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OMICS Group is an amalgamation of Open Access publications and worldwide international science conferences and events. Established in the year 2007 with the sole aim of making the information on Sciences and technology 'Open Access', OMICS Group publishes 500 online open access scholarly journals in all aspects of Science, Engineering, Management and Technology journals. OMICS Group has been instrumental in taking the knowledge on Science & technology to the doorsteps of ordinary men and women. Research Scholars, Students, Libraries, Educational Institutions, Research centers and the industry are main stakeholders that benefitted greatly from this knowledge dissemination. OMICS Group also organizes 500 International conferences annually across the globe, where knowledge transfer takes place through debates, round table discussions, poster presentations, workshops, symposia and exhibitions.

About OMICS International Conferences

OMICS International is a pioneer and leading science event organizer, which publishes around 500 open access journals and conducts over 500 Medical, Clinical, Engineering, Life Sciences, Pharma scientific conferences all over the globe annually with the support of more than 1000 scientific associations and 30,000 editorial board members and 3.5 million followers to its credit.

OMICS Group has organized 500 conferences, workshops and national symposiums across the major cities including San Francisco, Las Vegas, San Antonio, Omaha, Orlando, Raleigh, Santa Clara, Chicago, Philadelphia, Baltimore, United Kingdom, Valencia, Dubai, Beijing, Hyderabad, Bengaluru and Mumbai.

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Monitoring disassembly of biodegradable nanoparticles designed for targeted delivery

Michael Chorny, Ph.D.

The Cardiology Research Laboratory

Perelman School of Medicine at the University of Pennsylvania &

The Children's Hospital of Philadelphia

Polylactide (particle-forming material)

Polylactide (PLA) is a synthetic, nontoxic, biodegradable aliphatic polyester. The biodegradation products of aliphatic polyesters are nontoxic, noncarcinogenic, and nonteratogenic. Due to their safety and biodegradability, these polymers are used to formulate implantable and injectable drug delivery systems for human and veterinary use.

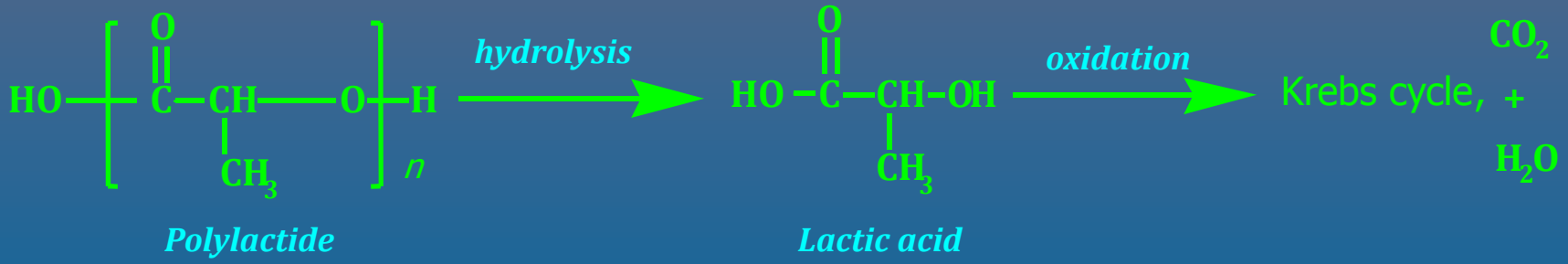
(Handbook of Pharmaceutical Excipients)

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Polymer biodegradation:



An ideal quantitative approach should

An ideal quantitative approach <u>should</u>

- ***give best approximation of the overall degradation status of polymeric NP***

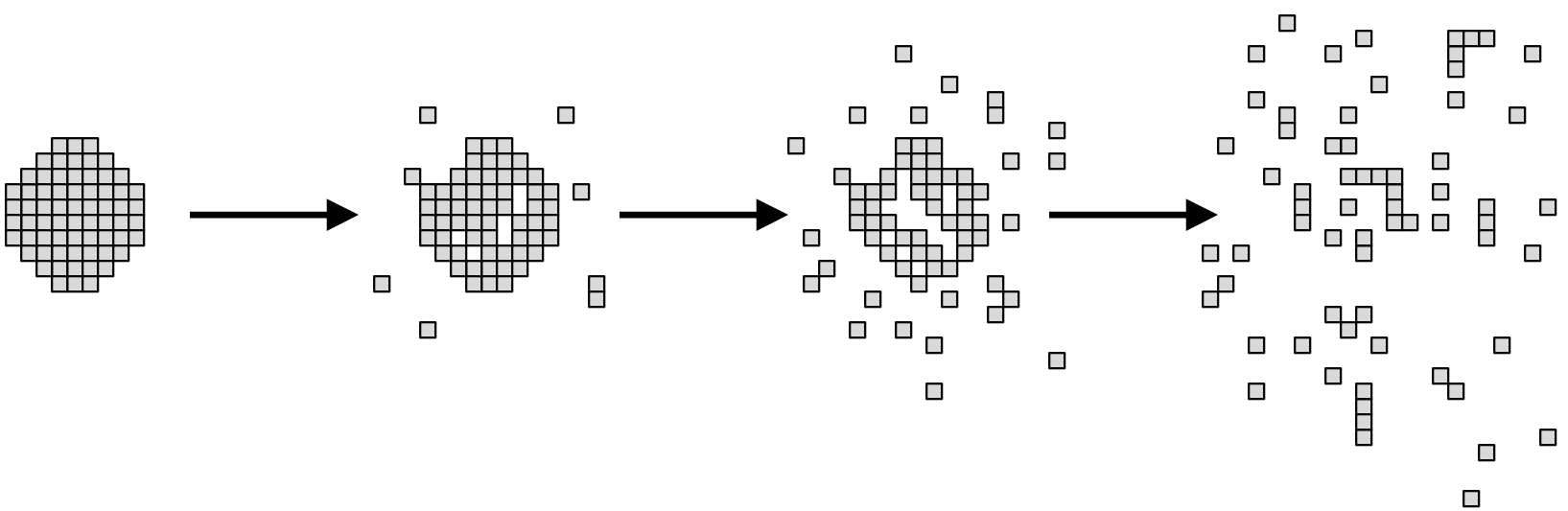
An ideal quantitative approach should

- *give best approximation of the overall degradation status of polymeric NP*
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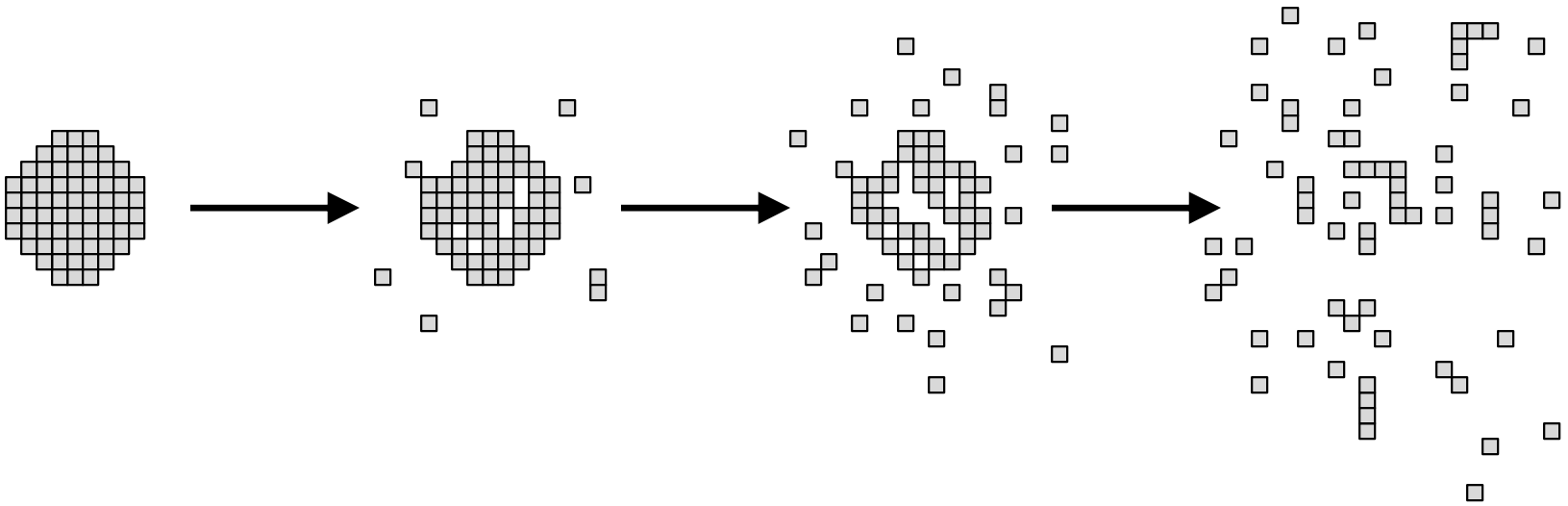
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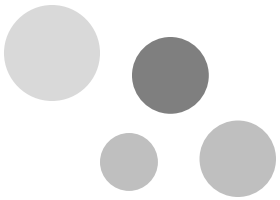
- *give best approximation of the overall degradation status of polymeric NP*
- *allow real-time kinetic measurements without the need for time-consuming sample preparation*
- *be potentially applicable to live cells (or live animals), as well as in vitro*

Simplified model of NP degradation (building blocks)

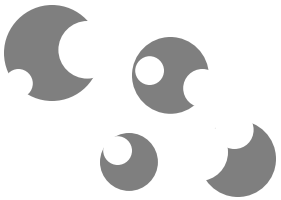


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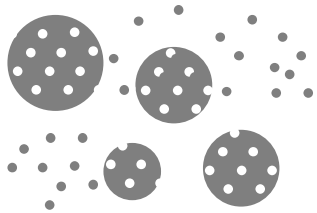




changes in Mw

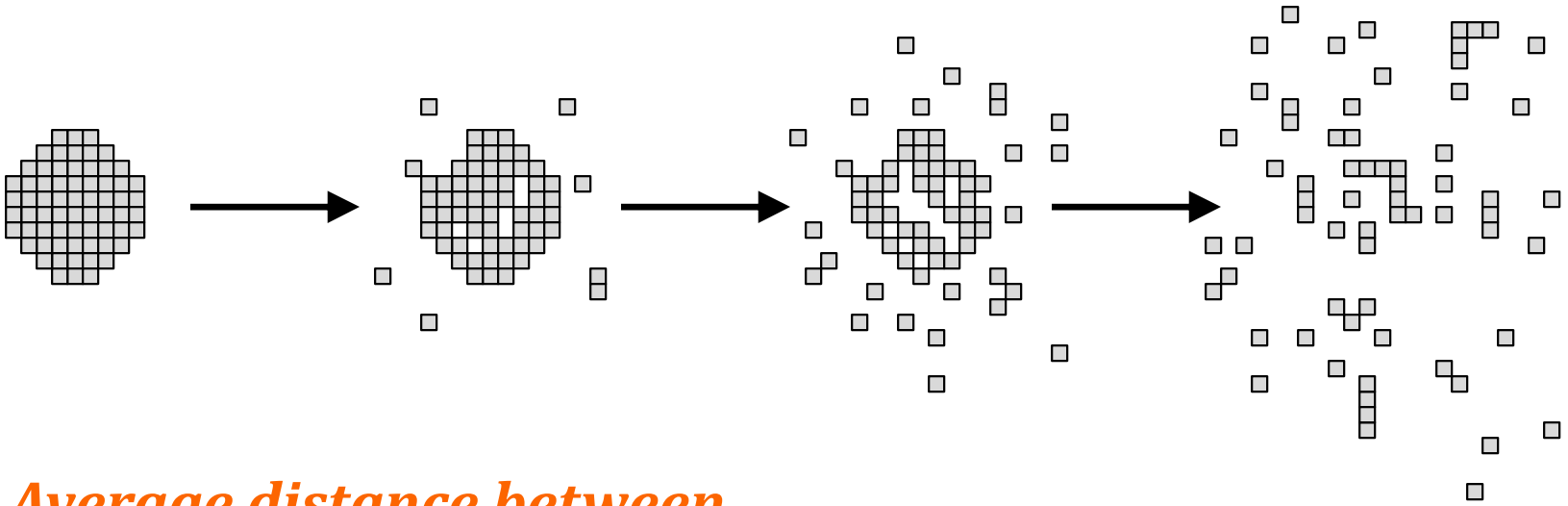


NP weight loss



polymer decomposition

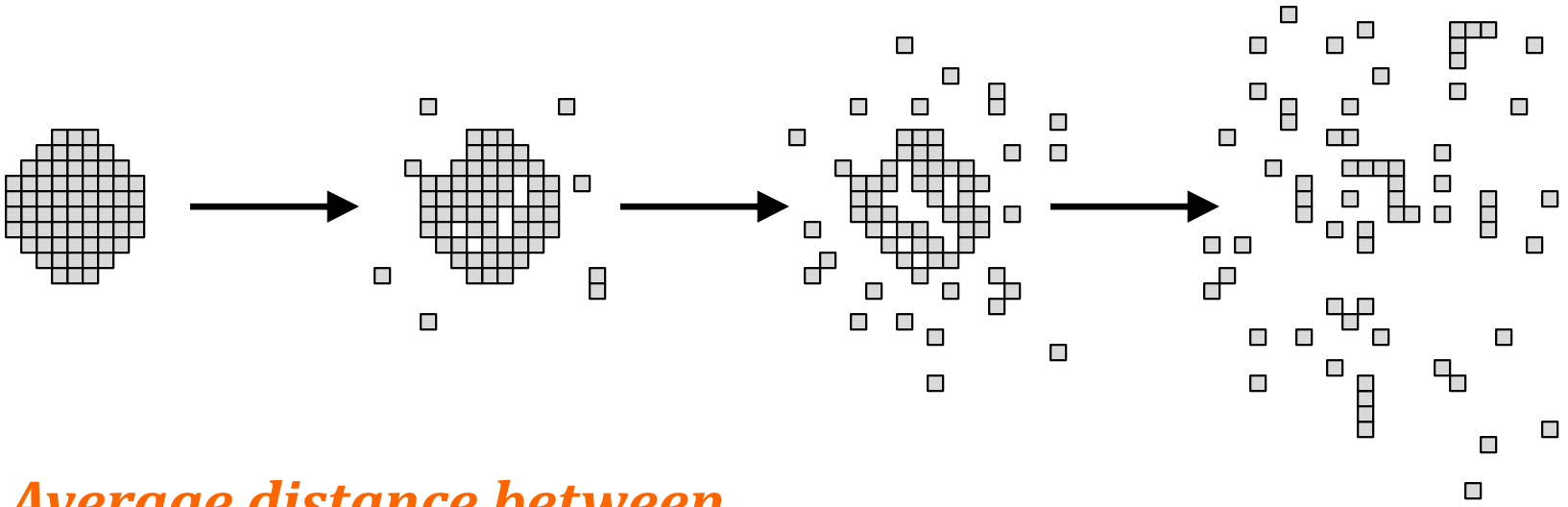
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Average distance between building blocks:

$\Leftrightarrow$

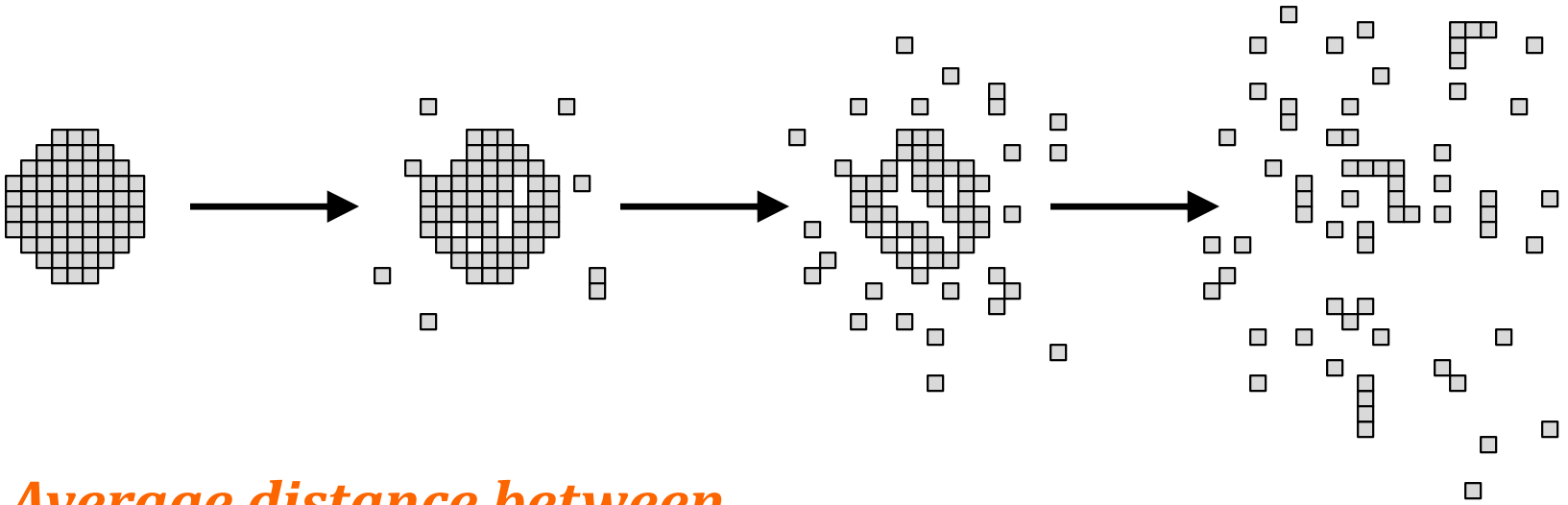
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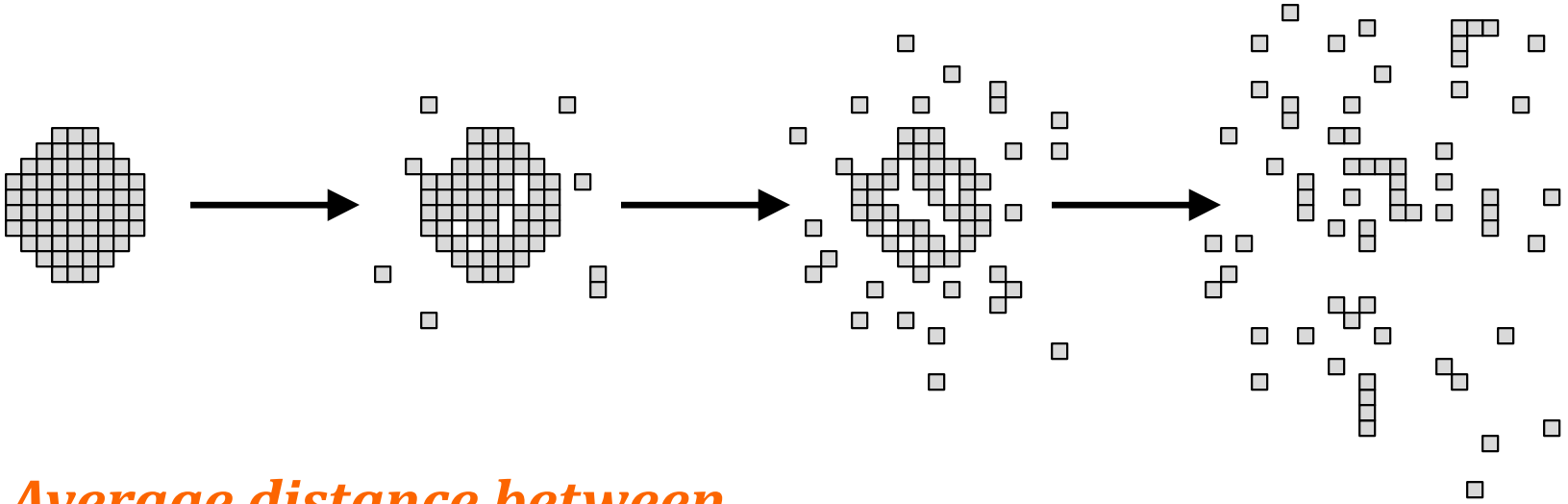
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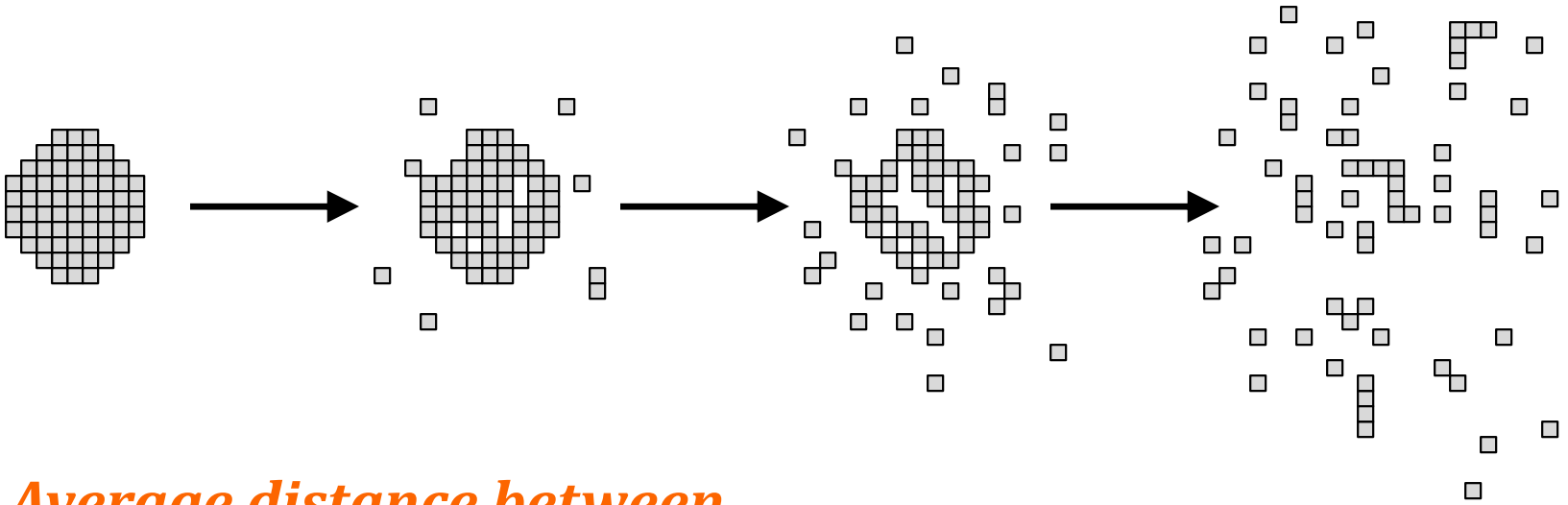


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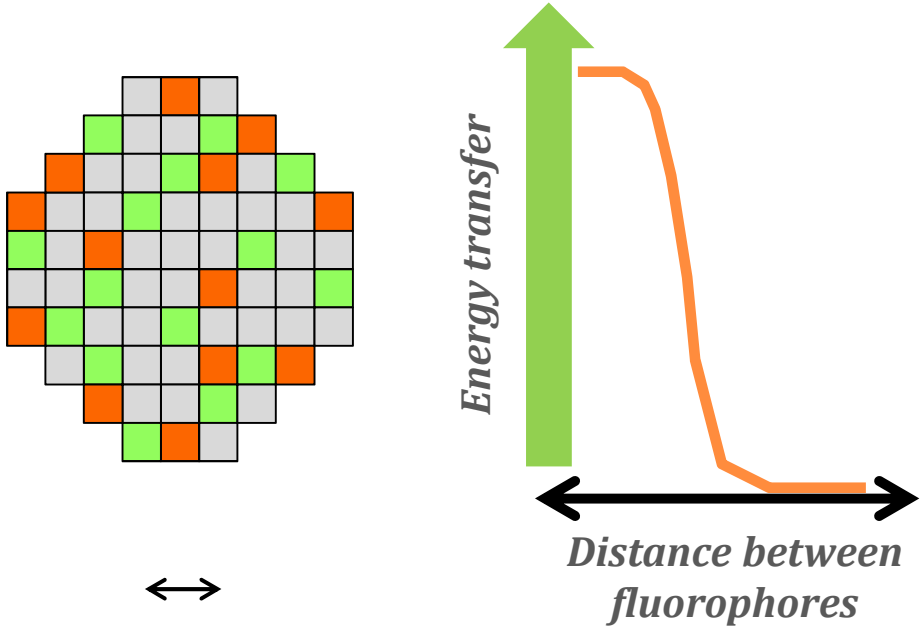


Requires a "ruler" that can reliably measure distances on this scale in real time…

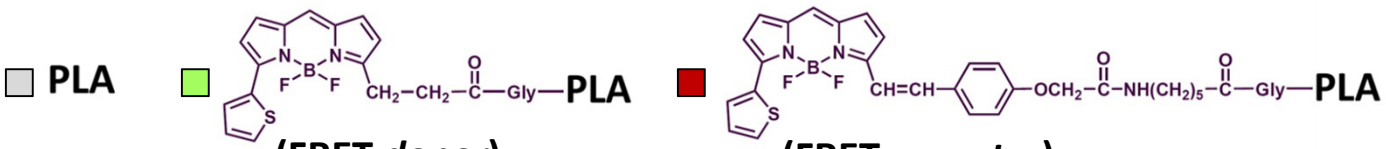
FRET applied to NP degradation according to the 'building blocks' model

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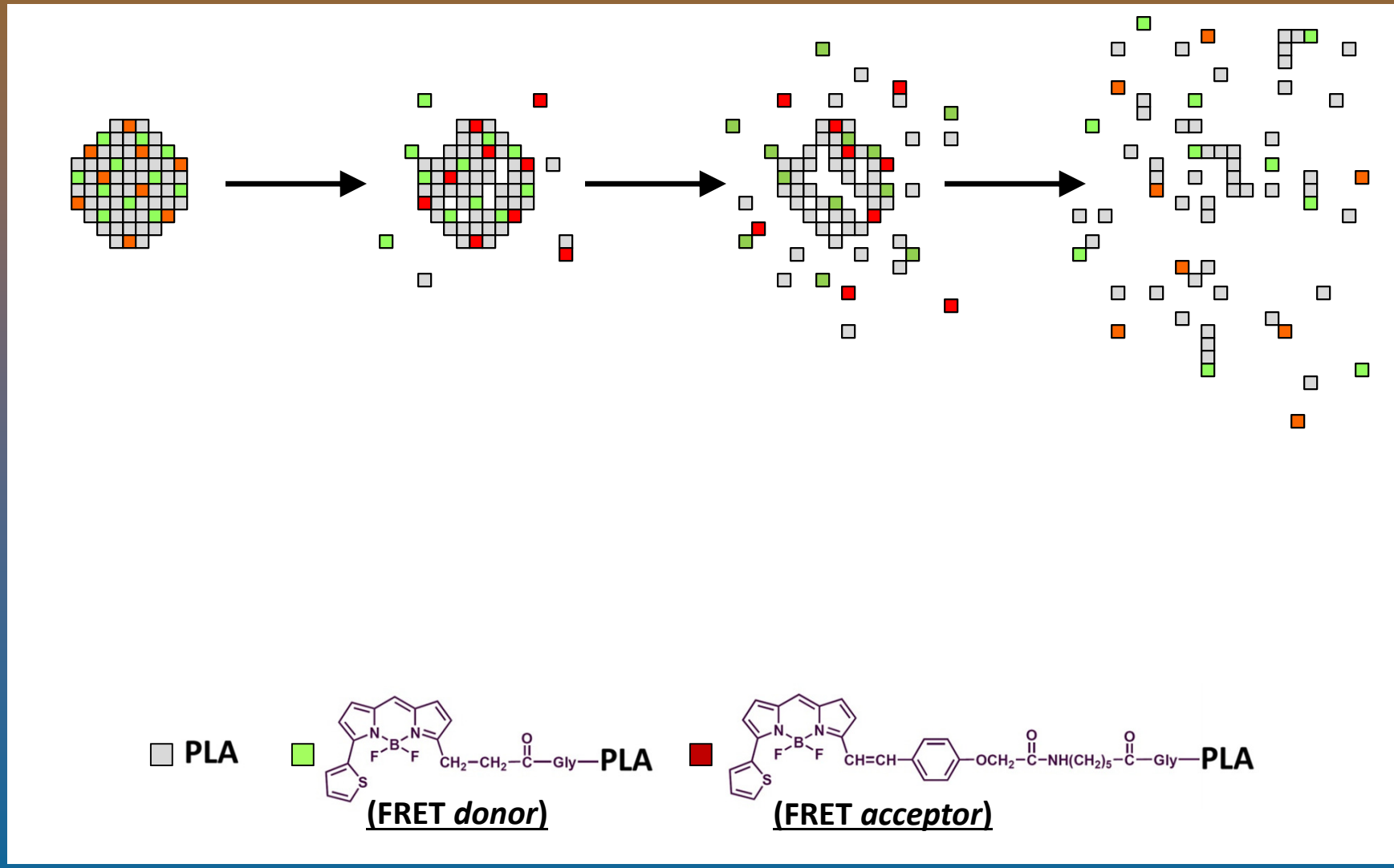
- Förster Resonance Energy Transfer (FRET) is a radiationless energy transfer mechanism between two (donor and acceptor) fluorophores in close proximity (typically < 10 nm).
- Transfer efficiency is extremely sensitive to the separation distance between the fluorophores, and thus can be used as a ruler.



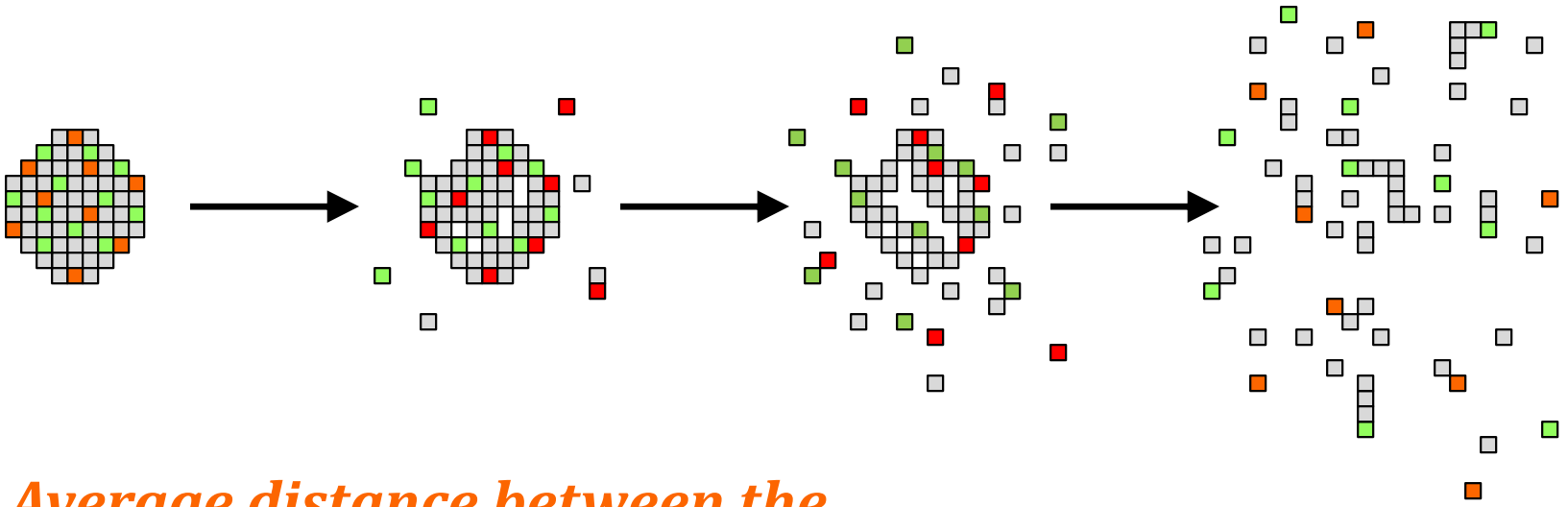
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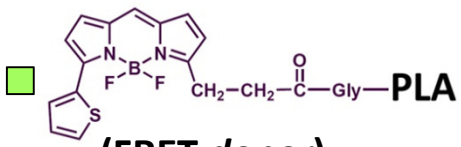
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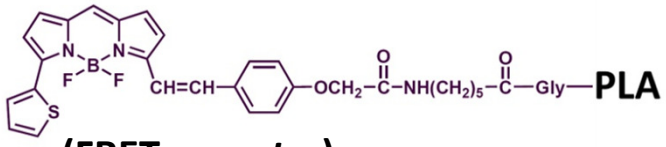
Average distance between the fluorescent-labeled blocks:



PLA

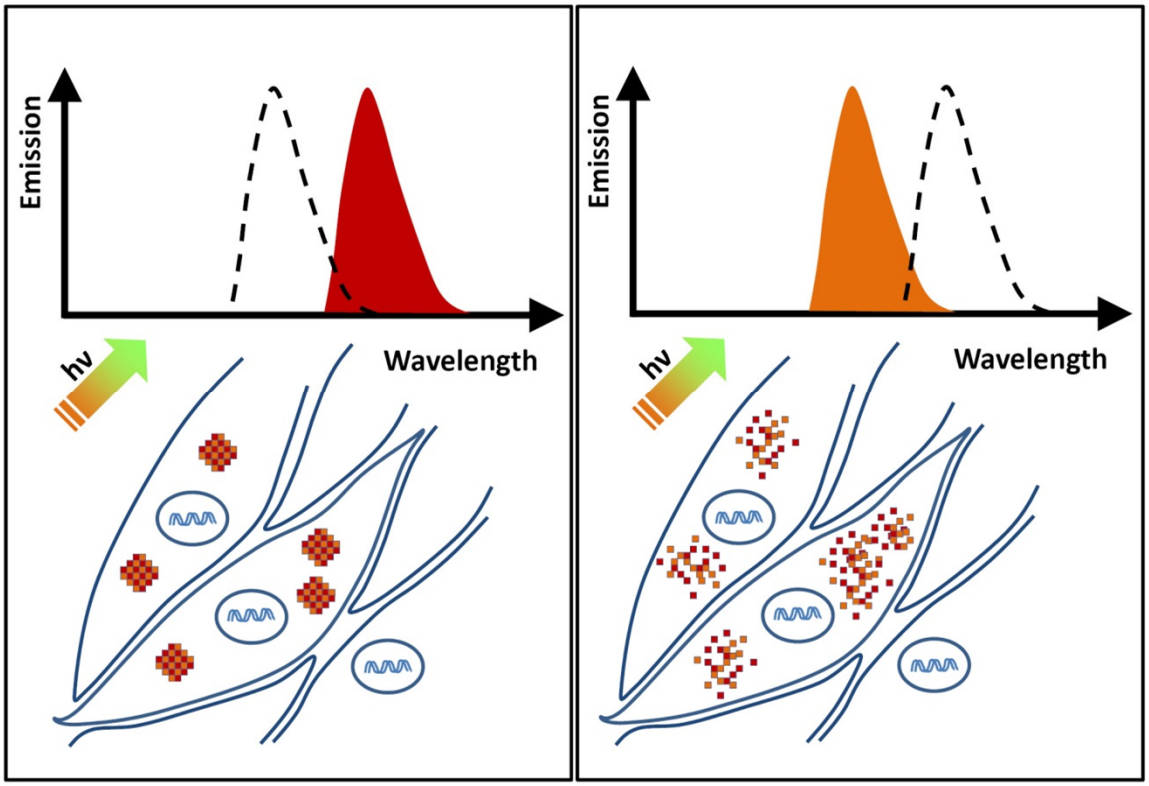


(FRET *donor*)

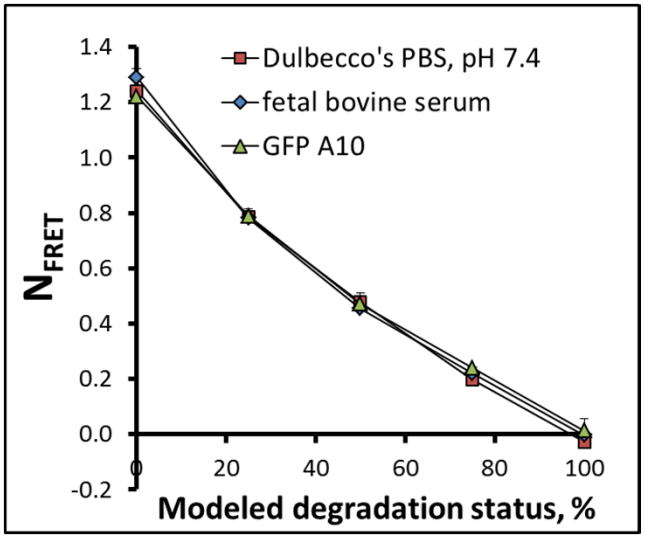


(FRET *acceptor*)

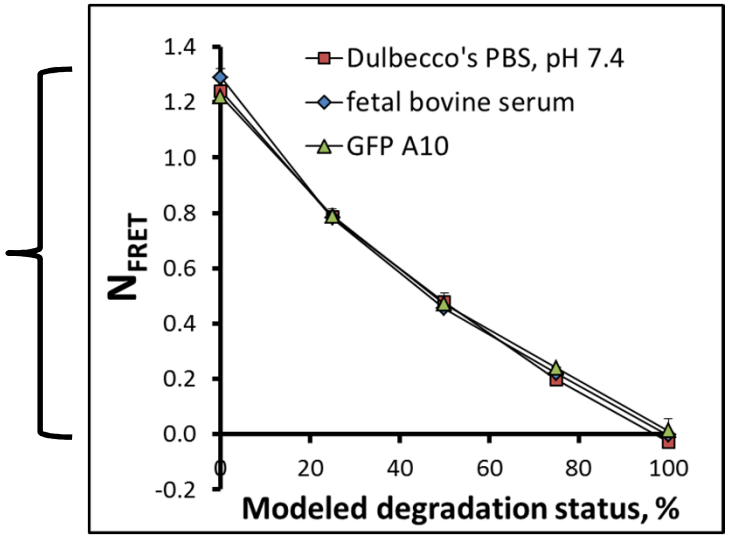
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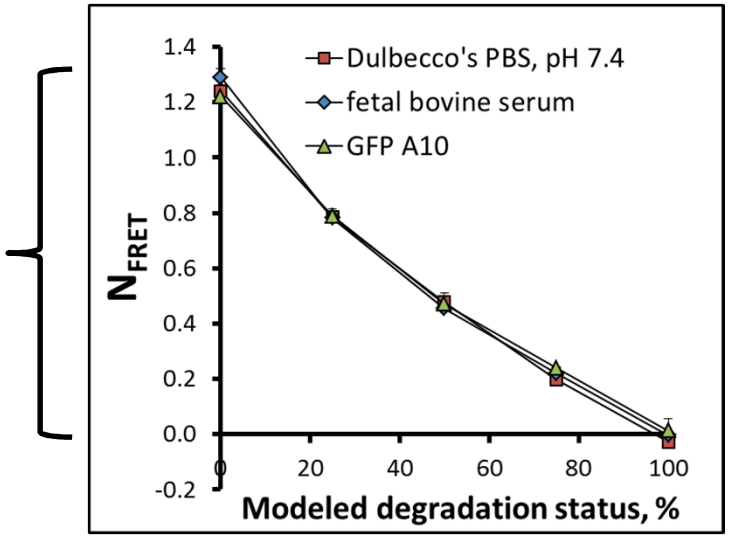
FRET-based assay of MNP disassembly

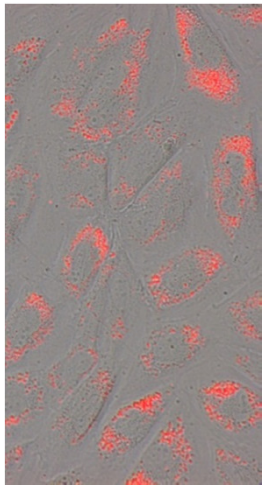


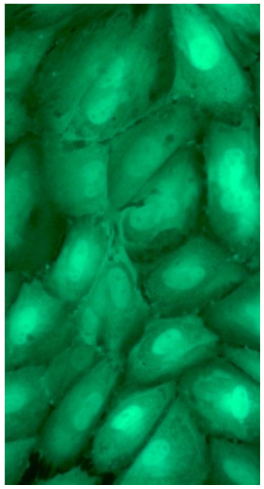
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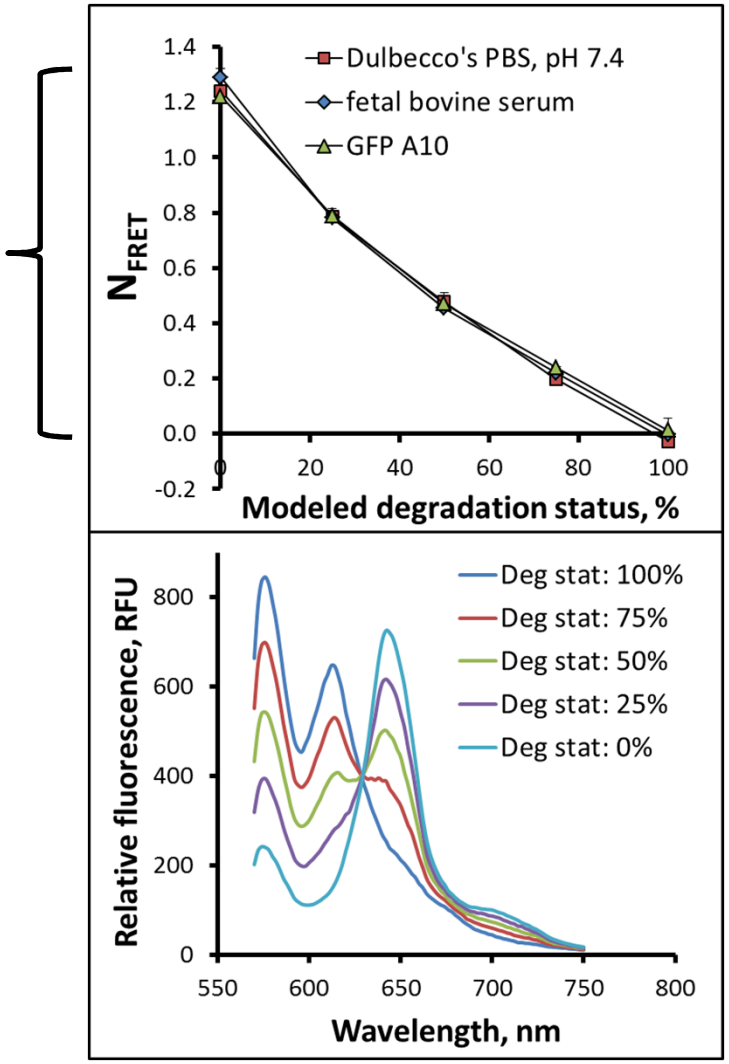
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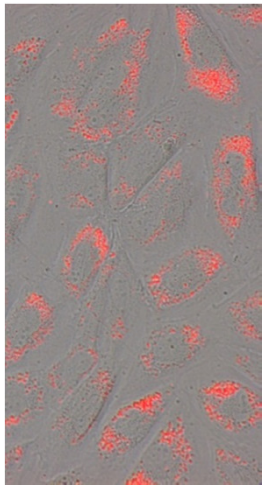


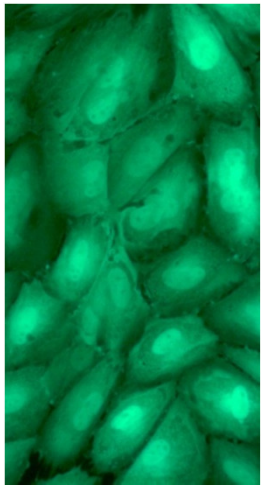




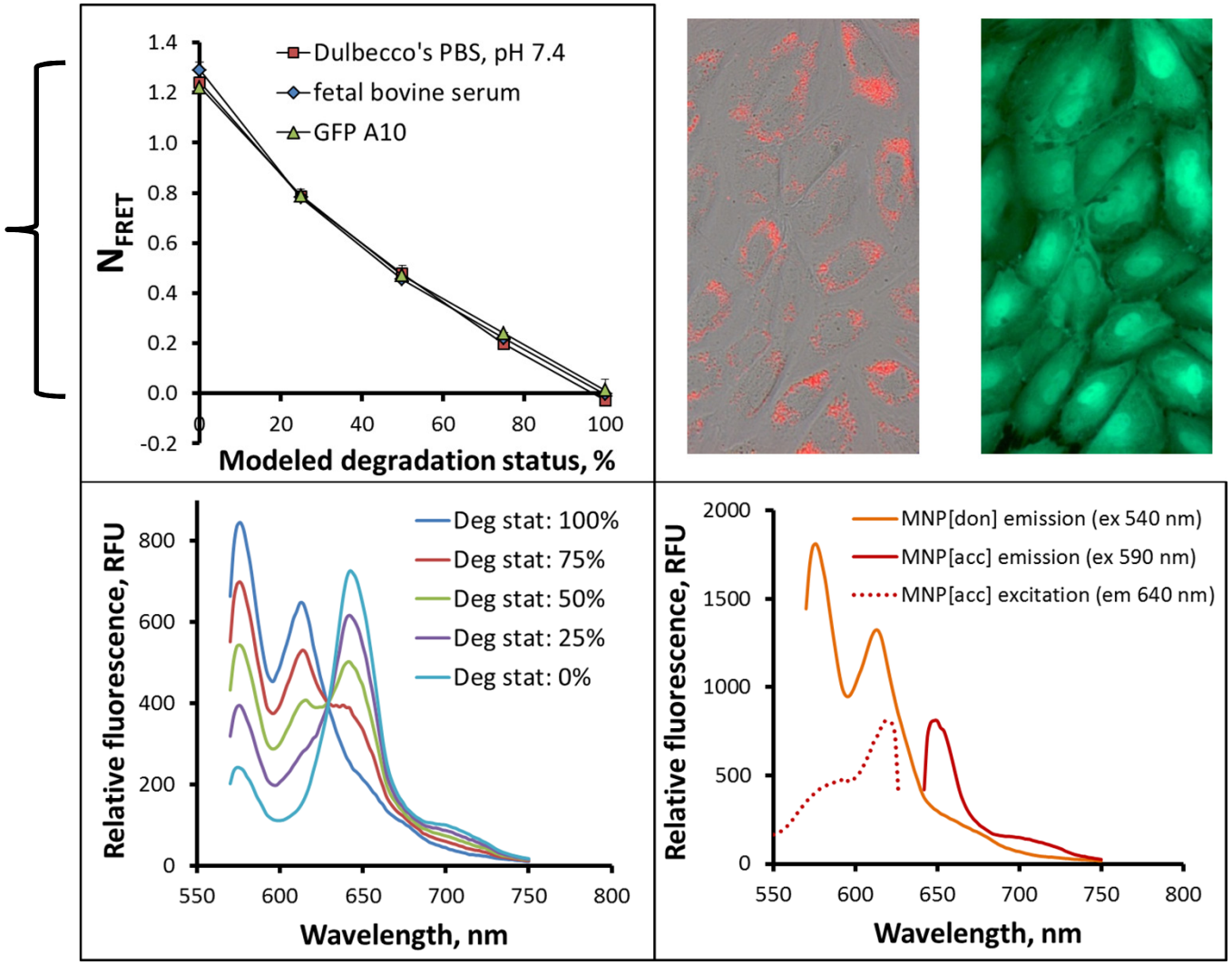
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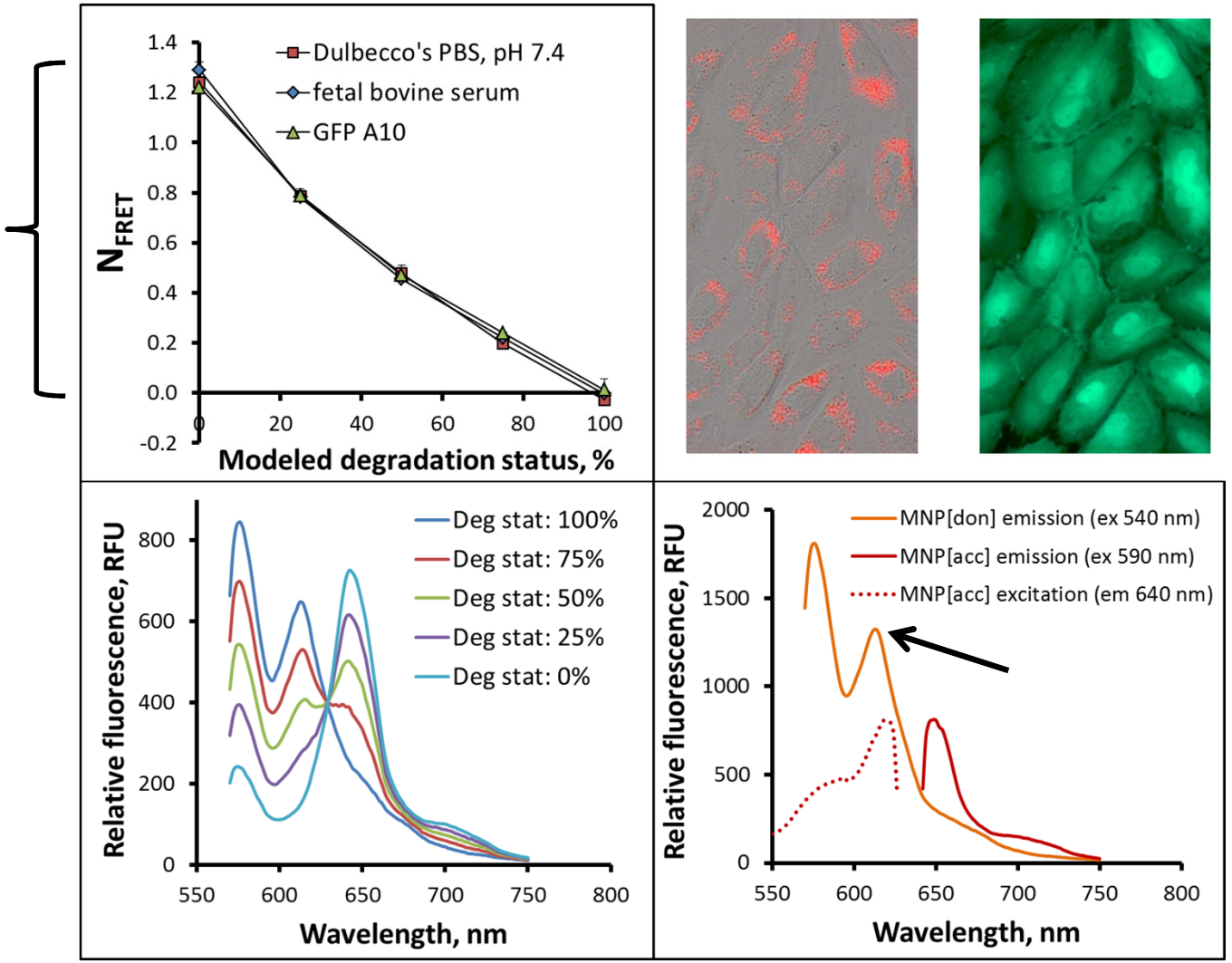




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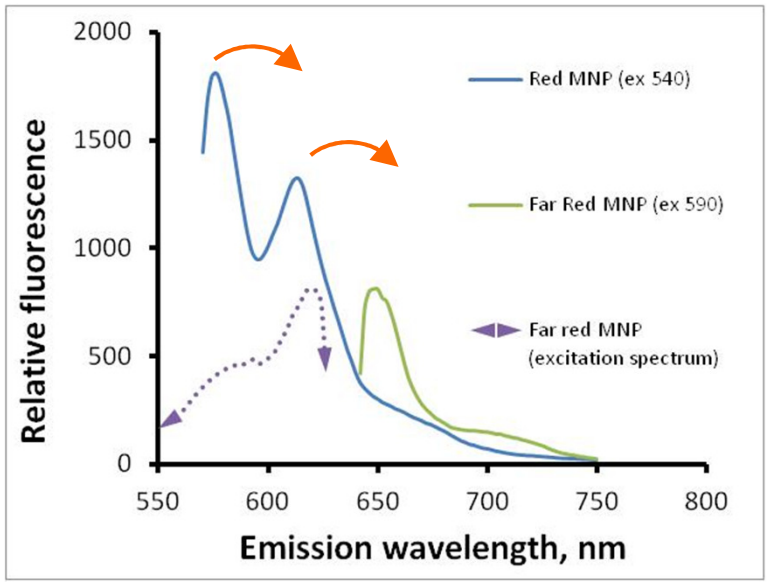
FRET-based assay of MNP disassembly



Two-step energy transfer improves dynamic range and sensitivity of the FRET-based assay

Spectra

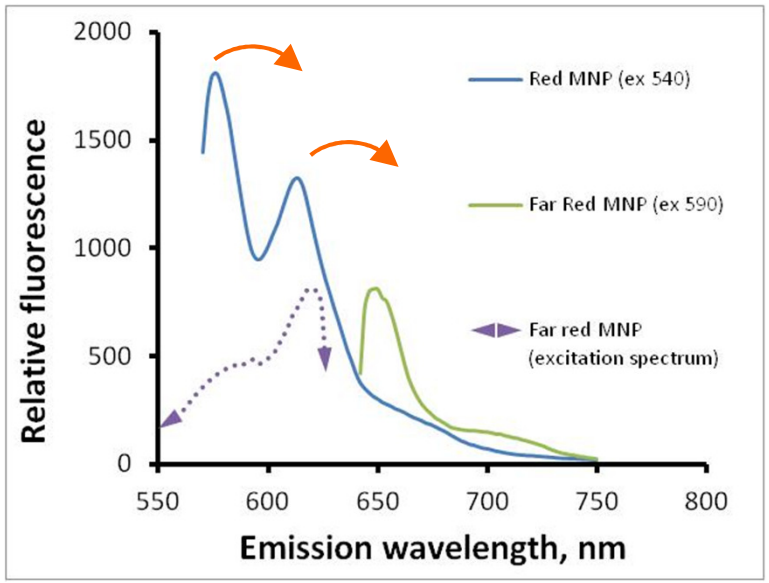
Singly labeled MNP spectra overlaid



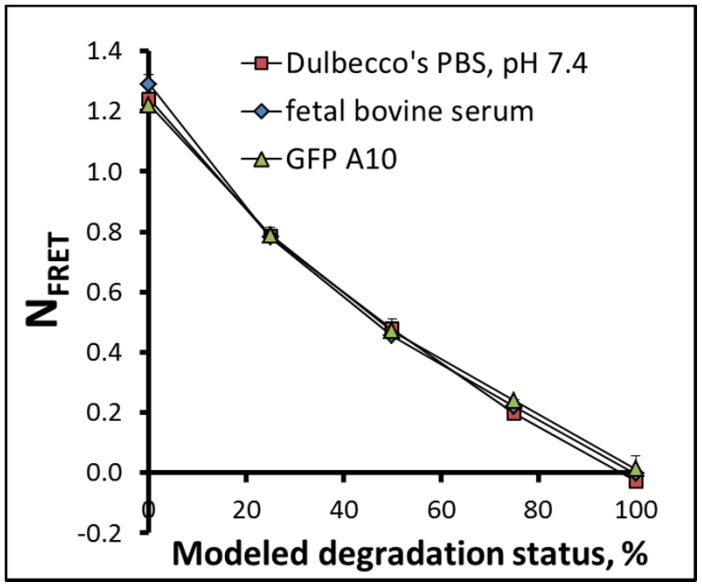
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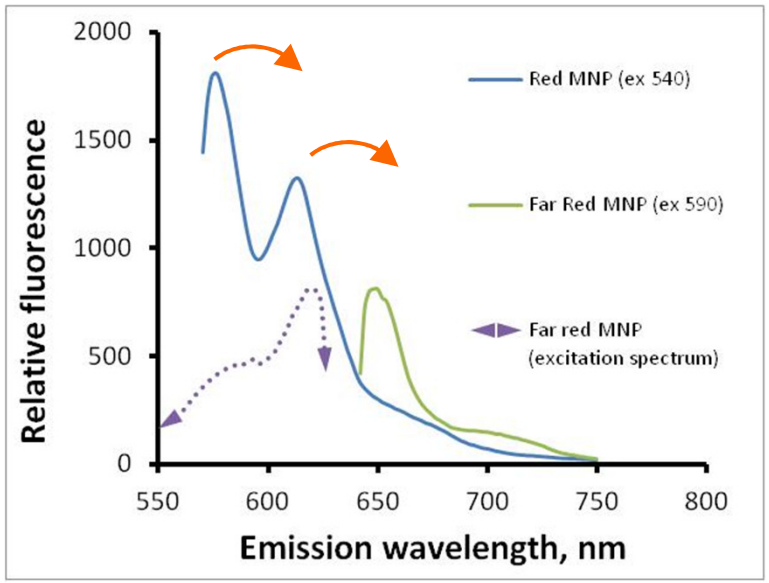
Co-labeled nanoparticles



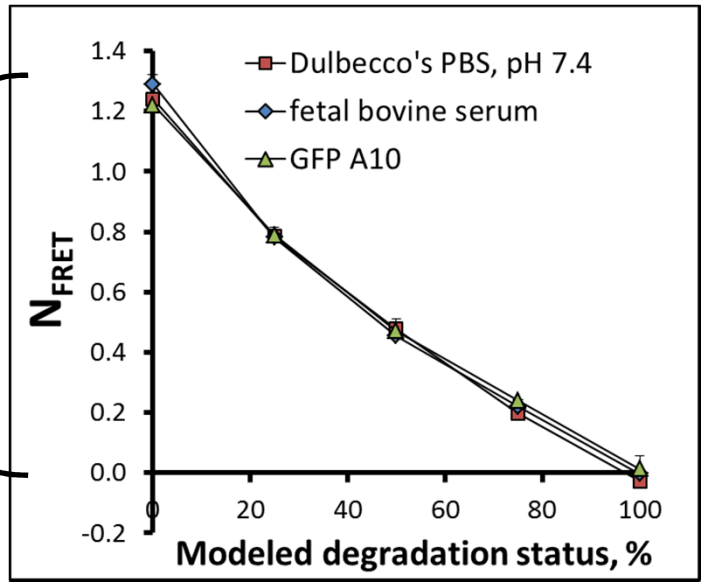
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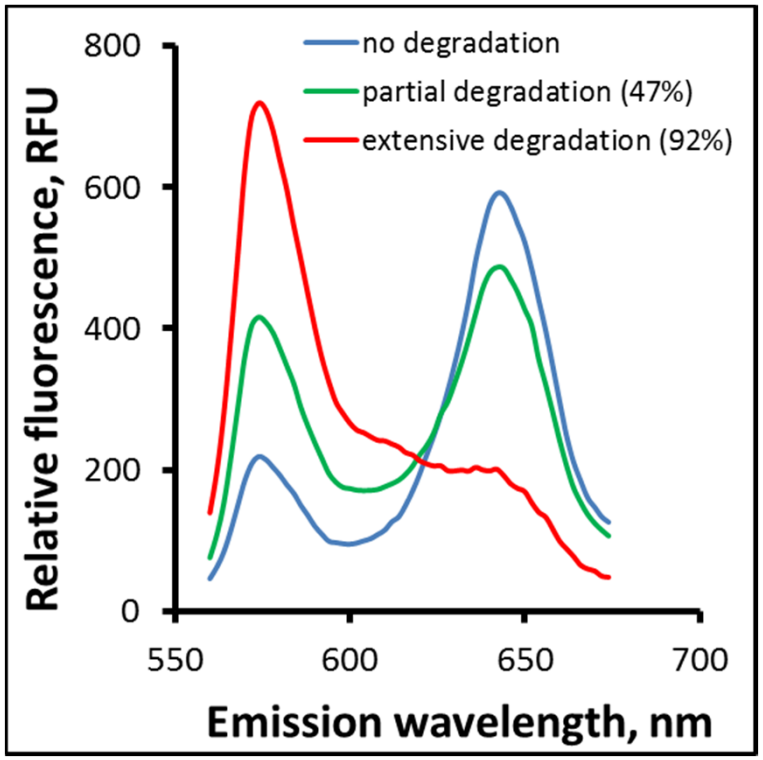


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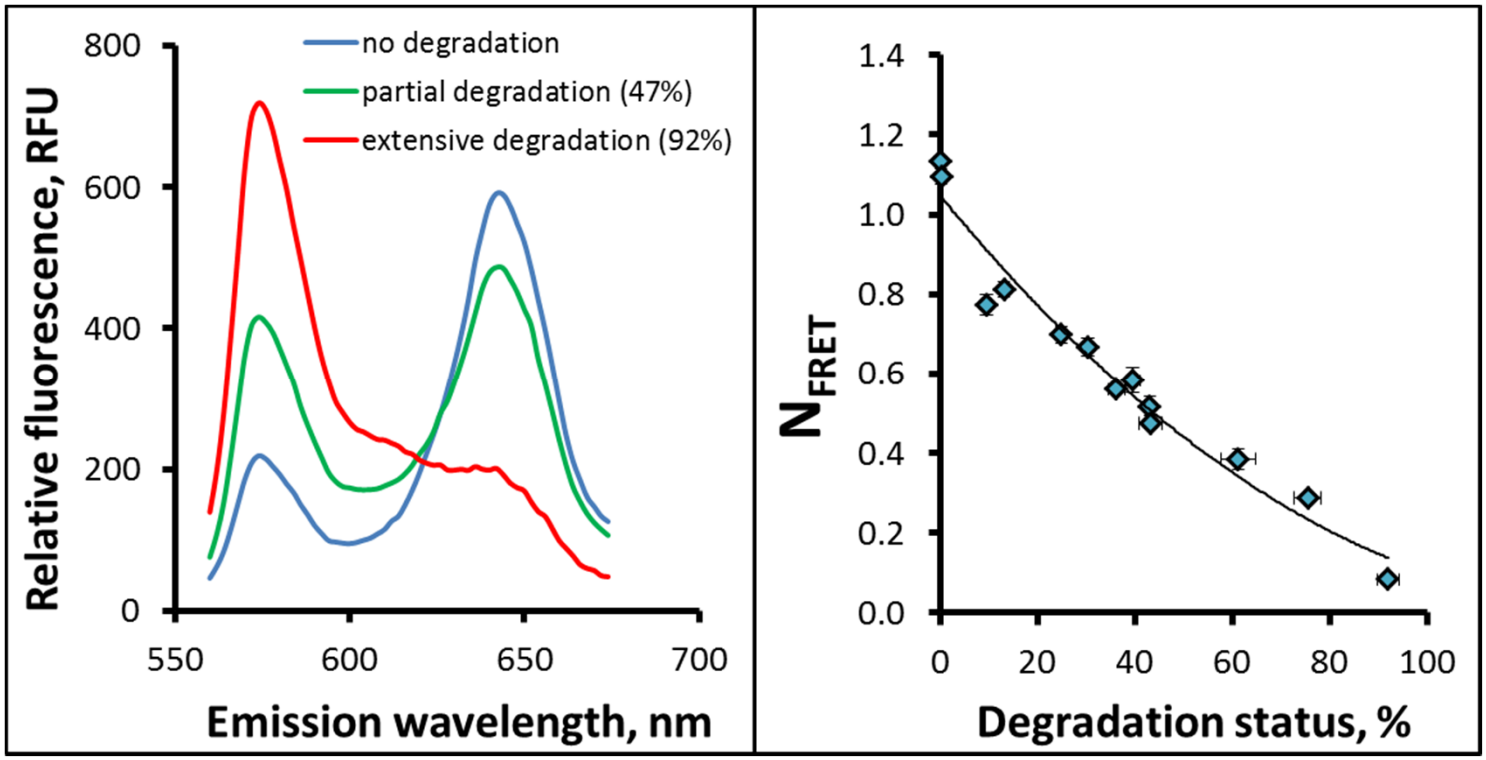
Proteinase K mediated MNP disassembly (validation)

Spectral changes and FRET scale

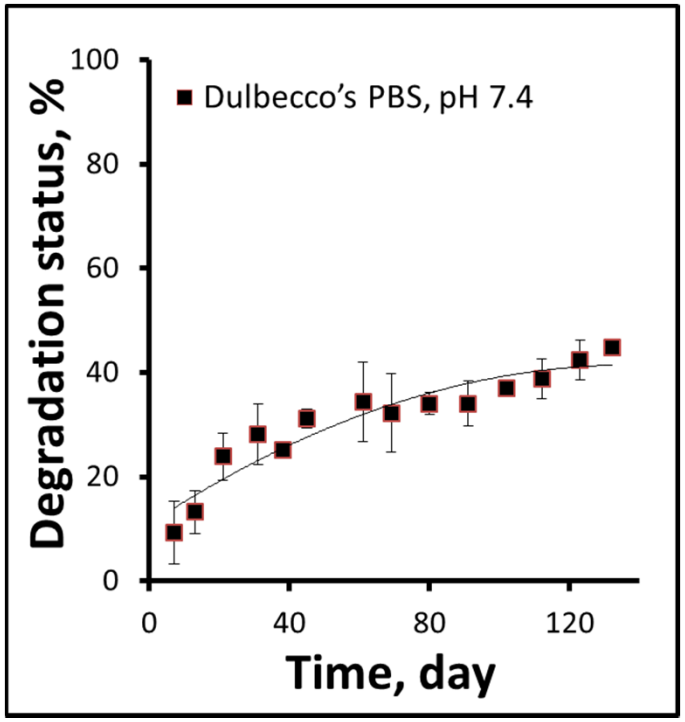


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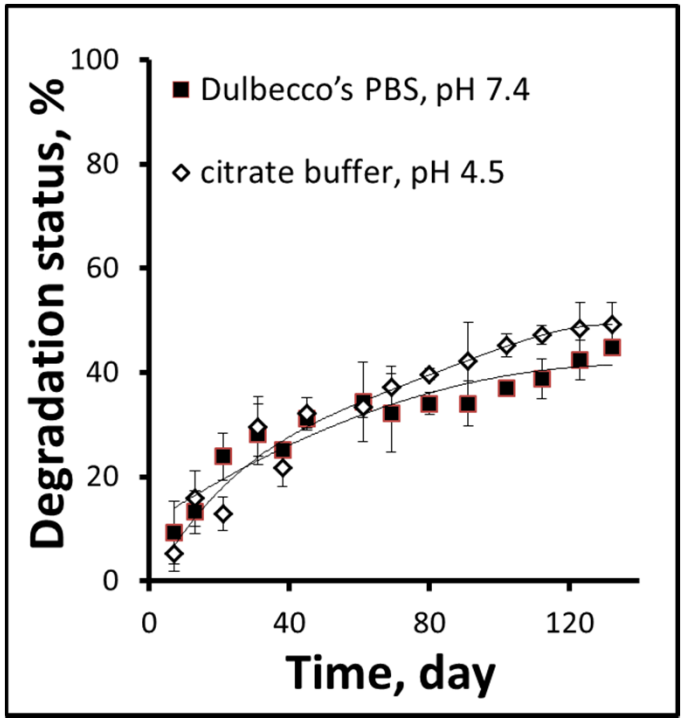
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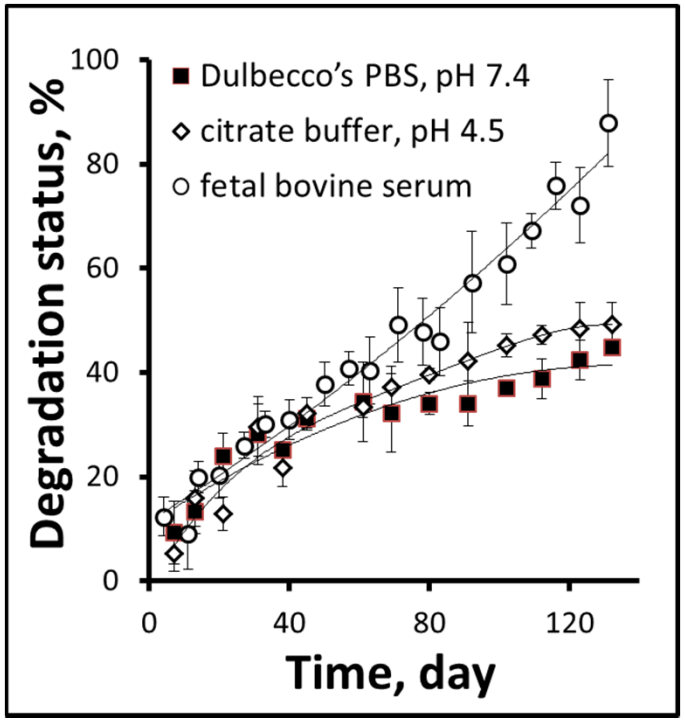
MNP disassembly in model liquid and semisolid media



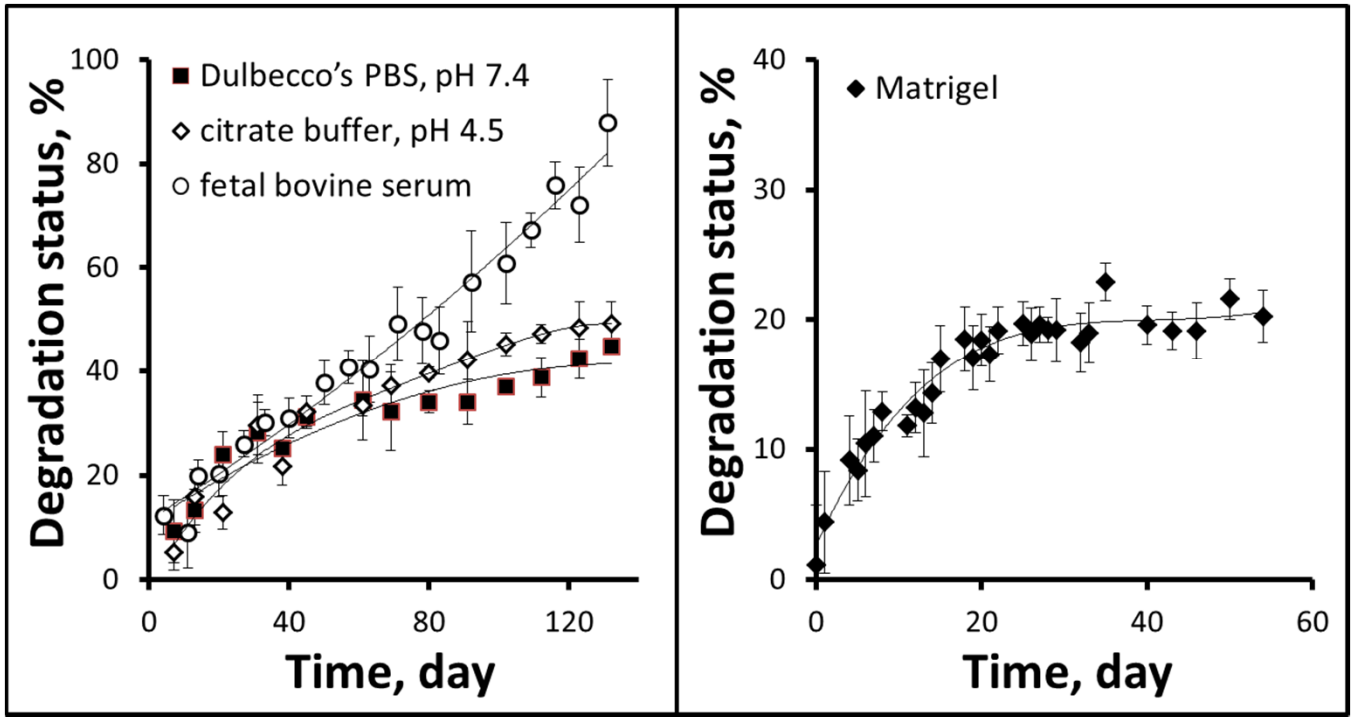
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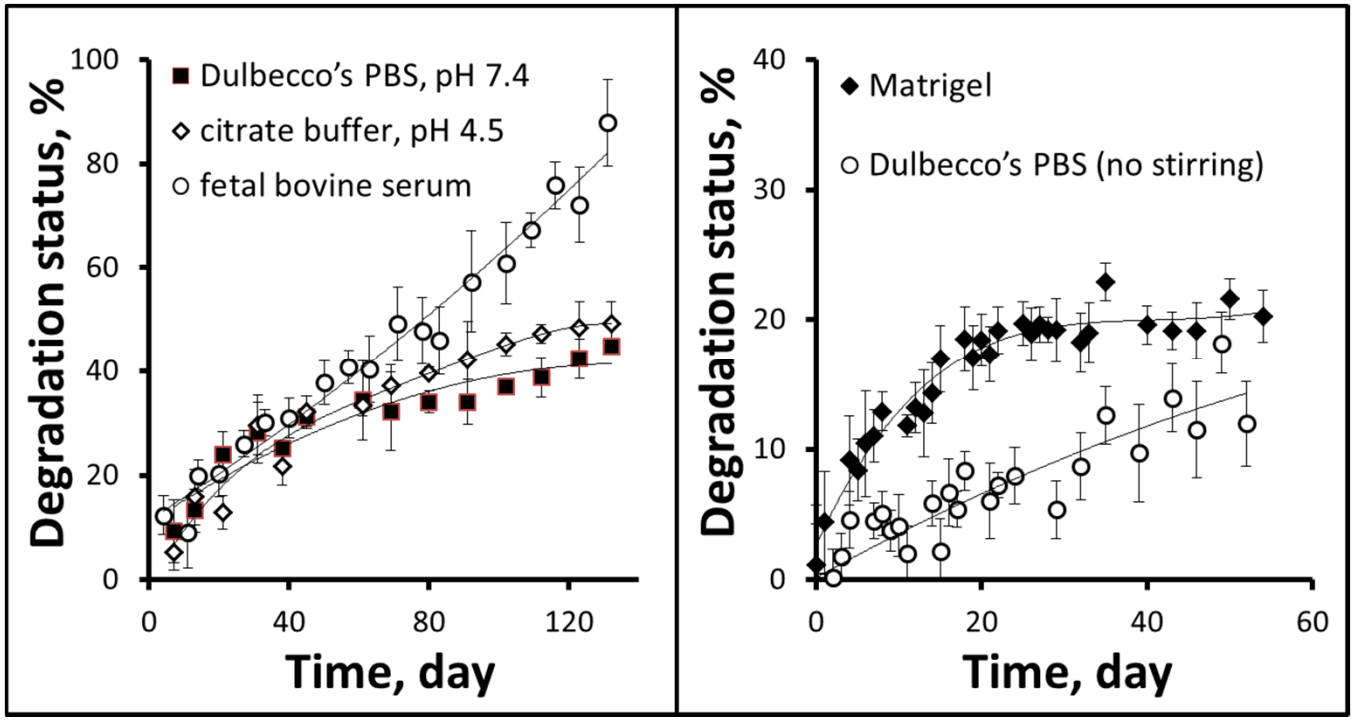
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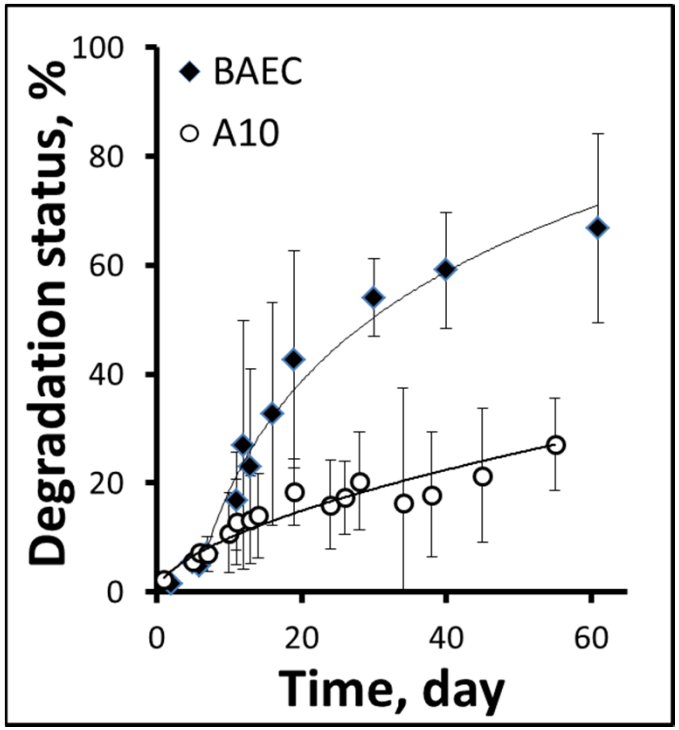
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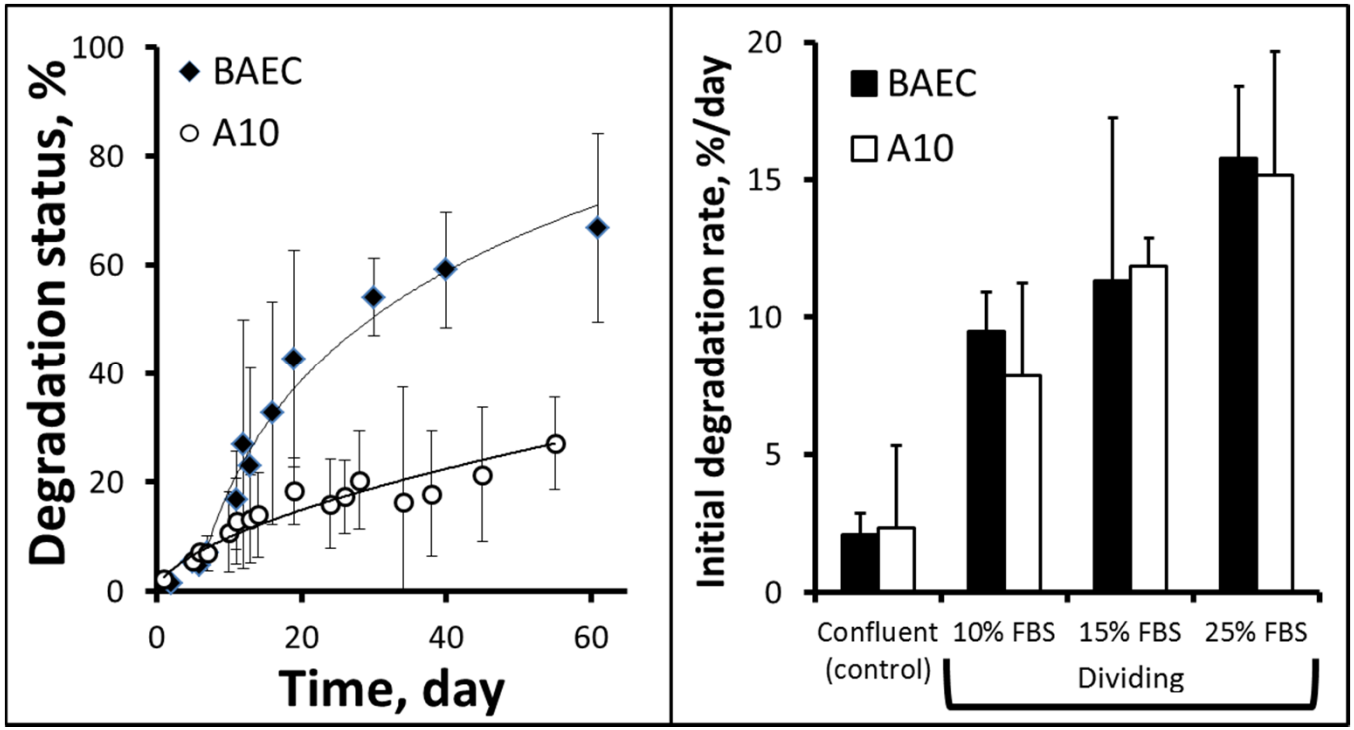
MNP disassembly in model liquid and semisolid media



Intracellular MNP disassembly in arterial smooth muscle and endothelial cells



Intracellular MNP disassembly in arterial smooth muscle and endothelial cells



Summary

- *The use of FRET as a molecular ruler potentially enables real-time measurements of NP integrity. FRET-based analysis can be applied as a tool for direct, undistorted kinetic studies of NP disassembly in complex environments.*

- *FRET-based analysis shows that NP disassembly is driven by diffusion-reaction mechanisms. Disassembly kinetics of NP endocytosed by vascular cells is strongly proliferation rate-dependent, which may be of relevance to the design and optimization of therapeutic nanocarriers for treating vascular disease*

Tengood J. E., Alferiev I. S., Zhang K., Fishbein I., Levy R. J., and Chorny M. (2014) Real-time analysis of composite magnetic nanoparticle disassembly in vascular cells and biomimetic media. Proc Natl Acad Sci U S A 111, 4245-4250.

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PNAS

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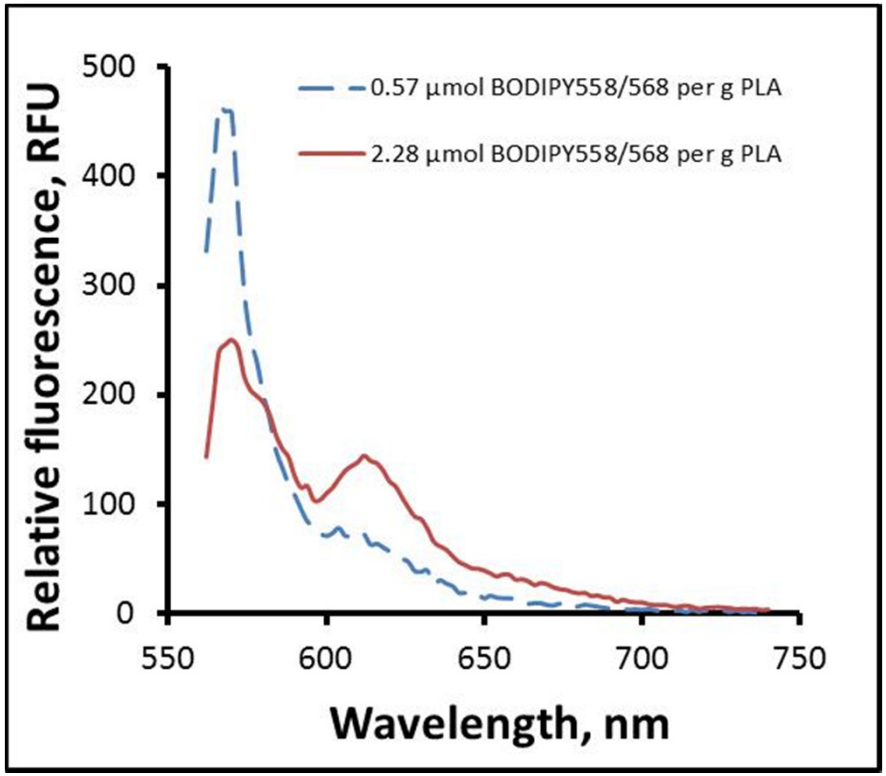
Jillian E. Tengood, Ivan S. Alferiev, Kehan Zhang, Ilia Fishbein, Robert J. Levy, and Michael Chorny[1]

Division of Cardiology Research, The Children's Hospital of Philadelphia, Philadelphia, PA 19104

PNAS | March 18, 2014 | vol. 111 | no. 11 | 4245–4250

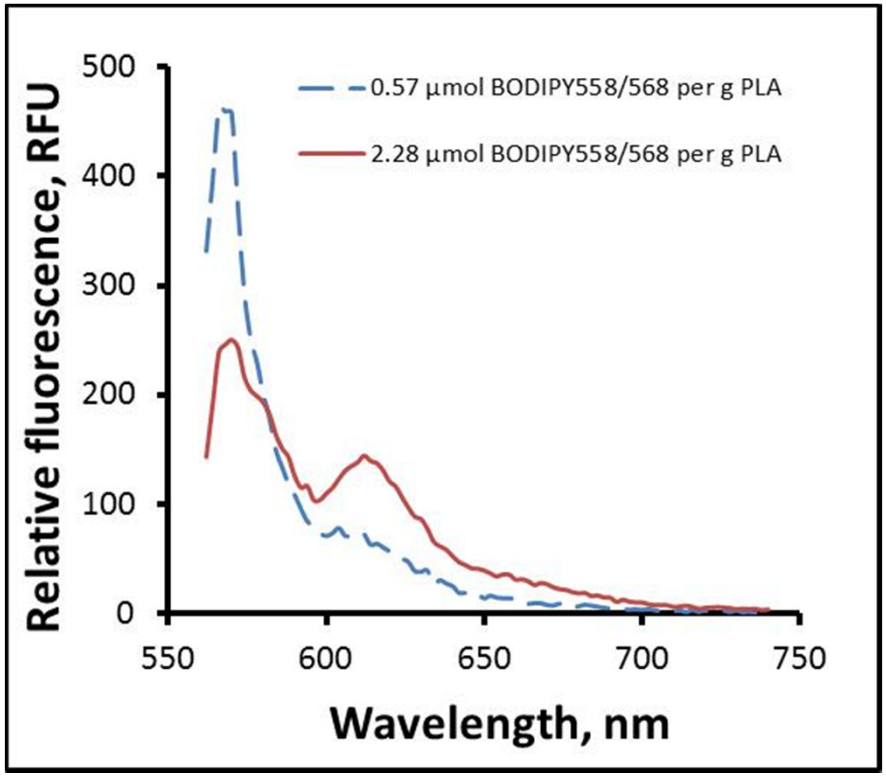
Monitoring particle disassembly using a single probe (PLA-BODIPY$_{558/568}$)

MNP spectrum as a function of the probe packing density

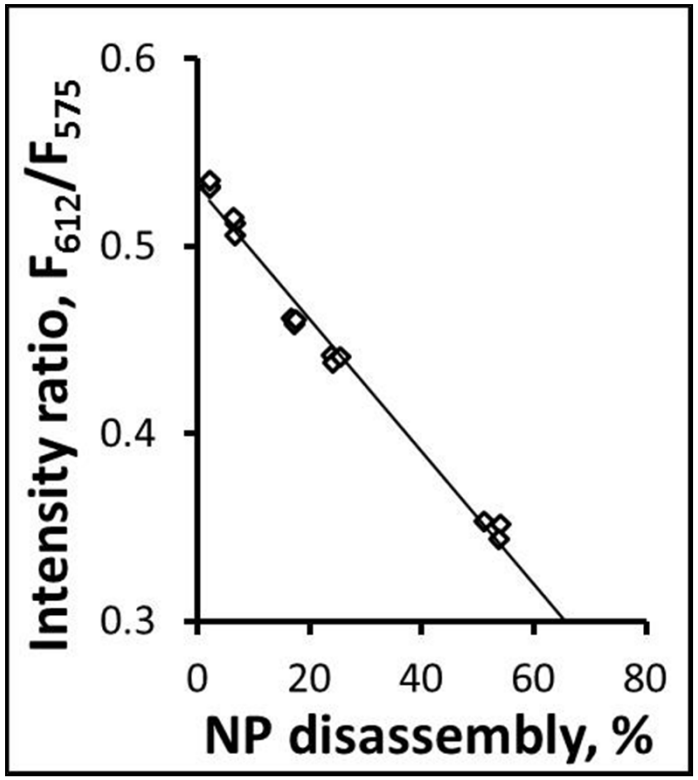


Monitoring particle disassembly using a single probe (PLA-BODIPY$_{558/568}$)

MNP spectrum as a function of the probe packing density



Fluorescence pattern reflects particle disintegration



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