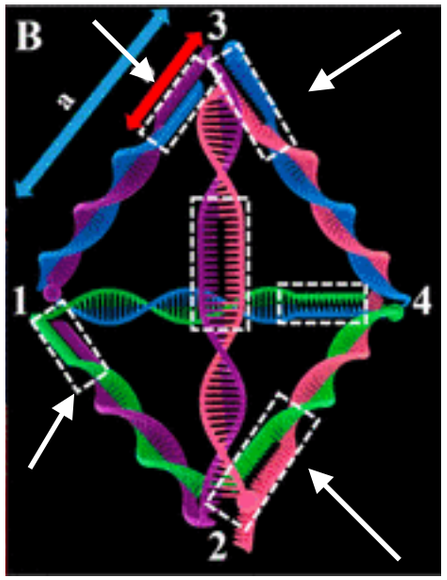
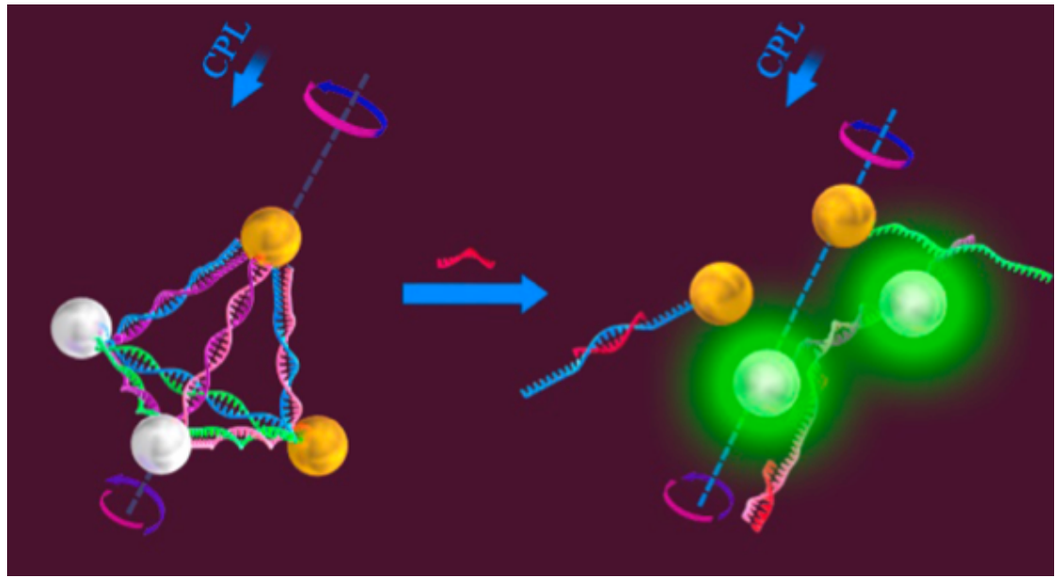
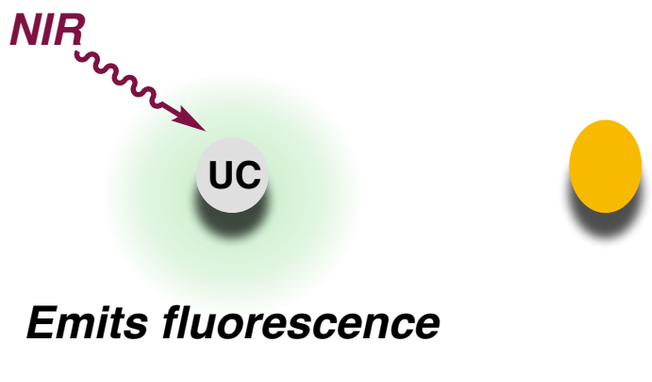




target miRNA binding

induces disassembly



Emits fluorescence

Non-complemented

DNA base pairs

Sequences complementary to target miRNA

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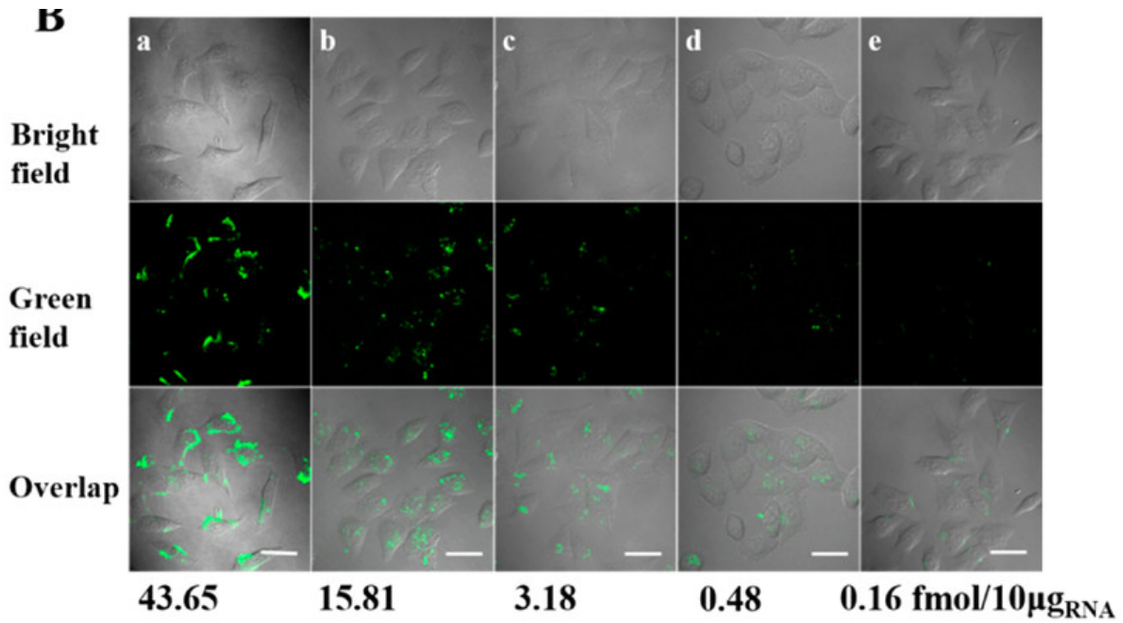
Intracellular miRNA detection

Upconversion towards intracellular miRNA detection

- ***Inside the cell:***

Live cell

Fluorescence imaging



Concentration gradient miRNA

Li, S., Xu, L., Ma, W., Wu, X., Sun, M., Huang, H., Wang, L., Kotov, N. A., Xu, C. *J. Am. Chem. Soc.* **2016**, *138*, 306–312.

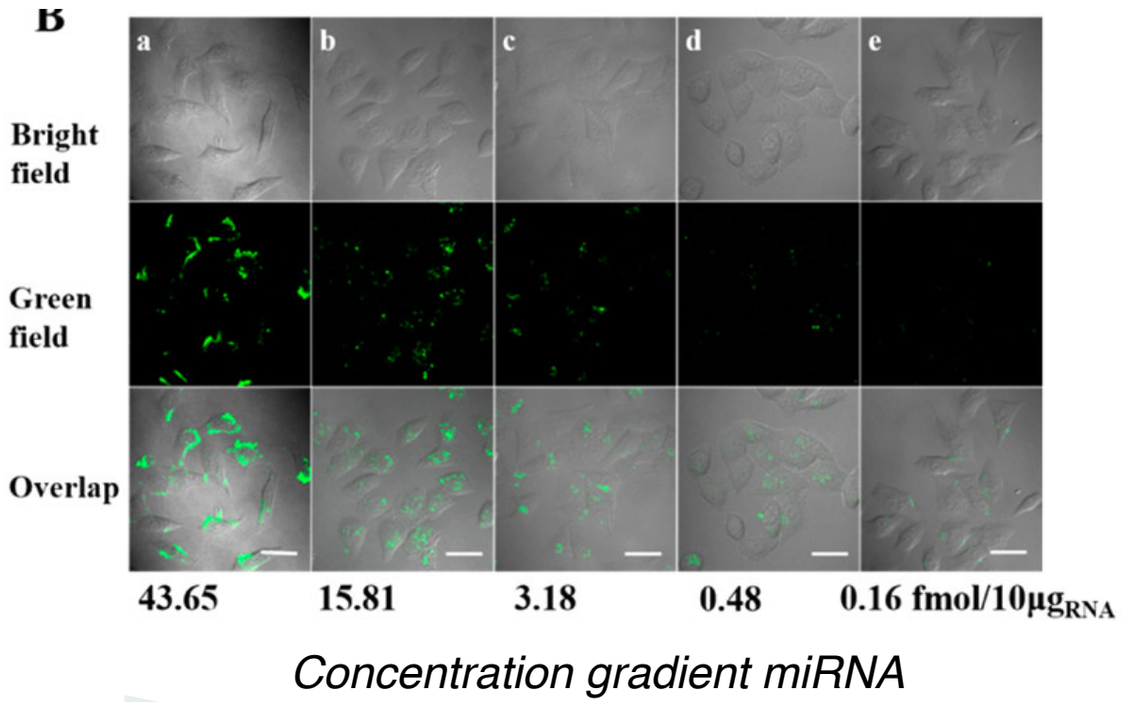
Intracellular miRNA detection

Upconversion towards intracellular miRNA detection

- ***Inside the cell:***

Live cell

Fluorescence imaging



Concentration gradient miRNA

Greatest fluorescence emission correlates to [miRNA]

Li, S., Xu, L., Ma, W., Wu, X., Sun, M., Huang, H., Wang, L., Kotov, N. A., Xu, C. *J. Am. Chem. Soc.* **2016**, *138*, 306–312.

Intracellular miRNA detection

Upconversion towards intracellular miRNA detection

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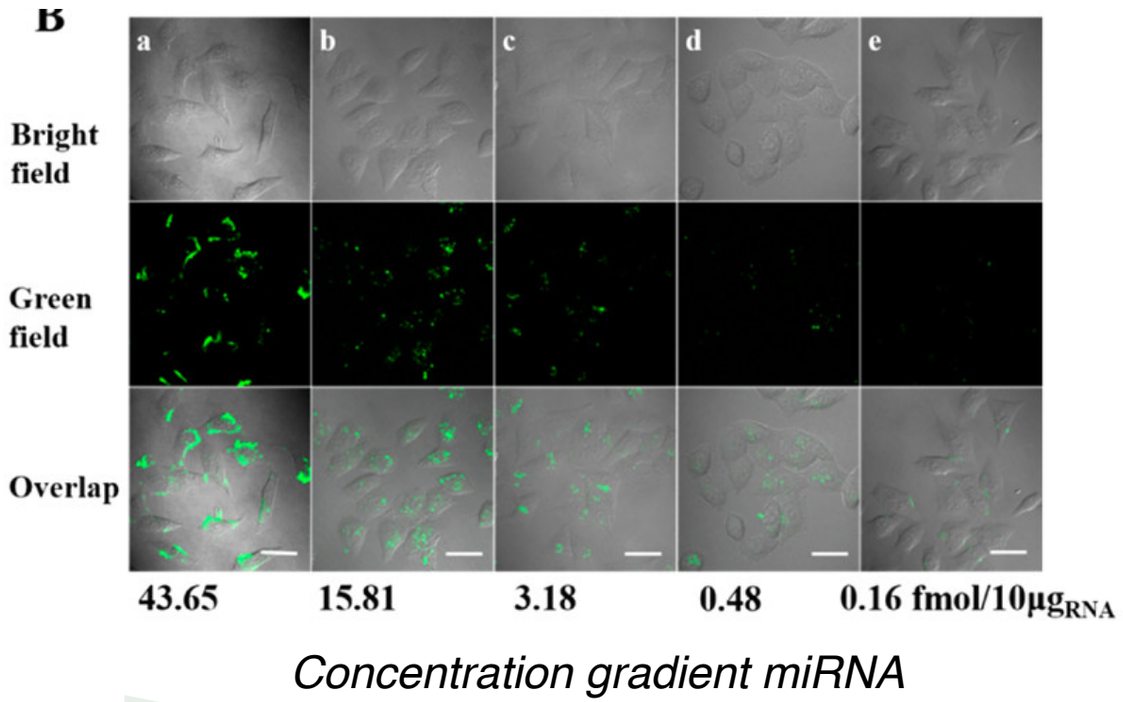
Live cell

Fluorescence imaging



Concentration gradient miRNA

Greatest fluorescence emission correlates to [miRNA]

✔ ***Upconversion fluorescence induced by miRNA binding***

Li, S., Xu, L., Ma, W., Wu, X., Sun, M., Huang, H., Wang, L., Kotov, N. A., Xu, C. *J. Am. Chem. Soc.* **2016**, *138*, 306–312.

Overview

Upconversion in Organic Materials

Upconversion in near-IR (NIR) and Visible light photocatalysis

Upconversion in Inorganic Materials

Overview

Upconversion in Organic Materials

Upconversion in near-IR (NIR) and Visible light photocatalysis

Upconversion in Inorganic Materials

Questions

Applications of upconversion

Fluorescence Φ

$$\textit{Quantum yield } \Phi = \frac{\textit{\# photons } \textbf{\textit{emitted}}}{\textit{\# photons } \textbf{\textit{absorbed}}}$$

Processes which decrease Fluorescence Φ

1. *Intersystem crossing (ISC)*
2. *Förster resonance energy transfer*
3. *Internal conversion*