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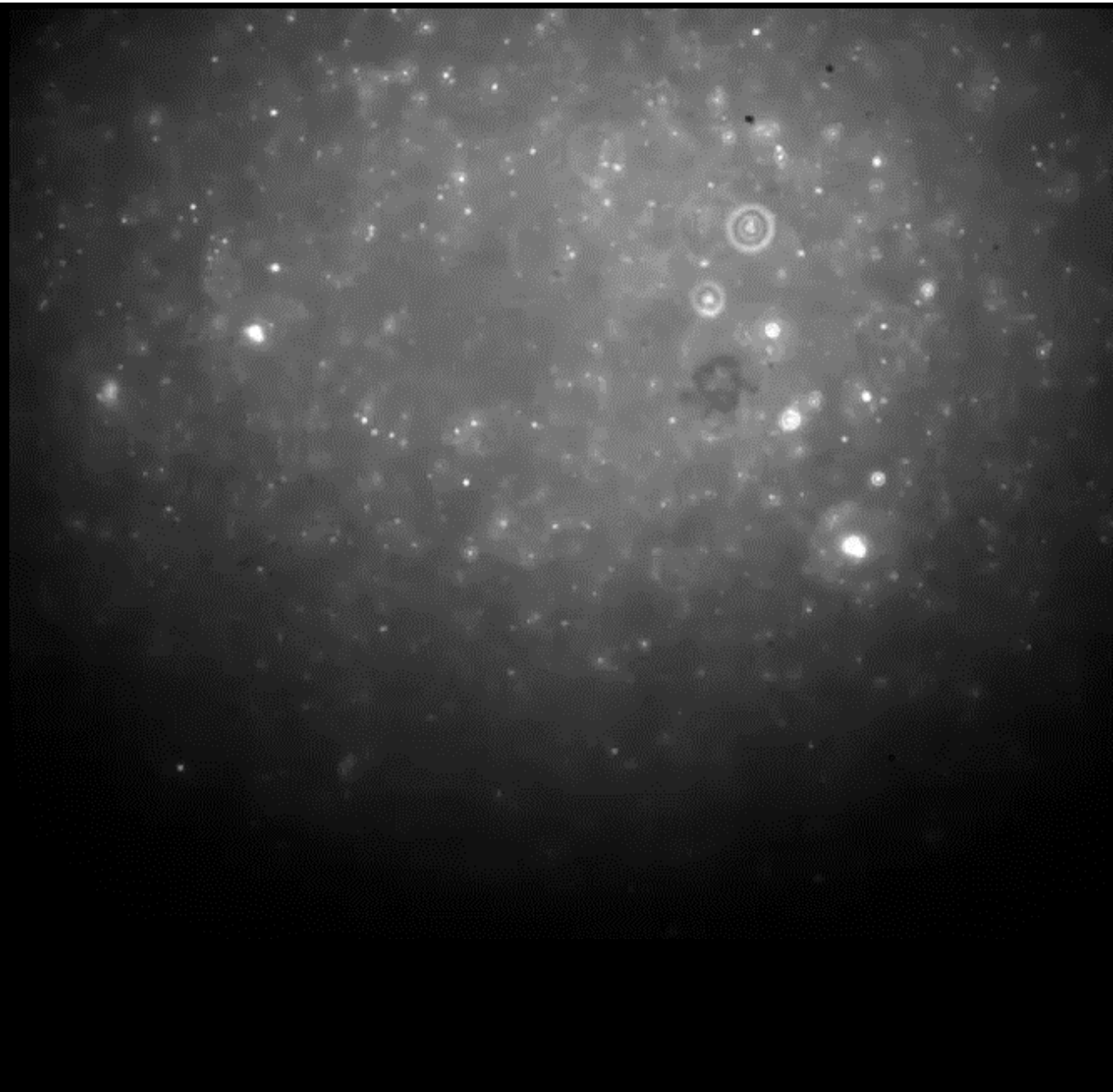
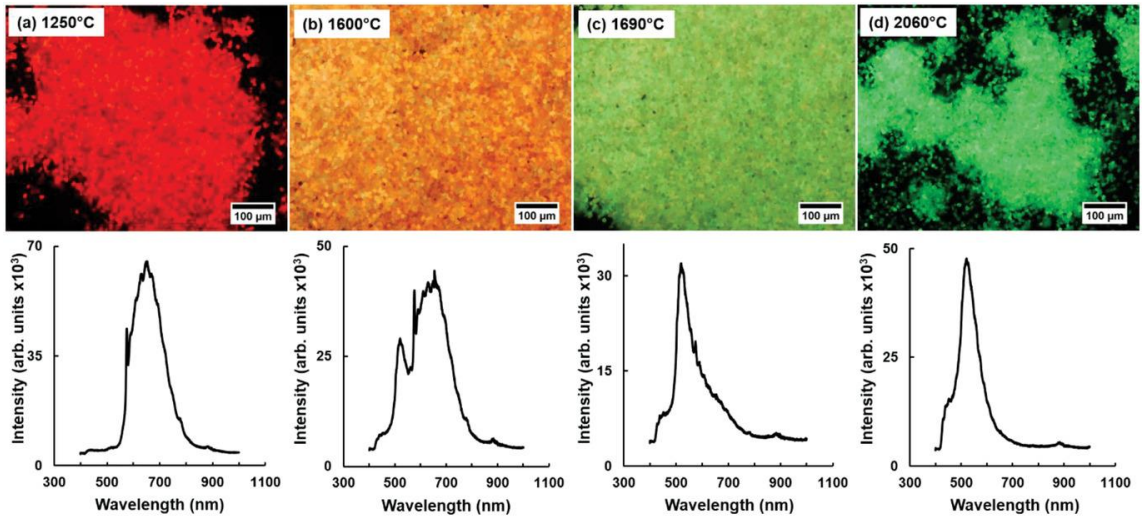
Method for in-solution, high-throughput, T_1 relaxometry using fluorescent nanodiamonds

Erin Grant, Mina Barzegar Amiri Olia, Brant Gibson, Liam Hall, Gawain McColl, Philipp Reinick, David Simpson, Ella Walsh and Avan Whaite

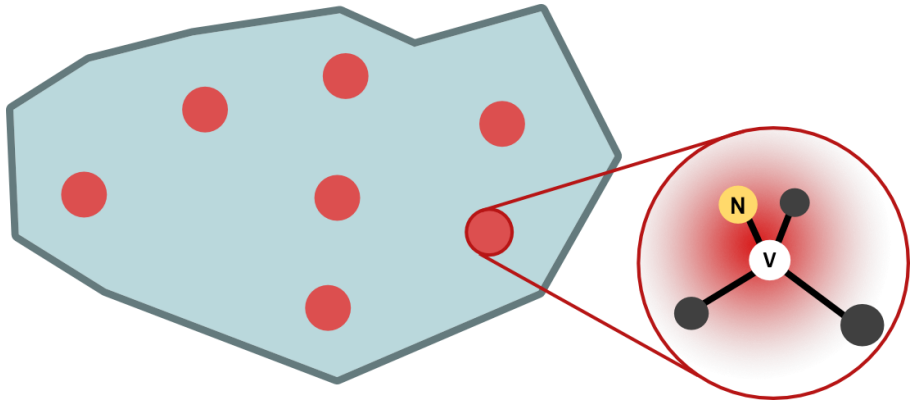
@GrantApplctns



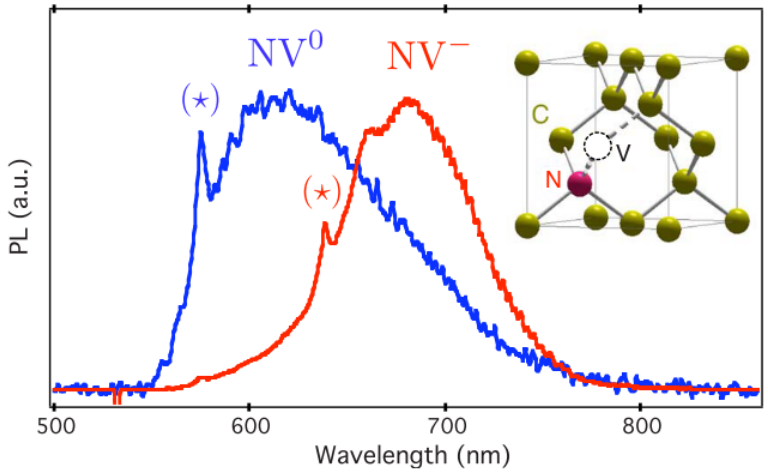
NV Nanodiamonds for Biology



Dei Cas, L. Adv. Func. Mat. 2019, 29



- Do not photobleach
- Are not cytotoxic
- Uses:
  - fluorescence marker
  - quantum sensing



Rondin, L., PHYS. REV. B, 2010, 82, 115449

Current Uses

Fluorescence Tracking

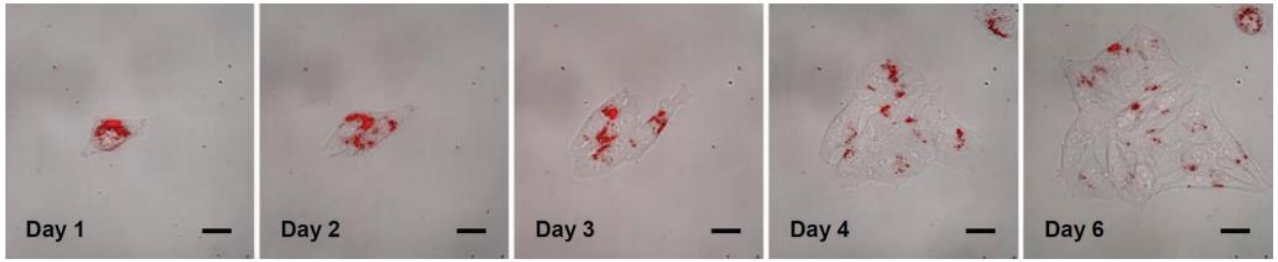
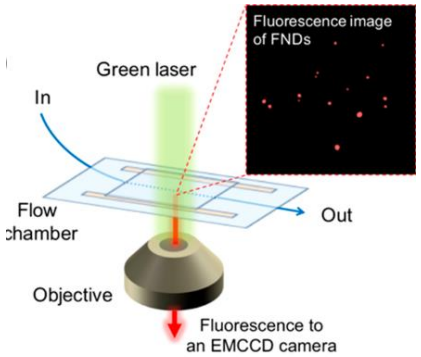
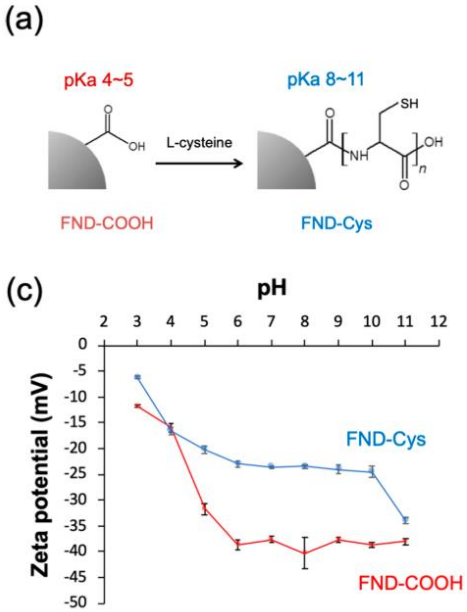


Figure 3. Tracking cell division of FND-labeled HeLa cells by DIC/epifluorescence microscopy. The tracking was conducted for up to 6 days of post-labeling incubation as indicated. Scale bars are 20 μm.

Fang, C., Small 2011, 7, No. 23, 3363–3370

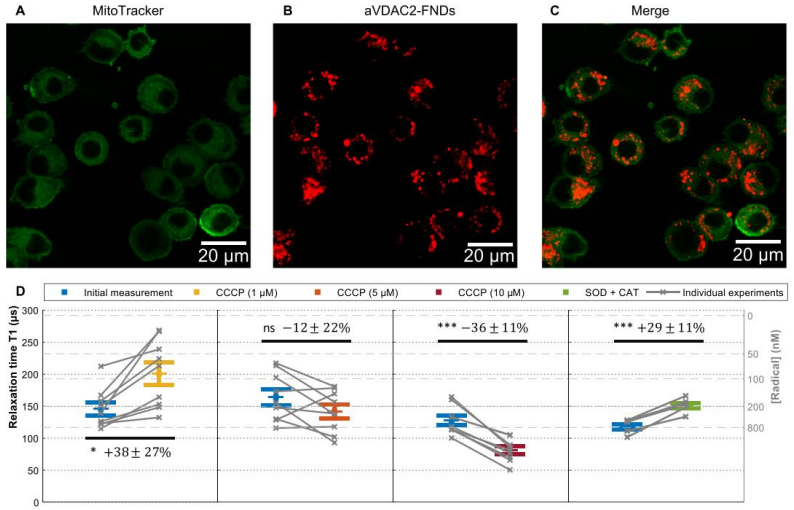
pH





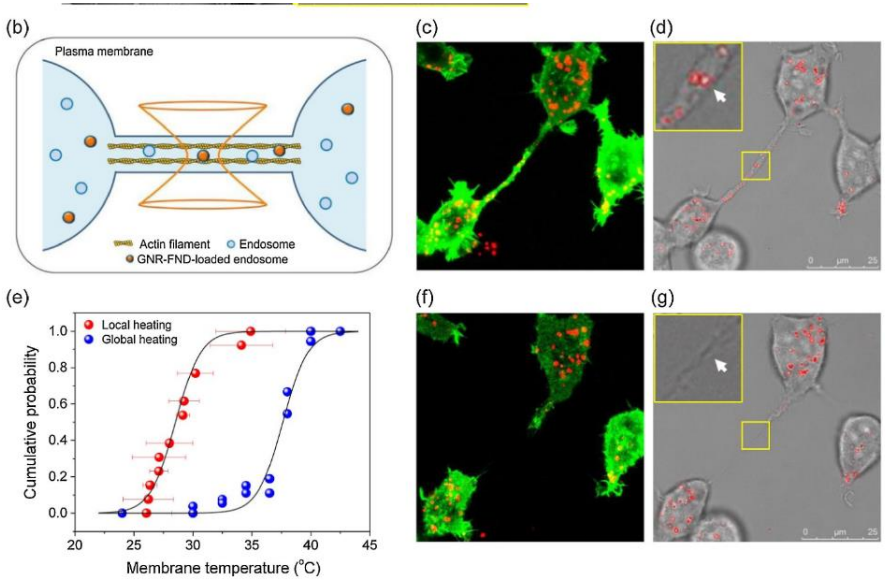
Fujisaku, T., ACS Nano 2019, 13, 11726−11732

Free radicals



Nie , Sci. Adv. 2021; 7 : eabf0573

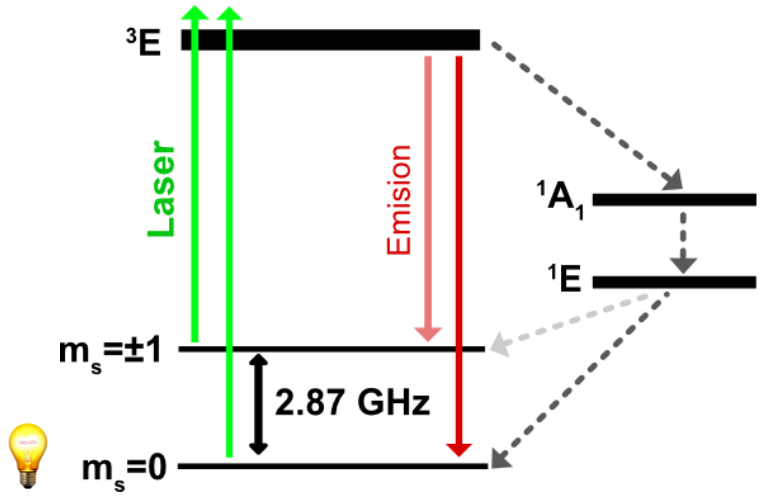
Temperature

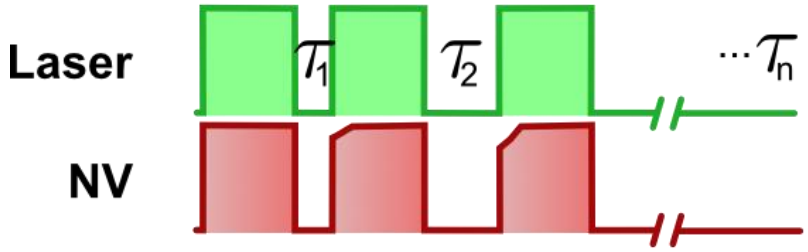


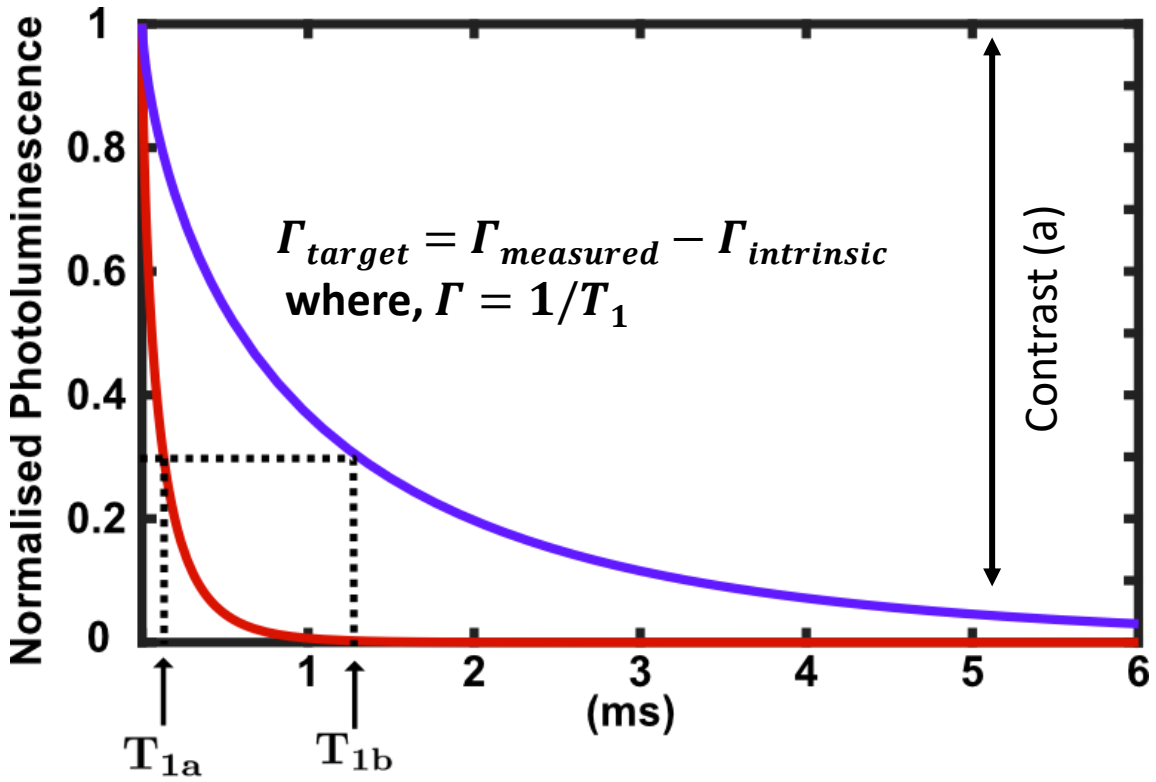
Tsai, PC., Angew.Chem. Int.Ed., 2017, 56,3025 –3030

T_1 Relaxometry

- Spin 1 defect.
- Optical polarisation and read out

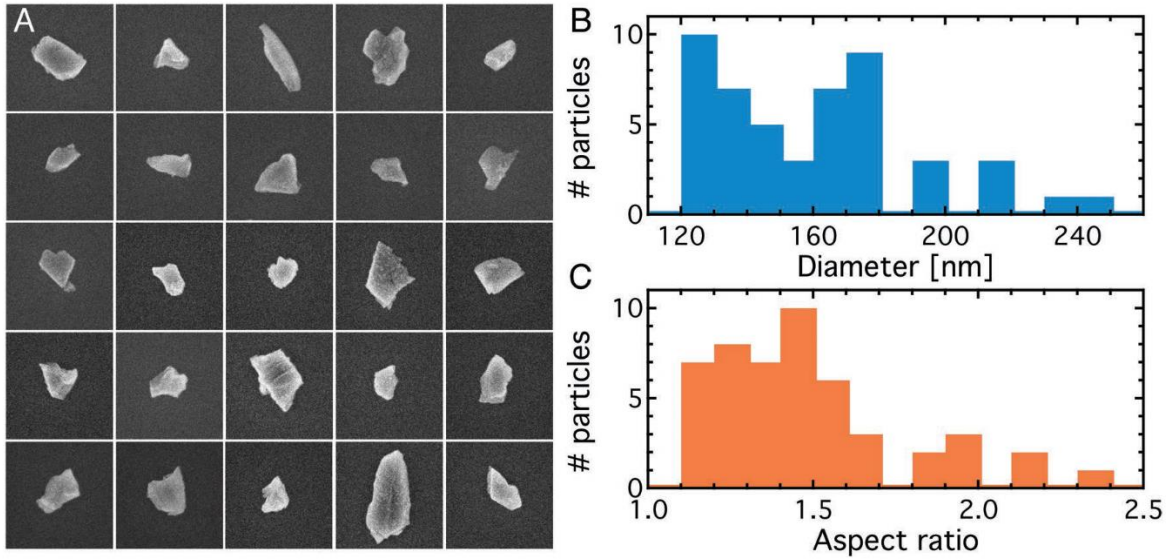






Current Limitations

- Inhomogeneous size, shape, brightness

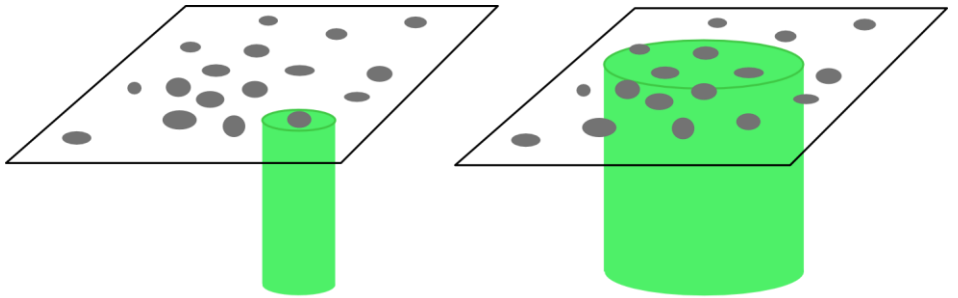


Reineck, P., Part. Part. Syst. Charact. 2019, 36, 1900009

- Unfavourable $\Gamma_{intrinsic}$

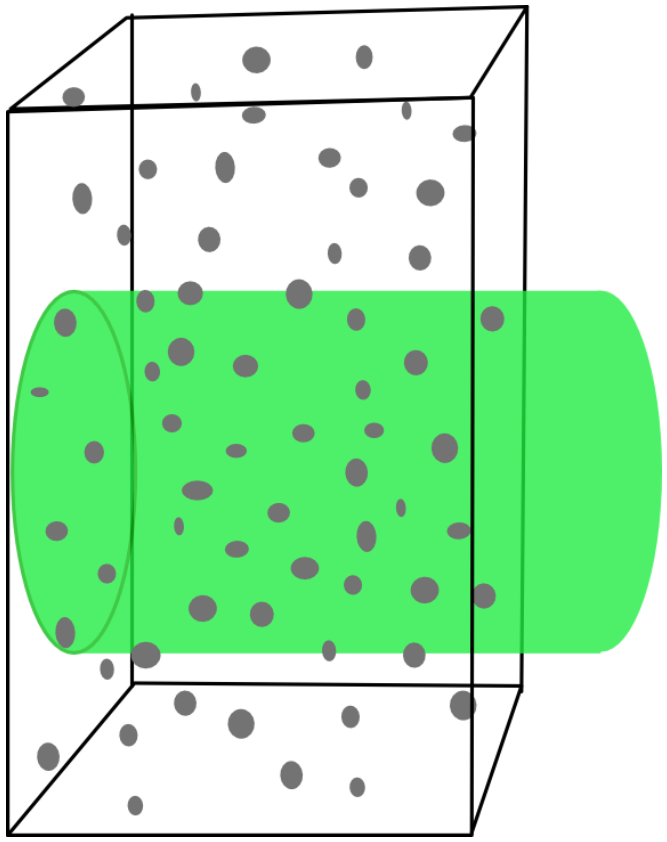
Single crystal $\Gamma_{intrinsic}$	Nanodiamond $\Gamma_{intrinsic}$
~1000 Hz	3000 - 10,000 Hz

- Current modalities require selection step and are non-ideal for sensing in-solution



Confocal Widefield

Motivation for In-Solution Measurements



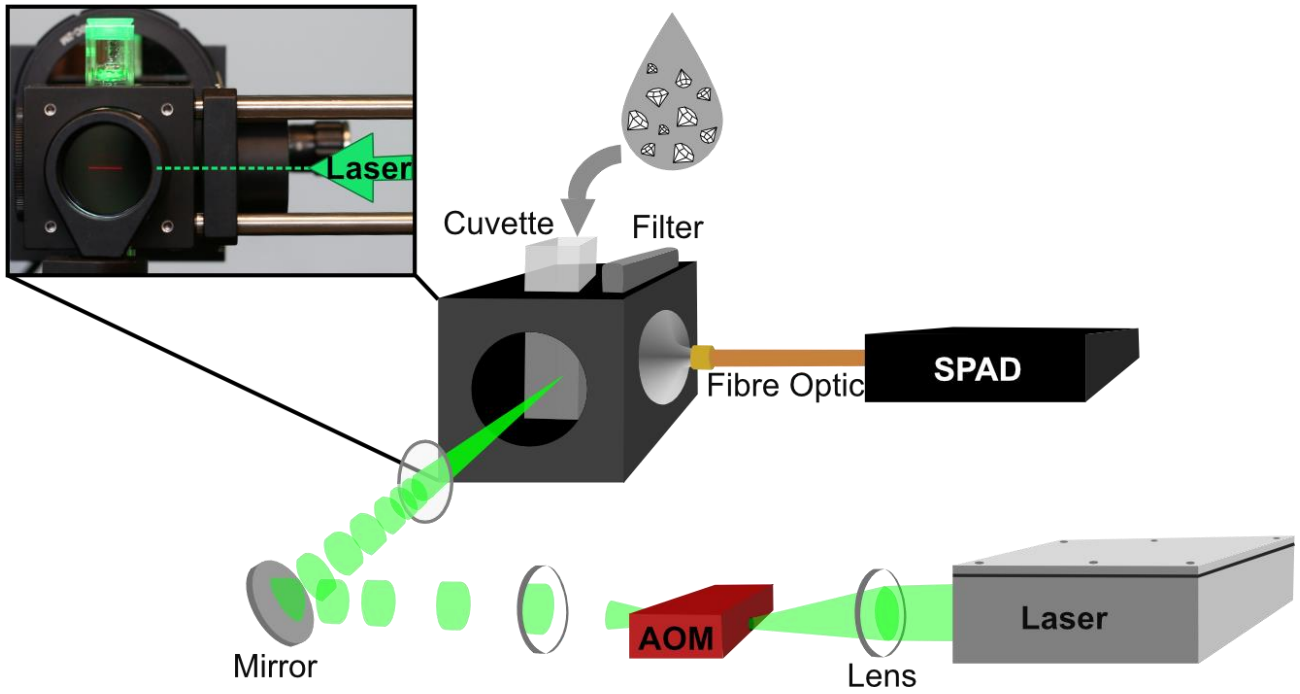
1. Efficient material characterisation
2. Paramagnetic sensing of dispersed targets

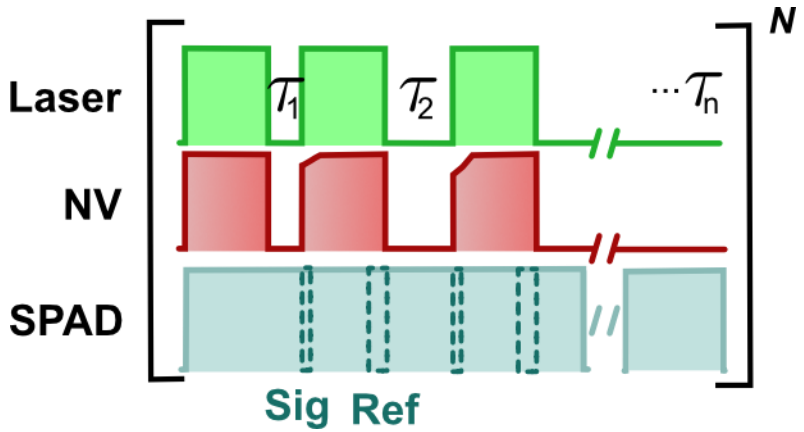
Benefits

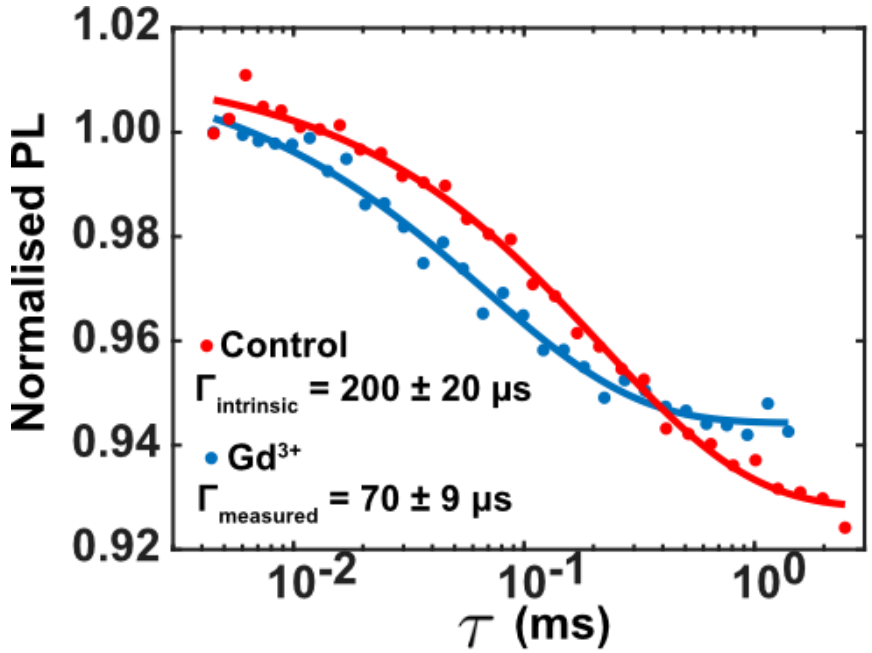
- Ensemble averaging
- High throughput
- Simple apparatus/operation

In-solution Apparatus

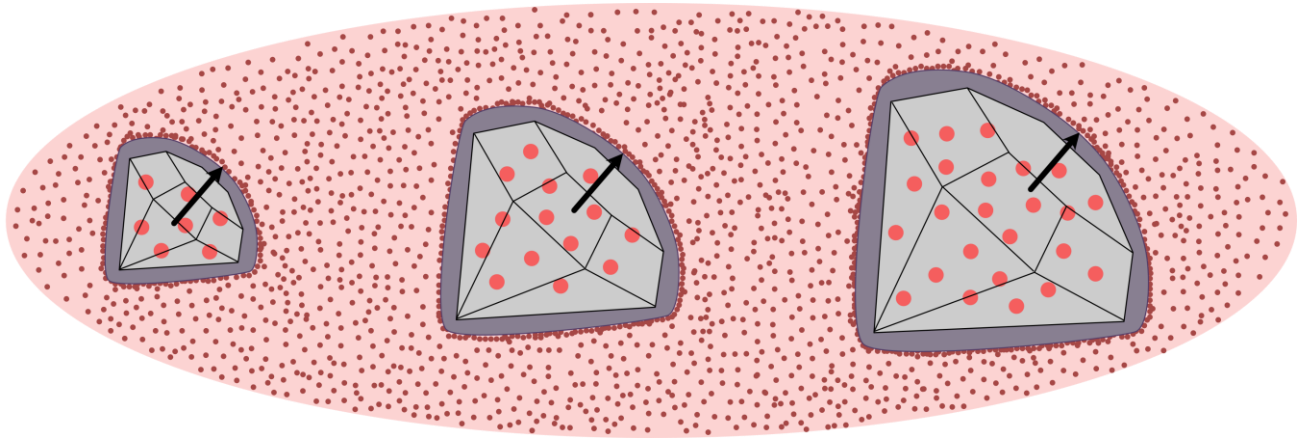
- 10 µg/ml sample
- 200 µL
- 15-50 mins/measurement



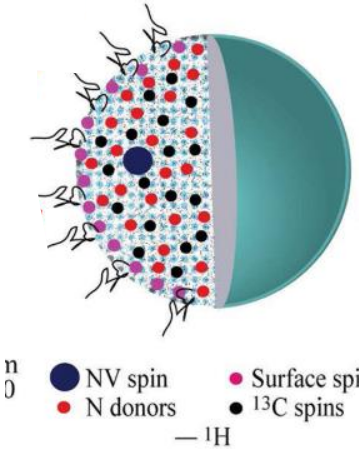




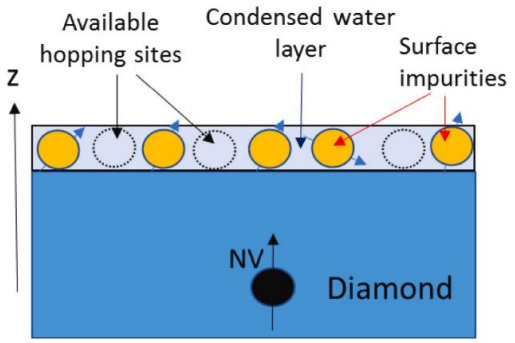
Which size is the most sensitive?



$\Gamma_{target} \propto 1/r^3$



A. Laraoui, Nano Lett. 2012, 12, 3477−3482



P. Chrostoski, Physica B: Physics of Condensed Matter 605 (2021) 412767

Suggests smaller is better.

However, $\Gamma_{target} = \Gamma_{measured} - \Gamma_{intrinsic}$

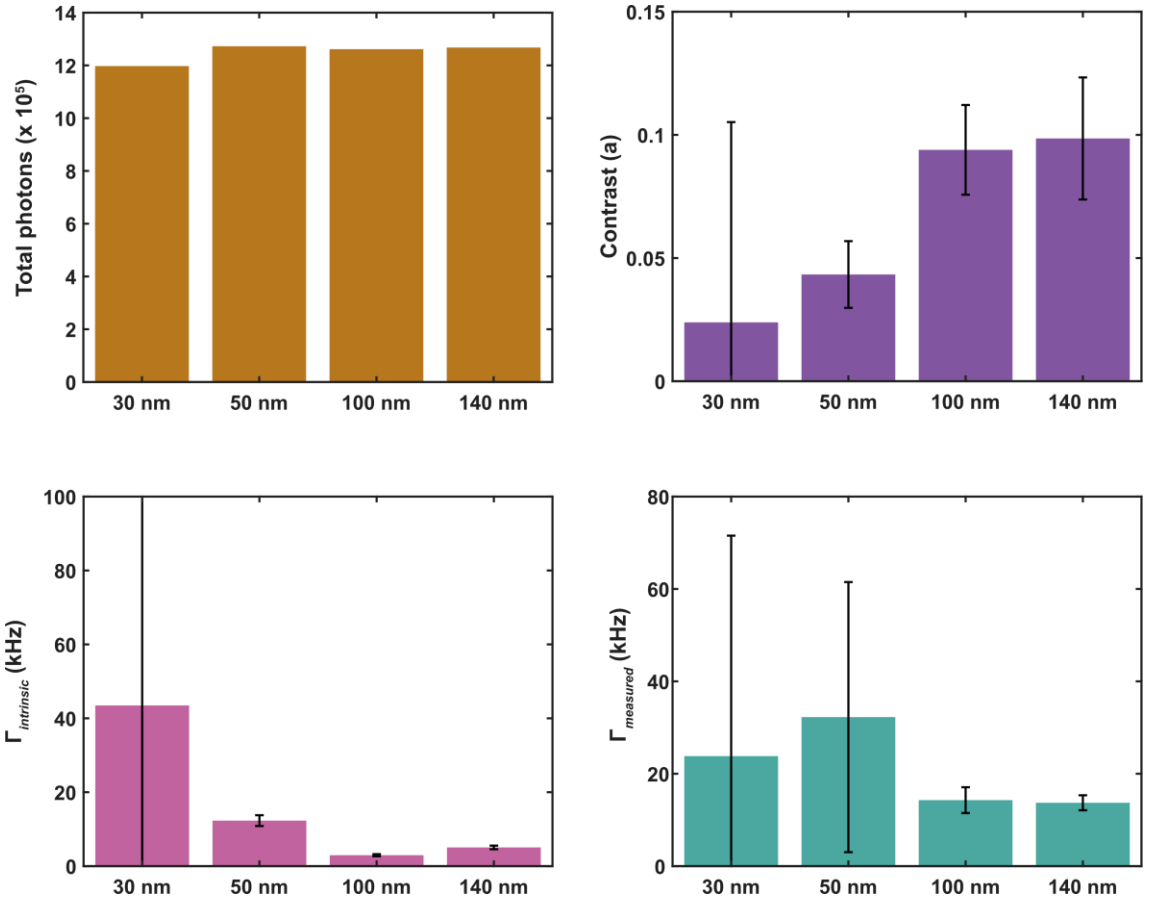
Single crystal $\Gamma_{intrinsic}$ =1000 Hz compared to 5000-10,000 Hz in nanodiamonds.

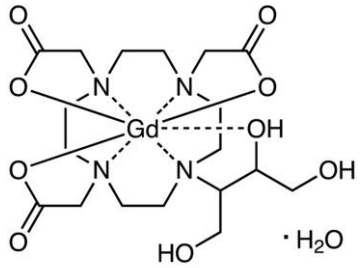
The sensitivity for a particular evolution time (τ):

$$SNR \approx \sqrt{\frac{Rt_{RO}T_{tot}}{\tau}}\frac{3a}{4}e^{-\Gamma_{intrinsic}\tau}(1-e^{-\Gamma_{measured}\tau})$$

Contrast (a)
Number of photons collected ($\frac{Rt_{RO}T_{tot}}{\tau}$)
Intrinsic relaxation rate ($\Gamma_{intrinsic}$)
Measured relaxation rate ($\Gamma_{measured}$)

Which size is the most sensitive?





-Tested sensitivity using gadobutrol – MRI contrast agent.

-Gd^{3+} has spin = 7/2

-Should be no binding, between ND and gadobutrol.

$$SNR \approx \frac{Rt_{RO}T_{tot}}{\tau}\frac{3a}{4}e^{-\Gamma_{intrinsic}\tau}(1-e^{-\Gamma_{measured}\tau})$$

Size (nm)	SNR
30	N/A
50	16 ± 9
100	43 ± 9
140	37 ± 10

Conclusions

- In-solution T_1 measurements are simple to perform with high throughput
- An attractive platform for characterisation studies
- A new modality for paramagnetic sensing

Next:

1. Improve collection efficiency to reduce acquisition time
2. Use surface functionalisation to specifically bind targets

@GrantApplctns

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