

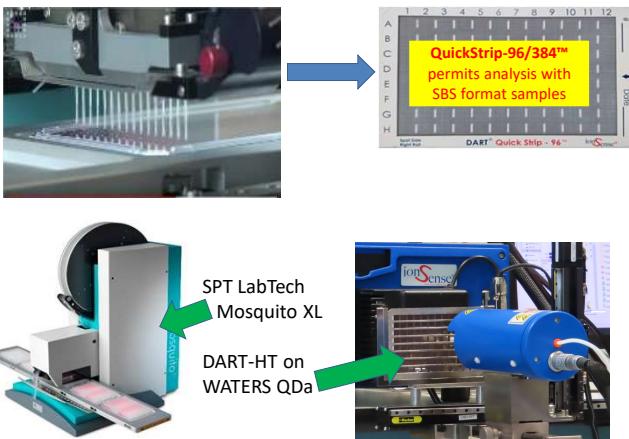
Rapid Analysis of Products from High Throughput Experimentation Utilizing a Novel Pulsed Gas Control System for an Ambient Ionization Source

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Abstract

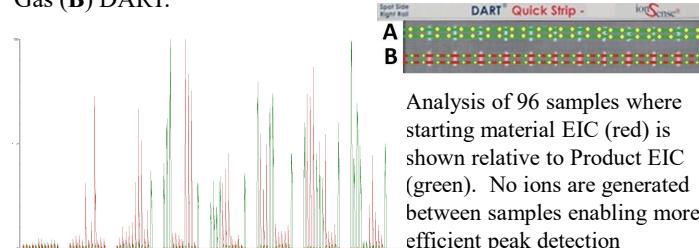
High Throughput Experimentation involves the use of small-scale samples to minimize chemical use while permitting synthesis route optimization, biocatalysts performance evaluation and bioanalytical assays while using very low volumes of chemicals, catalyst and reagents. HTE is conducted using microtiter plates potentially generating thousands of samples per cycle. Using nanoliter pipetting and a new pulsed ionizing gas system incorporated into the controller of a direct analysis in real time (DART) source an analysis rate of >20 per minute is demonstrated. Incorporating this pulsed gas method yields data with improved sensitivity, signal-to-noise, and permits simplified peak detection for targeted analytes.



Method: A series of samples were pipetted onto the wire mesh surface by using a Mosquito XL. Those sample strips were positioned on the digitally controlled linear rail which was programmed to move the sample into position, hold that position for a time, and then quickly move to the next sample in order to start the next sample analysis. Release of ionizing gas was coordinated to occur as the sample was positioned in the ionization region.

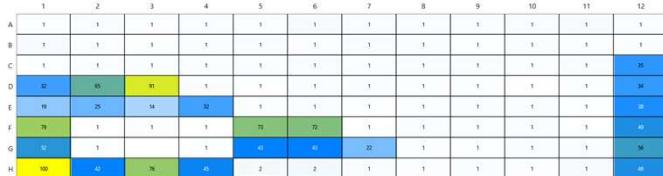
Experiment: What is Pulse Gas

Schemes for sample movement using continuous gas (**A**) or Pulse Gas (**B**) DART.



Analysis of 96 samples where starting material EIC (red) is shown relative to Product EIC (green). No ions are generated between samples enabling more efficient peak detection

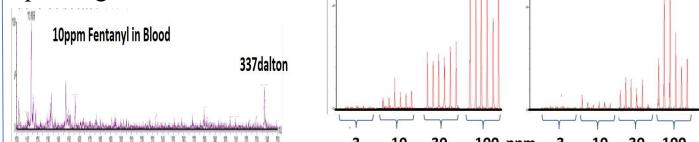
Data Analysis: Route Optimization



Due to time constraints the MS data system cannot collect this data as individual files and manual processing would require days. Here the user selects the mass values of the starting material and product. The Yellow highlights the wells with highest concentration of product. *Analyzer PRO XD SpectralWorks* used for data automated data reduction

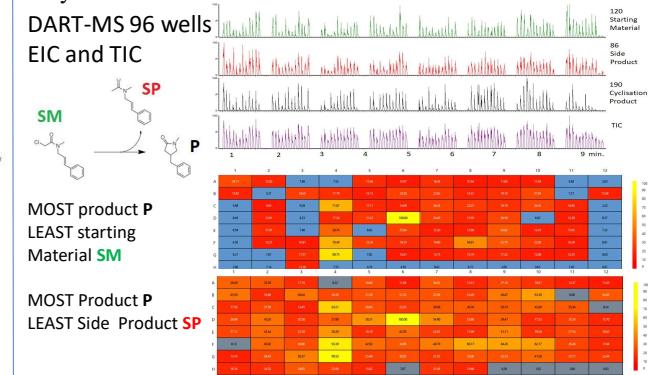
Experiment: Viscous Fluids

Analysis of blood and plasma using a single quadrupole MS operating in scan mode.



Experiment: Biocatalysis Performance

Optimization of the biocatalysts performance is demonstrated by testing the cyclization of a chloroacetamide to afford a gamma lactam with visible light irradiation, completed by using very low volumes of chemicals, catalyst and reagents. For this discussion HTE is conducted using a 96 well microtiter plate with varying reactant concentration and enzyme.



Heatmap permits rapid decision making facilitating progress

Conclusions:

- Utilizing a pulse gas DART source permit higher throughput ambient ionization of samples containing high concentrations of chemicals vs solvent ideal for HTE
- Analysis of 6 -10 samples per minute is enabled with limited sample preparation using low volume samples
- Analysis of samples of biological origin is facilitated with small molecule detection using scanning or MRM

Authors thank Prof. Todd Hyster, and Bryce Nichols, Princeton U. for generous use of results from their samples. See Biegasiewicz et al., *Science* 364, 1166–1169 (2019) for details on their Biocatalysis efforts.

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