Barium Ion Sensing with Commercial IPG K+ Molecular Probes

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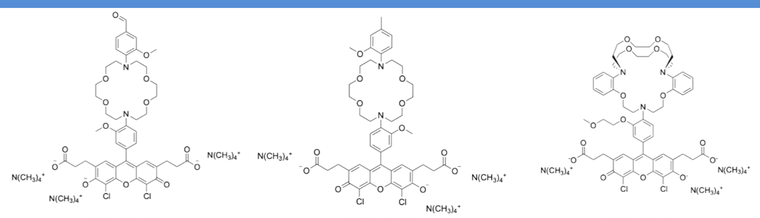
Introduction



IPG1 **IPG2** **IPG4**

- Fluorescence imaging of K^+ ions has significant biological relevance, leading to the discovery of highly selective molecular probes, including the IPG family.
- Detection of Ba^{2+}, Barium tagging, would enhance searches for neutrinoless double beta decay of atoms through the decay of xenon gas.
- The ionic radius of Ba^{2+}(149 pm) and K^+(152pm) are extremely well matched, meaning highly selective K^+ sensors are also selective for Ba^{2+}, such as the IPG family.
- We aim to characterize the ability of the IPG family to act as Ba^{2+} ion sensors.

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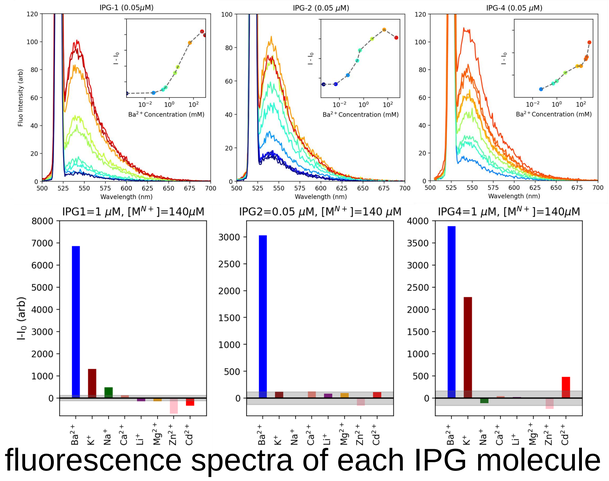
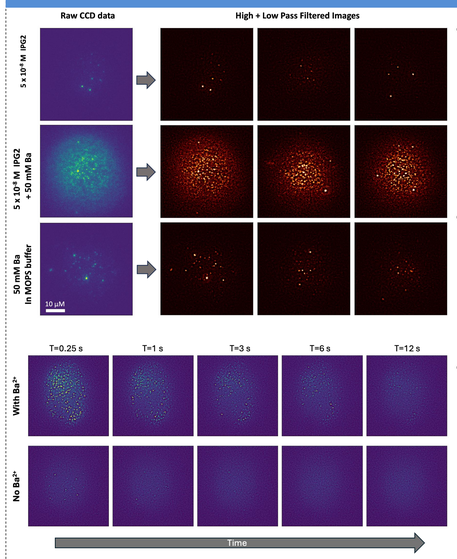
ION Biosciences, **2023**, https://ionbiosciences.com/wp-content/uploads/IPG-4-AM_SPEC.pdf.

Bulk Fluorescence Spectroscopic Studies

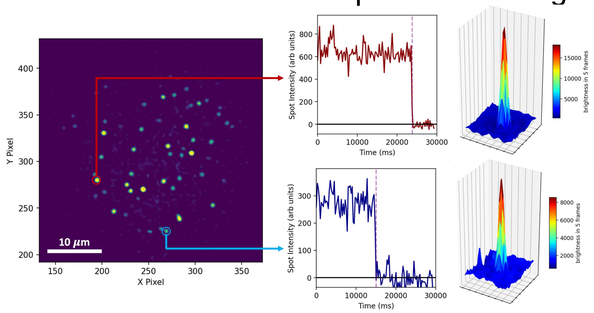


- The fluorescence spectra of each IPG molecule is very similar due to equivalent fluorescent groups.
- Each member of the IPG family showed stronger sensitivity to Ba^{2+} than K^+.
- IPG2's strong selectivity for Ba^{2+} led to its selection for further studies.

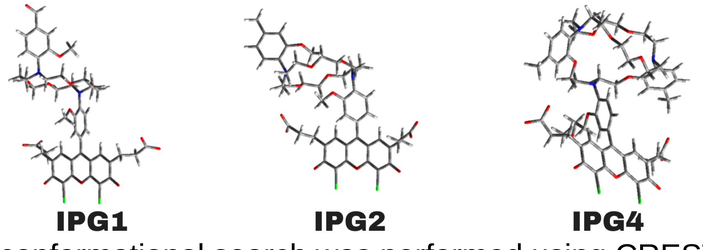
Single Ion Microscopy



- Small amounts of fluorescence activity are observed in both the IPG2 only and Ba^{2+} only control experiments.
- Combination of the IPG2 sensor and Ba^{2+} dramatically enhanced fluorescence.
- The combination of the sensor with Ba^{2+} shows single-molecule differentiation and characteristic photobleaching.



Structures Optimized with DFT



IPG1 **IPG2** **IPG4**

- A conformational search was performed using CREST across all molecules.
- Then, the lowest energy conformers of each molecule were optimized with Density-Functional-Theory (DFT), using the B3LYP/6-311G(d) functional and basis set.
- This reveals the lowest energy ground-state for each molecule, as seen above.

Frisch, M., et al. **2016**, Gaussian 16
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Mclean, A. D., Chandler, G. S. *J. Chem. Phys.* **1980**, 72, 5639-5648
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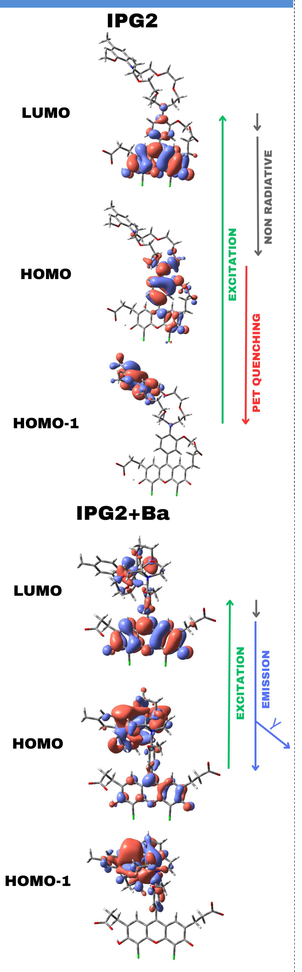
Fluorescence Mechanism with TD-DFT

- TD-DFT of this molecule led to a unique error which had not been seen before in literature.
- Screening of additional basis sets and functionals provided little help. Sometimes the error could be avoided but at a huge cost of accuracy.
- Found that the error could be avoided by simulating more excited states, but with seemingly no pattern.
- Once the unique error was avoided however, the binding of Ba^{2+} led to additional difficulties.
- Finally, once an optimized Ba^{2+}-bound geometry was found through the Def2TZVP basis set, the excitation could be simulated.
- Simulations of the sensor without Ba^{2+} show expected quenchable excitation.
- Simulations of the sensor with Ba^{2+} show a drop in energy of the HOMO orbital, allowing emission and pointing to a Photoinduced-Electron-Transfer (PET) Mechanism



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Conclusions

- Bulk fluorescence studies demonstrate the IPG family's strong sensitivity and selectivity for Ba^{2+}.
- Their suitability for single ion microscopy was confirmed and demonstrated characteristic photo-bleaching behavior.
- Computational studies with DFT/TD-DFT further demonstrate their suitability as sensors and point toward a PET mechanism.

Acknowledgements

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