Compact Optical Microfluidic Uric Acid Analysis System

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Why Uric Acid Analysis

\begin{itemize}
\item Uric Acid (UA) is clinically important.
\item Gout is a disease caused by the buildup of uric acid (UA) in the body leading to deposition of UA in joints, which causes joint swelling and debilitating pain.
\item UA level is a powerful biomarker or independent predictor of certain renal, cardiovascular, and cerebrovascular diseases.
\item Tumor lysis syndrome, which is caused by the breakdown products of dying cancer cells leading to hyperuricemia and acute renal failure, happens to 3%-22% patients who receive chemotherapy.
\end{itemize}

Current Technology: Large, slow, sample-to-analyzer

GW Point-of-Care Microfluidic UA Analyzer Prototype

This work developed and successfully tested a prototype handheld UA analyzer.

Three scientific papers and Two invention disclosures resulted.

Because of this work, we have a clear path to clinical testing.

Significant commercial interests are expected.

Recognition:

- Enzymatic Reactions to provide the selectivity and specificity
- Transduction:
  - Optical Fluorescence detection gives good sensitivity and signal to noise ratio, and reduces the interferences.

Two-Step Enzymatic Reaction (Invitrogen)

1. 1st Step: Uric Acid + O\textsubscript{2} (air) \rightarrow Allantoin + CO\textsubscript{2} + H\textsubscript{2}O
2. 2nd Step: H\textsubscript{2}O + Amplex Red \rightarrow Resorufin

Dramatically smaller analyzer size than conventional

Microfluidics technology of small sample about 1-2 drops

No pre-concentration, separations or sample mixing bench-top and desk-sized instruments!

Making and Using Functionalized Sample Holder

1. \textbf{1st Invention:}
   - Functionalized Sample Holder
   - Mesh to guide enzymes and chemicals.
   - A water-soluble polymer was used to entrap the enzyme and chemicals, and hold the mesh in place.
   - Simple fabrication: Low cost

2. \textbf{2nd Invention:}
   - Compact High-Performance Prototype
   - 3 inch (L) \times 2 inch (W) \times 2 inch (H)
   - Diffusional mixing can be achieved in about 100 seconds
   - Compact, robust

Overall Processing and Use Sequence

\begin{enumerate}
\item Overall Processing and Use Sequence
\item Microscope Slide
\item Lens Paper Mesh
\item Uricase
\item Glass Slide
\item Enzyme uricase
\item Enzyme HRP
\item Chemical Amplex Red
\item Mesh fiber
\item Microscope Slide
\item Lens Paper Mesh
\item Uricase
\item Glass Slide
\item Enzyme uricase
\item Enzyme HRP
\item Chemical Amplex Red
\item Mesh fiber
\end{enumerate}

Results: Two Calibration Curves

- Both calibration curves are plotted as initial reaction rate (slope: mV/sec) as a function of UA concentration
- Calibration Curve #1:
  - For clear diluted samples of saliva and urine
  - Developed by using 7 UA solutions of known concentrations
  - Data agrees with Michaelis-Menten Enzyme Kinetics
  - Data was obtained in 60 seconds

Calibration Curve #2:

- For opaque diluted blood
- Spiking unknown blood sample
- Results were obtained in 60 seconds

Our analyses are in these clinical ranges for all three sample types:

- Blood Sample Comparison with J&J VITROS 5600 Analyzer

Exciting Possibilities

- More applications, such as glucose and cholesterol.
- Truly handheld prototype integrated with display and microcontroller is planned.
- Proposals based on this work are possible: NIH (NIAID, NIMH, NCI R21), NSF (Biosensing, Biophotonics), and DHHS for clinical testing.
- Commercial licensing is expected.