

Introduction

- Current attempts to directly measure radiopharmaceutical uptake in single cells are limited both by spatial resolution and by the ability to localize a $\beta\pm$ emission to a specific cell. [1]
- Using microfluidic channels, we intend to separate cells on top of individual detector modules in order to determine the radiopharmaceutical uptake in each cell.
- Each detector module will need to have high detector efficiency for emissions coming from the cell placed directly atop it, and low background sensitivity for emissions coming from neighboring cells. These will primarily come from gammas due to positron annihilation.

Methods

The basic design for a single detector module in the Betabox 2.0 is seen below. It utilizes a thin layer of plastic scintillator sandwiched between a SiPM to read out the signal from the scintillator, and the microfluidic channels which deliver the cells atop the detector.

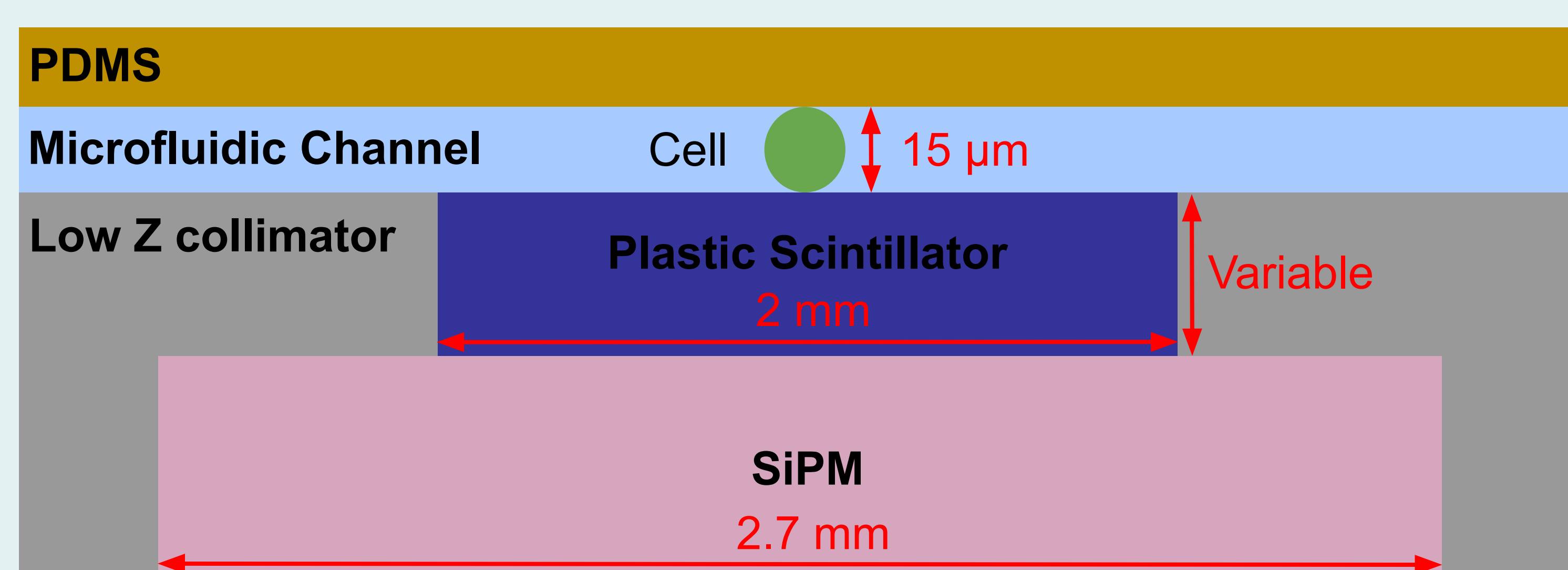


Figure 1. Design of a single detector module for the Betabox 2.0. The depth of the plastic scintillator was left variable to optimize for maximum detection efficiency and low background from neighboring detector modules.

A number of factors are worth pointing out about this geometry. First, a low Z collimator mold encapsulates the organic scintillators and SiPMs. This mold reduces any cross talk between detector modules due to energetic positrons. Second, a Broadcom AFBR-S4N22P014M SiPM with a 2.7x2.5 mm² surface area and 2x2 mm² active area was used. The small active area of the SiPM limits the dark count rate, which when compared to the average activity of a single cell ($\sim 10^{-1}$ Bq) is much larger than the signal count rate. A 2 mm diameter cylinder of plastic scintillator of variable height is optically coupled to the SiPM. The dimensions of this plastic scintillator must be optimized in order to maximize the sensitivity of the detector to the signal from the biological sample (cell) directly above it and minimize the amount of signal detected from neighboring cells. In order to perform this optimization, this geometry was built into an 8x8 array in GATE, a powerful Monte Carlo Toolkit that utilizes GEANT4. The GATE geometry is seen below.

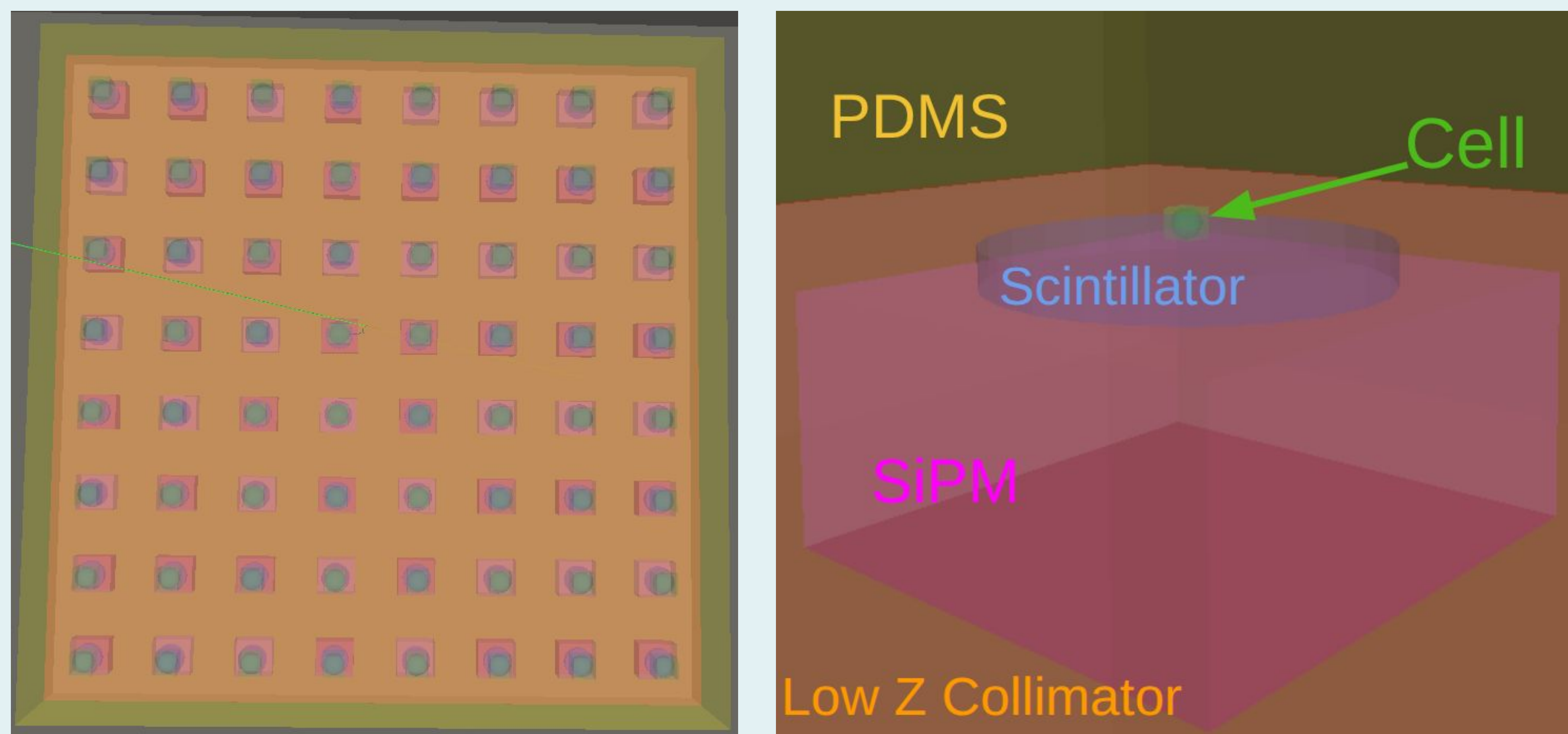


Figure 2. The geometry of the Betabox 2.0 detector in the GATE simulations. The cells in this figure have been artificially enlarged relative to the detector for improved visualization.

The GATE simulation was performed using the cells as 15 μ m diameter water spheres with uniformly distributed radioactivity. These cells were surrounded by water, which was in turn surrounded by PDMS, the polymer material that composes the microfluidic channels. The plastic scintillator was modeled as EJ-212 from Eljen Technology and the SiPM was made out of silicon. The low Z collimator for the simulation was made out of PMMA. The two isotopes used for this simulation were F-18 and Ga-68, which are commonly used β^+ emitters and represent two extremes in emitted positron energy. No optical photons were simulated, only charged particles and gammas were modeled in this simulation.

Results

Simulations were performed on a variety of scintillator thicknesses from 100 μ m to 1 mm to determine the optimal scintillator thickness. The simulated events were then filtered based on a minimum of 60 keV energy deposited in the plastic scintillator, assuming a minimum energy deposition required for detection. In order to determine the optimal scintillator thickness, two main metrics were balanced. The first is the detector efficiency. This was calculated as the total number of events which passed the energy cut in the plastic scintillator divided by the total number of simulated events. The second metric was the signal to background ratio. In this case, the signal were events from a source cell, and the background was any event detected from neighboring cells. The results for both F-18 and Ga-68 are shown below.

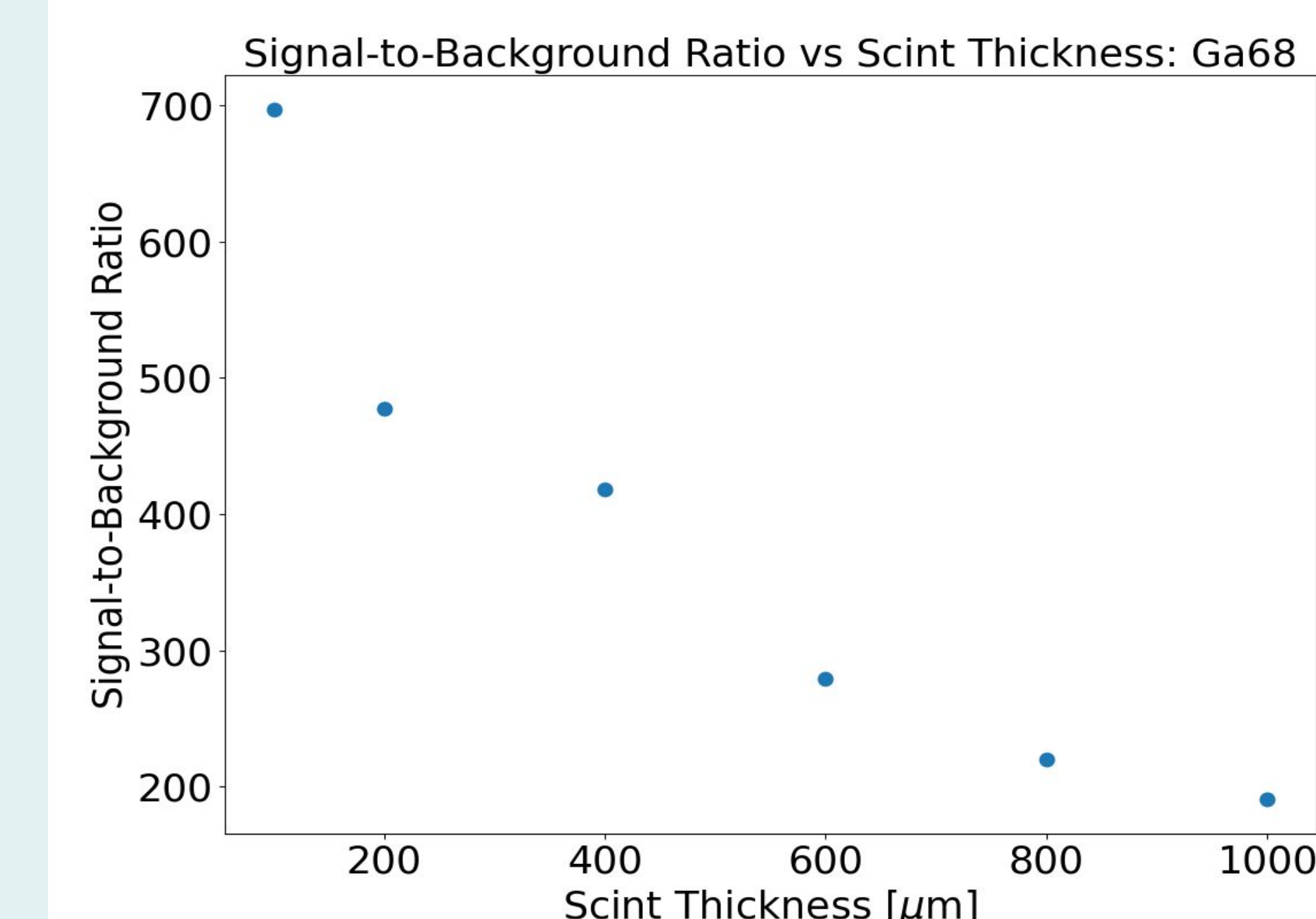
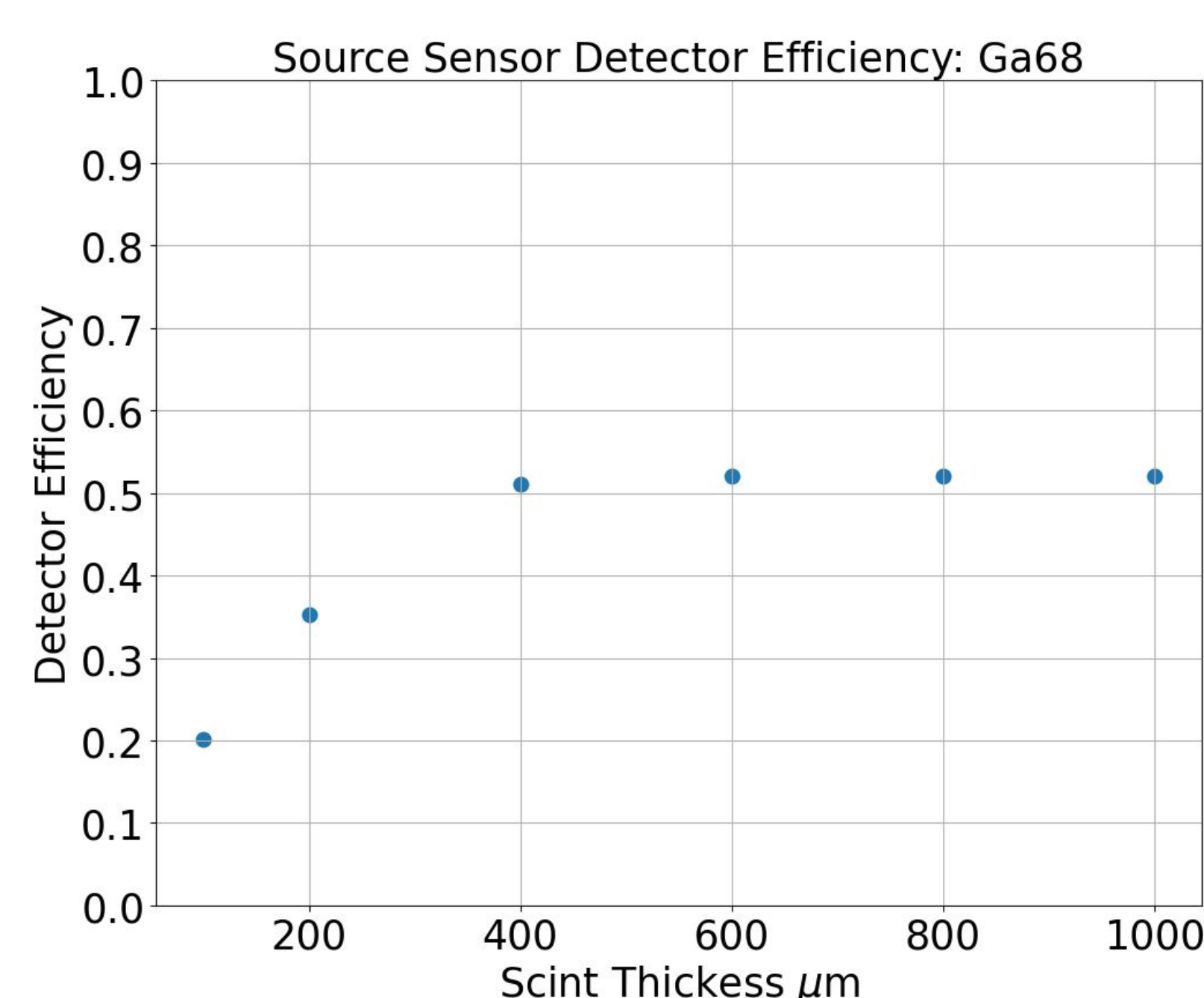
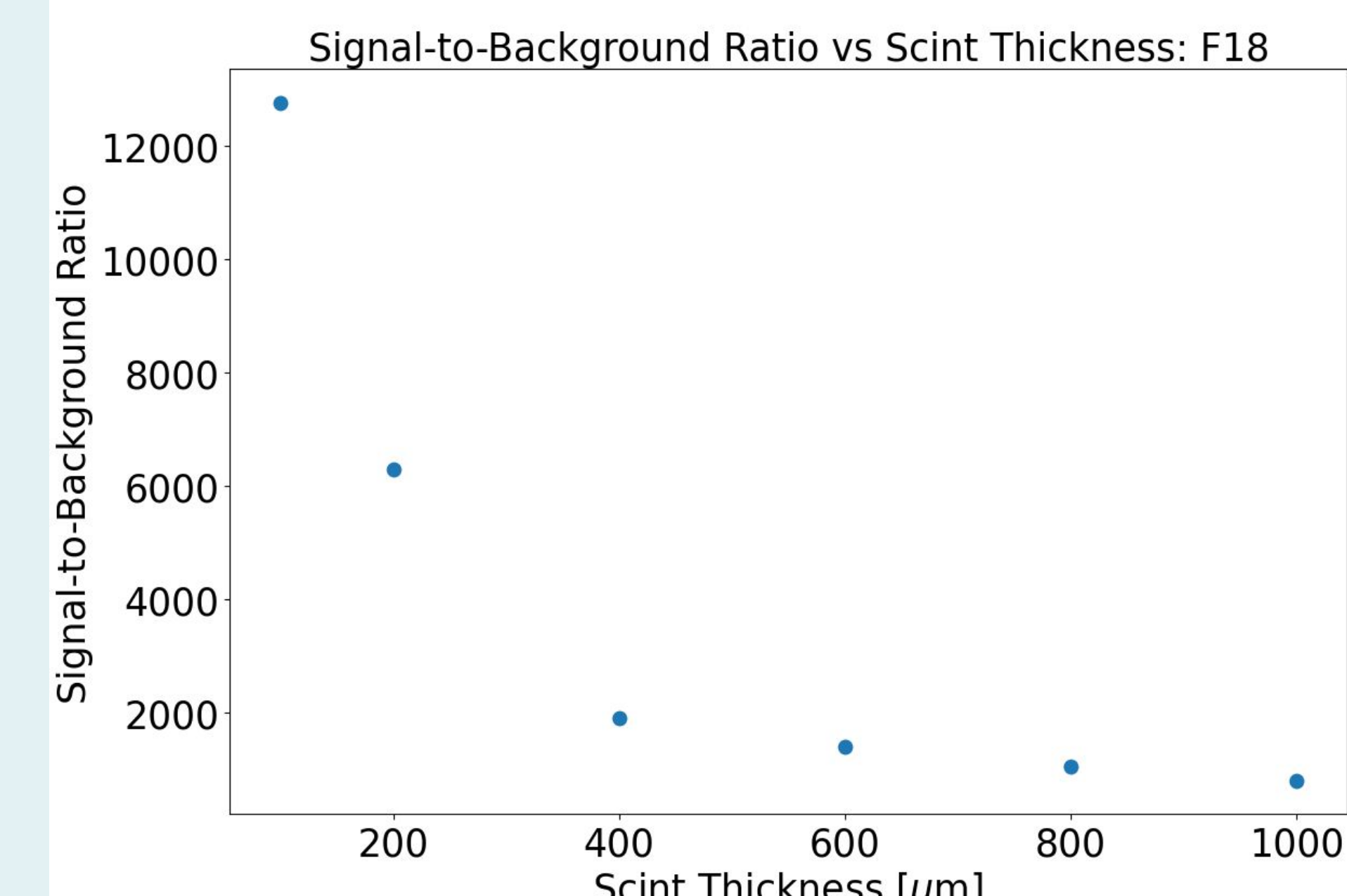
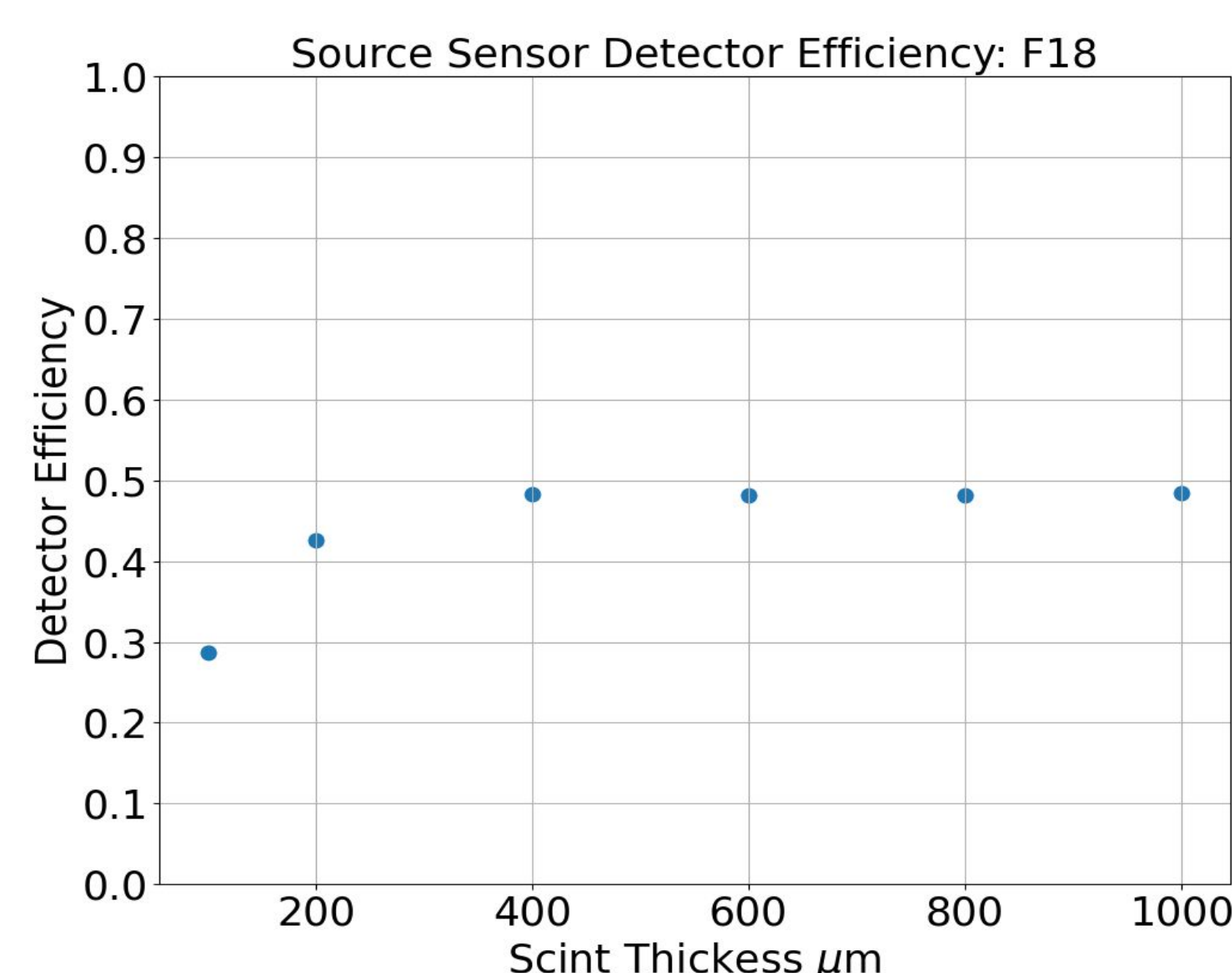


Figure 3. The detector efficiencies (left) and signal-to-background ratios (right) for F-18 (top) and Ga-86 (bottom) emitting cells. In both cases there is good separation between detector modules and high geometric detection efficiency.

Discussion & Future Work

- In order to balance the detector efficiency and signal-to-background ratio, an optimal scintillator thickness of 250 μ m was determined.
- Current further work is related to generating experimental data to verify this simulation work. Currently, a single detector module has been prepared and F-18 data has been acquired on it via PETsys electronics and a 500 μ m scintillator thickness.
- The goal is to optimize the thresholds on the readout electronics and maximize the device sensitivity, then expand to an 8x8 array as modeled in GATE.

Acknowledgements

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References

- [1] Pratz G, et al. High-resolution radioluminescence microscopy of 18F-FDG uptake by reconstructing the β -ionization track. J Nucl Med. 2013 Oct;54(10):1841-6. doi: 10.2967/jnumed.112.113365.
- [2] Jan S., et al. GATE: a simulation toolkit for PET and SPECT. Phys Med Biol. 2004 Oct 7;49(19):4543-61. doi: 10.1088/0031-9155/49/19/007. PMID: 15552416; PMCID: PMC3267383.