UNIVERSITY OF WASHINGTON

Yager Laboratory

Department of Bioengineering
University of Washington

Microfluidics for Point-of-Care Diagnostics

Advancing Diagnostics

Today's sophisticated laboratory techniques allow accurate diagnosis of disease in centralized labs of hospitals and other medical centers. These techniques are often slow and expensive because of the labor, reagents, and equipment involved.

Microfluidic "lab on a card" systems can accomplish the same diagnoses in a format that is portable, automated and inherently inexpensive.

In developed communities, these technologies could allow high-quality, rapid diagnosis at the point-of-care, decreasing wait times for test results while simultaneously reducing cost.

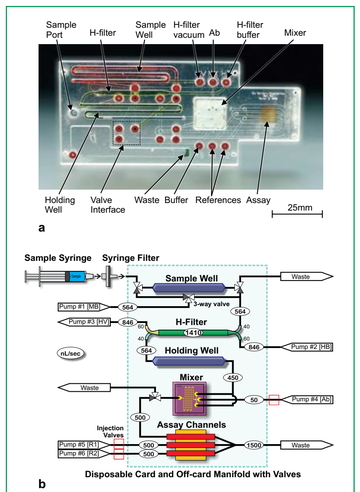
In under-resourced communities, high-quality diagnosis can be difficult or impossible to obtain, both in Washington state and abroad. In these settings, microfluidic systems are poised to bring robust diagnostic tests and a new standard of health care to people in need.

Microfluidic Technologies

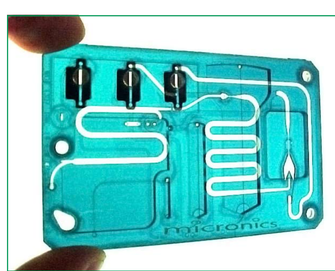
Many standard lab techniques have been adapted to the microfluidic environment, including technologies developed and used in our work or that of our collaborators:

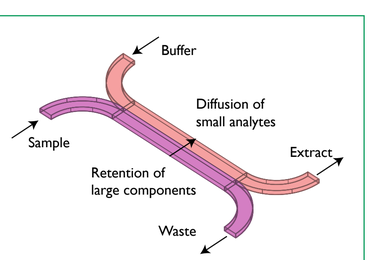
- Pumps
- Mixers
- Valves
- Filters
- Switches
- Fractionation
- Concentration
- Immunoassays
- Genetic Assays
- Cell Imaging

These are components that can be engineered into diagnostic systems.



Example of an integrated, disposable diagnostic card





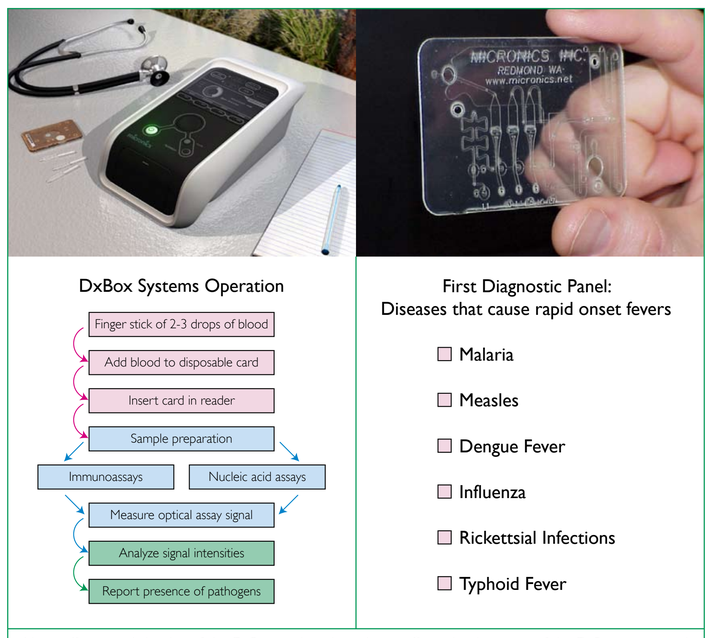
Microfluidic devices require very accurate control of fluid motion. Often, this is achieved by moving the fluid slowly enough that individual "layers" of fluid move parallel to one another in a condition known as "laminar flow." This state is contrasted with turbulent flow, where different layers of fluid mix with one another.

Left: One example of using laminar flow to control fluid motion takes place in a flow cytometer. Cells in one stream of fluid are made to flow in single-file by squeezing the stream with surrounding streams in a tapering channel. Because the stream of cells is so tightly positioned, individual cells can be interrogated optically. The device pictured was developed by Micronics, Inc.

Right: Another example of the importance of laminar flow is the H-filter, a device developed in the Yager Laboratory. In this filter, a sample stream containing small and large components is run parallel to a second stream. While the streams do not mix, particles can randomly migrate between them via diffusion. The small components diffuse quickly into the second stream, but the large components diffuse too slowly to leave the laminar flow stream. At the end of the channel the components that have diffused more are separated from those that have diffused less. In this way, small and large components are filtered from one another.

Point-of-care Diagnostics for the Developing World

Funded by the Bill & Melinda Gates Foundation's Grand Challenges in Global Health



Upper: Conceptual drawing of the DxBox card reader provided by DxBox collaborator Invetech, and an example of a microfluidic card produced by DxBox collaborator Micronics, Inc. Cards similar to this will be used with the DxBox system.

Lower: Operational concept of the DxBox system, and list of the diseases to be detected. The architecture of the DxBox system could be applied to many other diseases, simply by changing the microfluidic card.

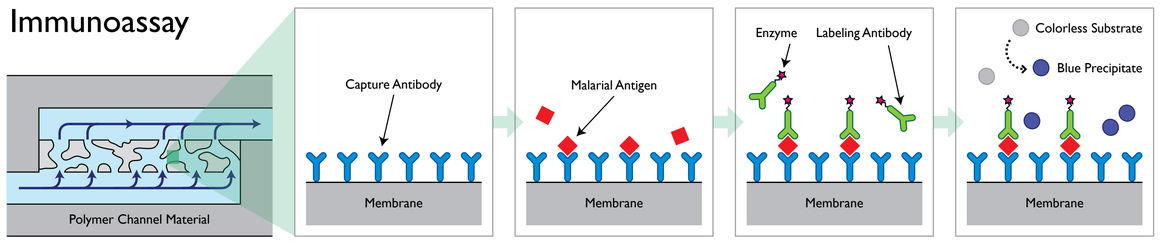
This project aims to improve health care in the developing world with a highly portable diagnostic system, the "DxBox," that:

- Requires only 2-3 drops of blood
- Uses inexpensive, disposable test cards and a battery-powered reader
- Tests for 6 diseases in parallel
- Looks for both protein and genetic markers
- Gives a diagnosis in under 10 minutes
- Meets or beats the highest standards of clinical diagnostic accuracy

The five-year project involves two UW and four industry collaborators working on an array of design challenges. The Yager Laboratory is developing the device's microfluidic immunoassays, which identify protein markers that indicate disease states.

Example of a DxBox Immunoassay

The DxBox will look for proteins that are indicative of various diseases. The diagram on the right shows an example of one of these immunoassays: a test for malaria. Because different parts of the membrane are coated with different "capture" molecules, diseases can be determined by which coated area turns blue at the end of the assay. This approach allows testing for many diseases with a small sample.



A porous membrane seals a microfluidic channel. Pumps drive fluid through the membrane.

1: The membrane has been coated in antibodies that capture the analyte of interest

2: The analyte flows in and is bound to the antibodies on the membrane. Other molecules are not bound.

3: A labeling antibody flows in and binds only to the captured analyte. Unbound antibodies flow away.

4: The enzyme label on the second antibody converts a molecule in a colorless solution to a blue product.

Salivary Diagnostics System

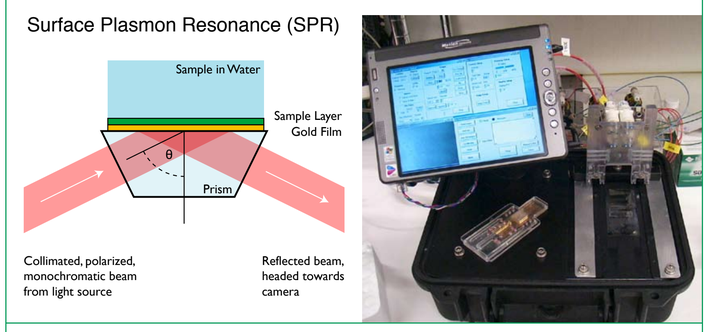
Funded by the National Institutes of Health (NIDCR)

Saliva is an under-utilized sample in point-of-care testing, containing most of the molecules found in blood. Giving a saliva sample is painless and requires no specialized training. Our project will:

- Develop an integrated system for measuring analytes in saliva
- Validate the system using model analytes
- Apply the system to optimize drugs for treating epilepsy, which affects 1% of the US population

The Yager Laboratory has led the development of the detection technology and immunoassays. The device has already been reduced to a portable size and is undergoing continuing miniaturization.

Detection System for Salivary Diagnostics



Left: A diagram of the surface plasmon resonance measurement scheme. Light is reflected off the inside face of a prism – the amount of light reflected depends on the refractive index of the material near the gold. The gold is coated with molecules that capture only specific molecular targets from the sample. If these targets are present, their binding to the capture molecules changes the index of refraction at the gold surface. This binding thus causes the amount of light reflected to change. In this way, the presence or absence of a target molecule can be detected by watching the reflected light levels.

Right: A portable prototype of the salivary diagnostics instrument. The computer-controlled device integrates a surface plasmon resonance (SPR) imaging system, a disposable microfluidic card, syringe pumps, and off-card valves.

Contact

Department of Bioengineering, Box 355061, University of Washington, Seattle, WA 98195

Dr. Paul Yager	*206 543 8063*	*yagerp@u.washington.edu*	*http://faculty.washington.edu/yagerp/*
Dean Stevens	*206 616 3129*	*yasuo@u.washington.edu*	
Katherine McKenzie	*206 616 3129*	*kmckenz@u.washington.edu*	