

Multifluorescent, disposable phantoms for calibration of a quantitative fluorescence-guided resection instrument in neurosurgery

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INTRODUCTION

- A new point measurement quantitative fluorescence-based fiber-probe has been developed at UHN to identify malignant tissues in neurosurgery, based on ALA-induced PPIX fluorescence.
- Designed to assist in fluorescence-guided brain tumor resection, based on absolute measurements of local PPIX concentration.
- Fluorescence is excited at 405 nm and reemits in the 600-720 nm window.
- Quantification of fluorescence is achieved using a closed-form analytical model that decouples fluorescence from the tissue optical properties, using spectrally-constrained diffuse reflectance spectroscopy.¹⁻⁴

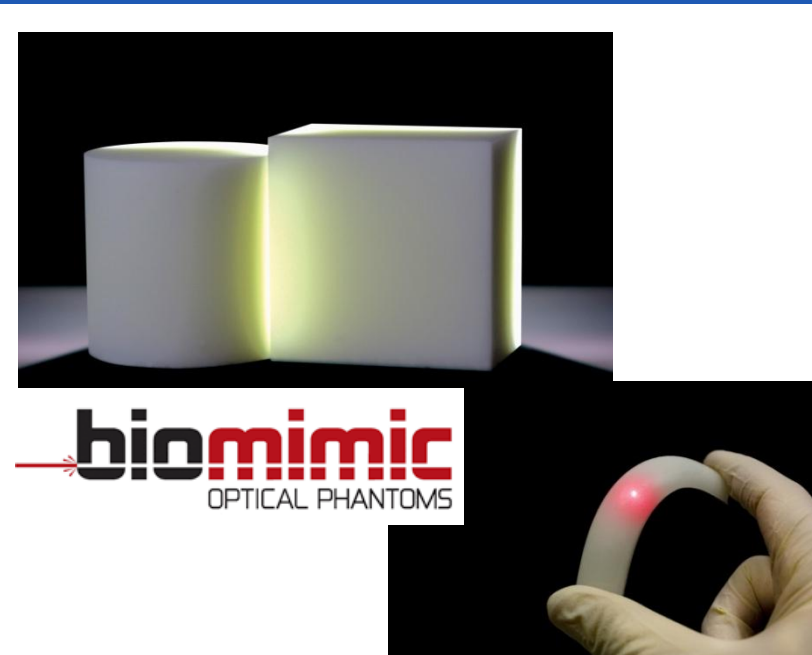
MULTIFLUORESCENT PHANTOMS

- Provide an *in situ* performance check of the instrument in the operating room during neurosurgery procedures
- Phantom designed as a sterilizable, disposable, single-use item

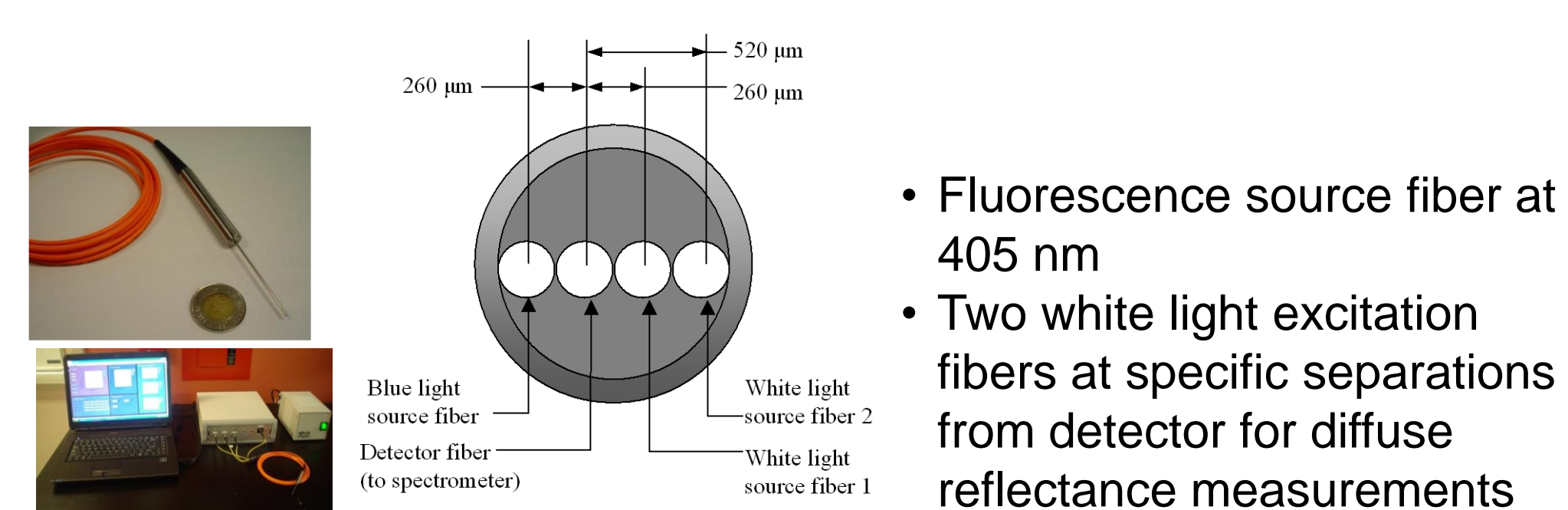
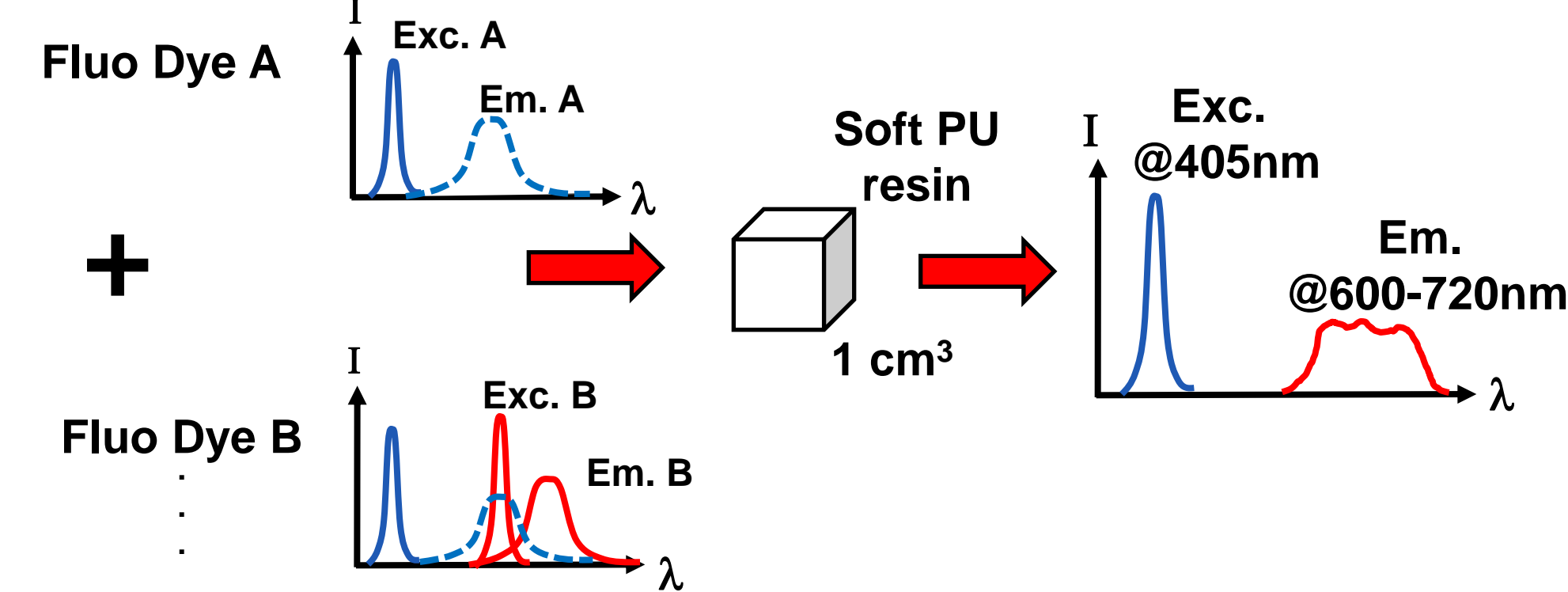
IMPORTANT DESIGN CRITERIA:

- Large Stokes Shift
- Broad flat emission
- High reproducibility between phantom units
- Good optical coupling to device

Design Methodology



- Polyurethane (PU) solid phantoms⁵⁻⁷
- Control and reproducibility of optical properties @635 nm within ±10%
- Recent development of a soft PU matrix version



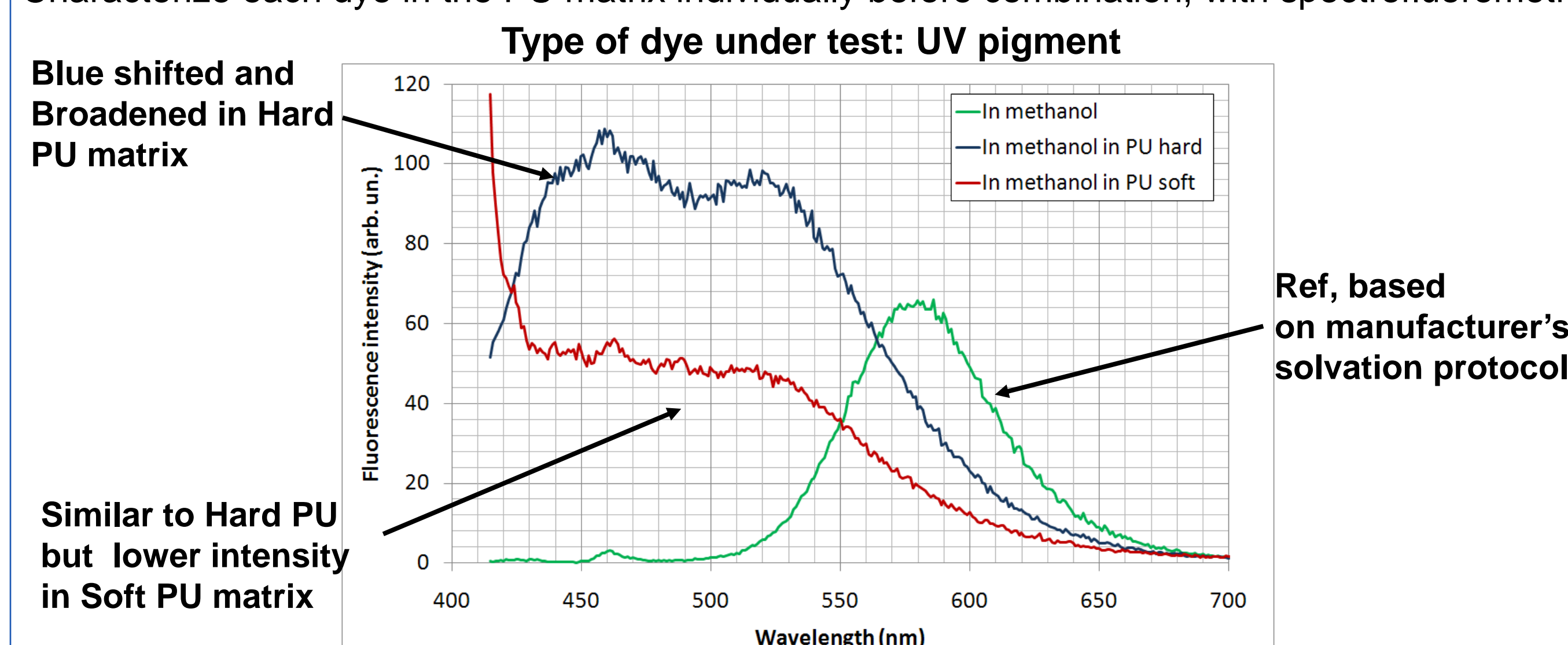
- Fluorescence source fiber at 405 nm
- Two white light excitation fibers at specific separations from detector for diffuse reflectance measurements

Challenges in Dye Selection

- A PU matrix is a complex solvent with generally undocumented effects on fluorescent dyes optical properties.
- Solvent polarity and viscosity shift the spectral bands.
- The PU matrix fabrication and curing process can strongly modify the spectra during and after casting.
- Commercially-available PU resin molecular structure is generally a trade secret.
- Fluorescent dyes can potentially interact chemically.

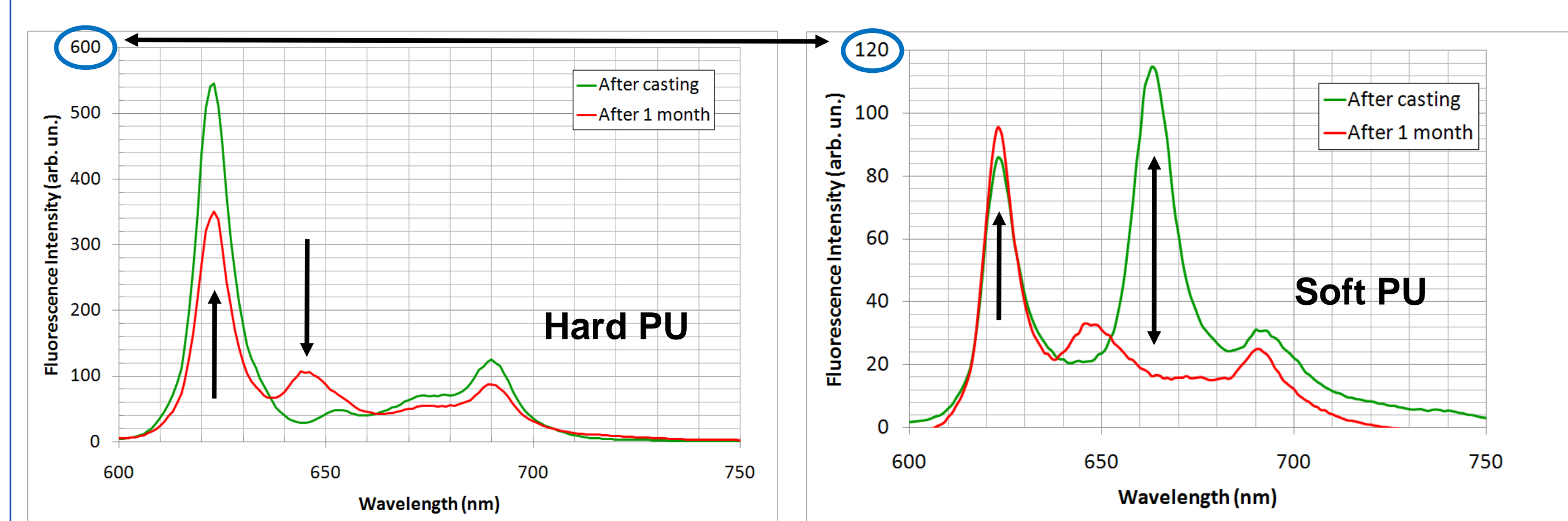
Spectral and Fluorescence Intensity

Characterize each dye in the PU matrix individually before combination, with spectrofluorometry



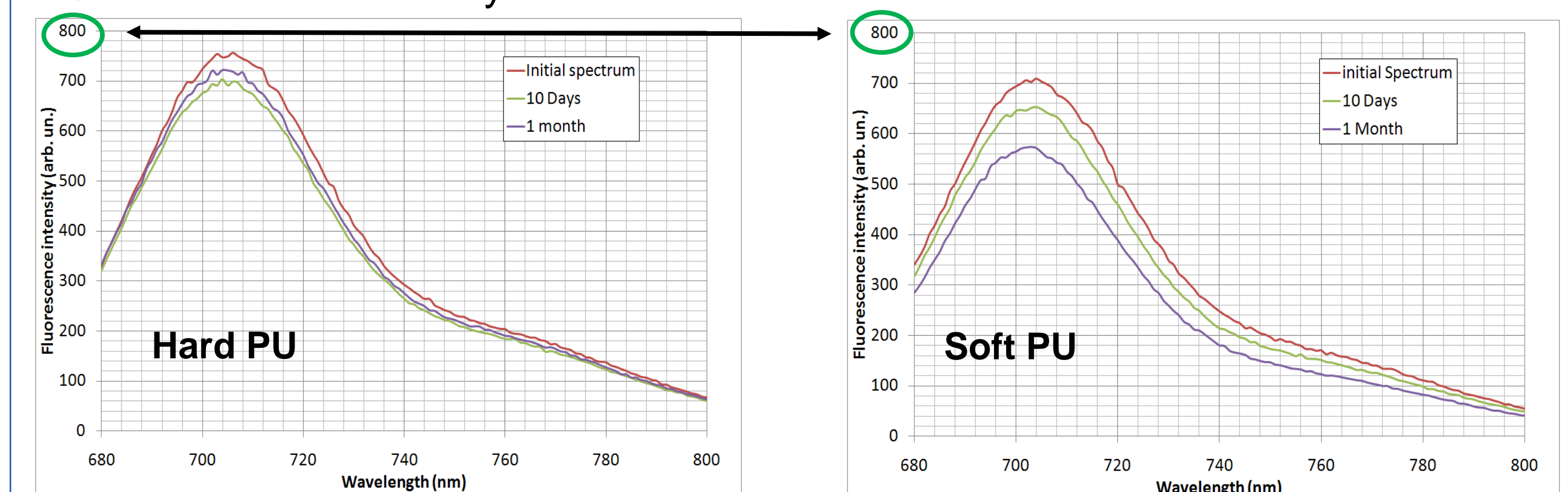
Stability in time: Porphyrin example

- Changes in spectral features over 1 month time in both PU matrices
- Lower overall intensity in soft PU matrix



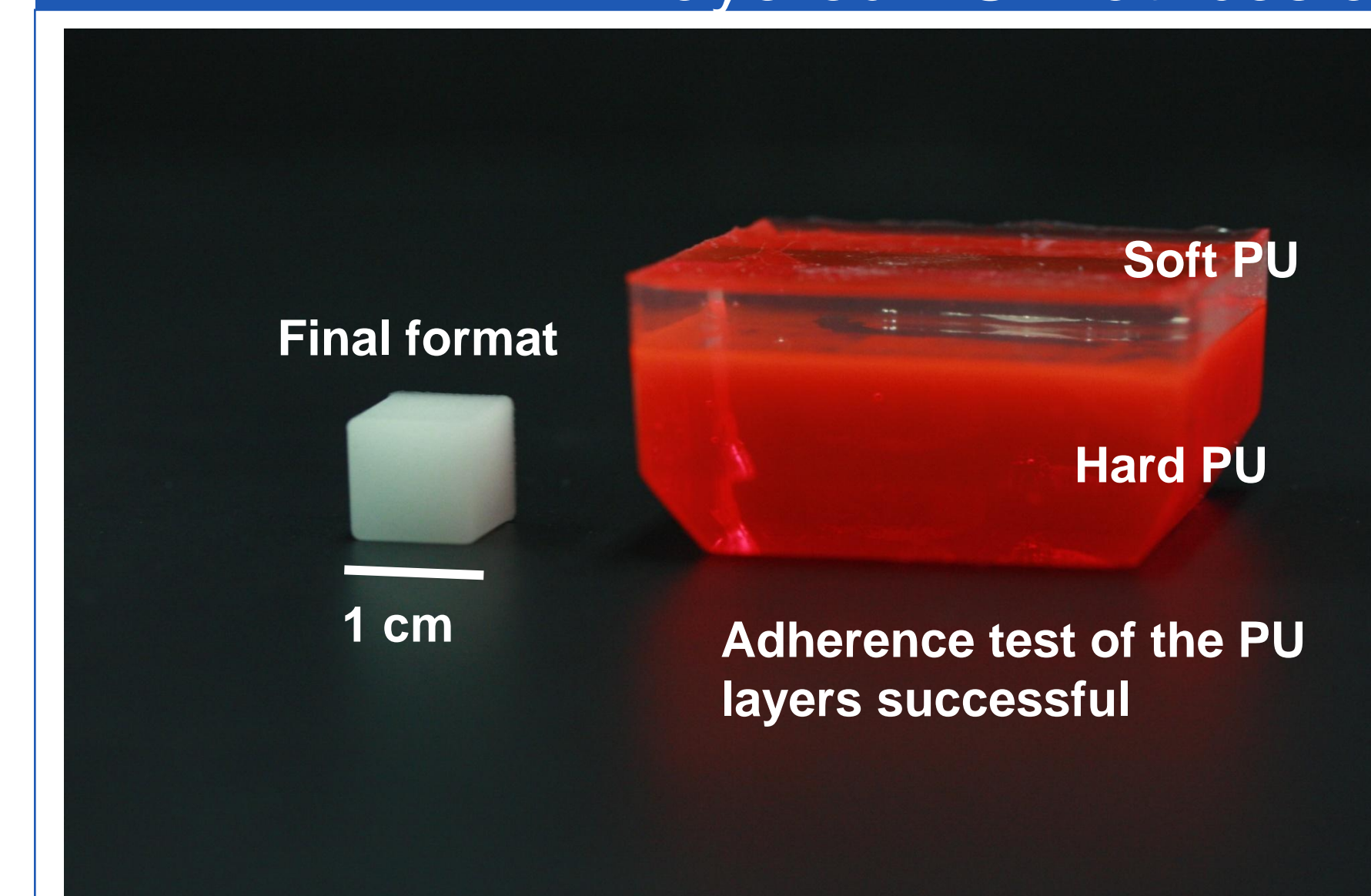
Known stable dye: Cy5.5

- Fluorescence stability in soft PU is not appropriate → >20% decrease
- Minimal changes in Hard PU matrix
- Similar overall intensity in both matrices

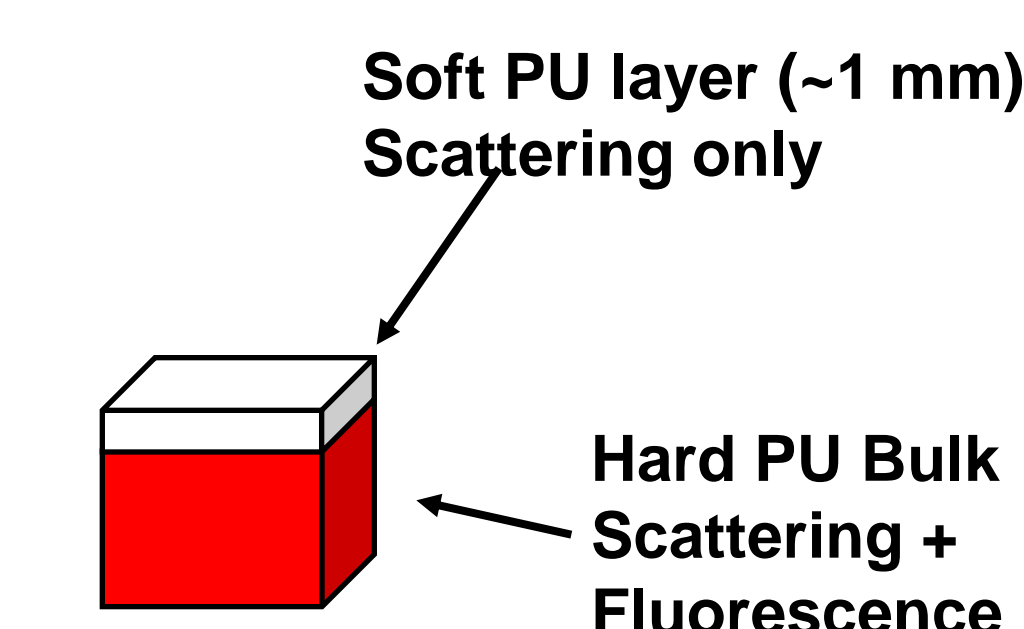


Current Design

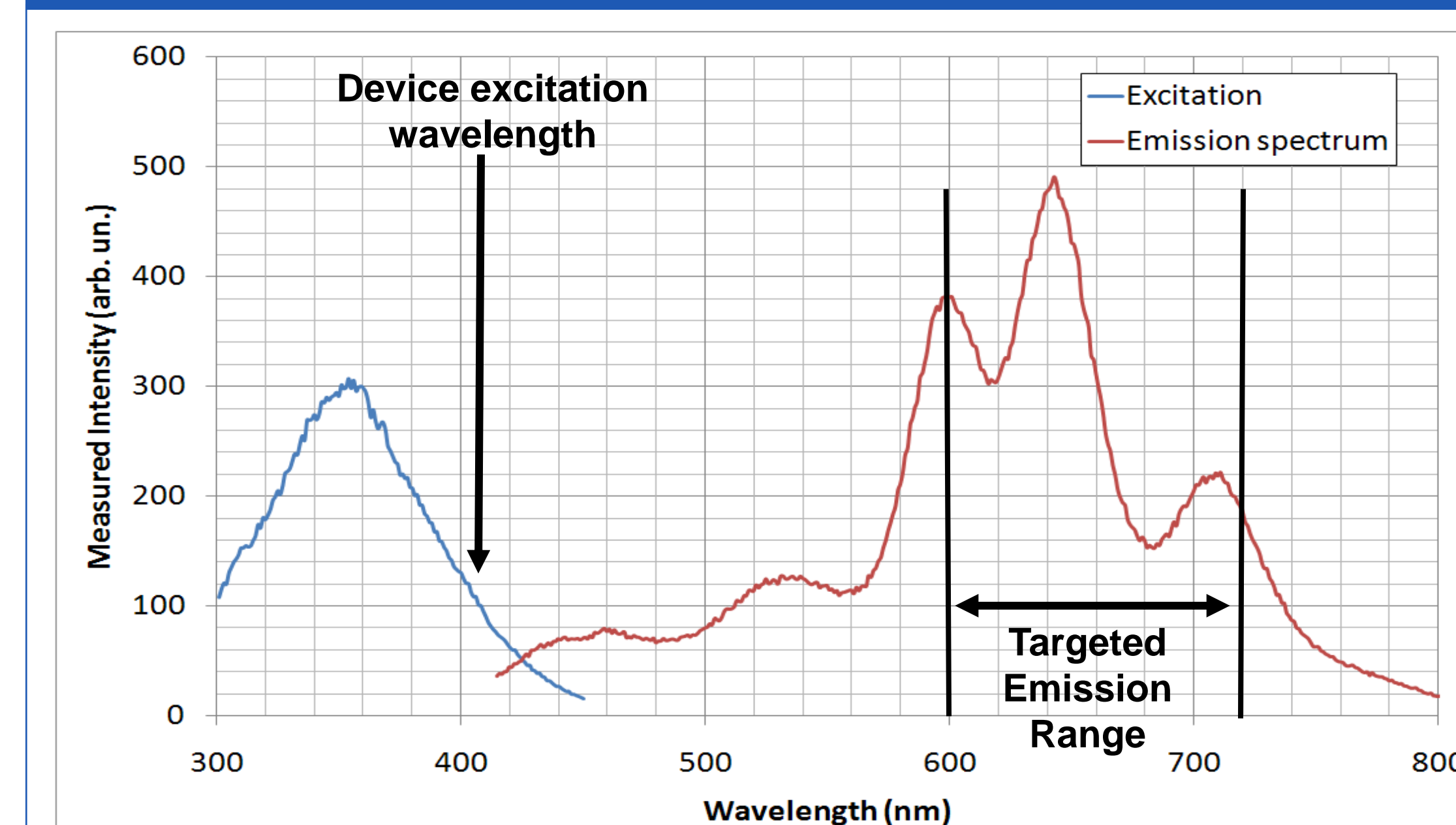
Layered PU matrices approach



- Benefit from the stability and intensity performance of the Hard PU matrix
- Combine with the optimal coupling of the soft PU matrix



First multifluorescent mixture



- Combination of 4 fluorescent dyes, to exploit overlaps of excitation and emission bands.
- Selected dyes are all stable in time
- Concentrations are to be optimized to improve flatness of emission spectrum
- Dye used for 405 excitation not optimal after blue shift of the excitation band

CONCLUSIONS AND FUTURE WORK

- Interactions of the various components (multiple dyes, PU matrix and unknown intrinsic additives of the matrix) make phantom fabrication challenging
- Soft PU matrix appears problematic for fluorescence stability with most dyes. Use of a hybrid layer design should circumvent the problem
- First operational fluorescent dye mixture in hard PU matrix shows promises
- NEXT STEPS:
 - Optimize mixture for better match of the excitation band
 - Refine mixture to obtain a flatter emission spectrum
 - Test the hybrid PU layered design with the device

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