Development of a Low-Cost Photon Correlation System for Measuring HIV-1 Viral Load

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Problem Statement

An HIV positive infant will spend over $3,600 in a lifetime for viral load tests alone.

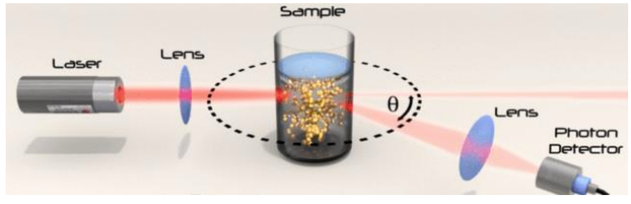
The Macha Hospital in Zambia requires an HIV viral load test that is:

- Low Cost: less than $10 per test
- Quick: Under 1 hour
- Accurate: Sensitivity of 1000 viruses/ml

A viral load test requires the detection of activated complexes through the use of dynamic light scattering, data acquisition and signal processing.

Dynamic Light Scattering

Dynamic Light Scattering is a laser-based optic technique that can be used to determine the size of nanoparticles in solution
Methodology:
(1) Laser beam projects onto a sample containing nanoparticles
(2) Particles within the sample scatter light
(3) The fluctuations in the intensity of scattered light are related to the size of particles in the solution.



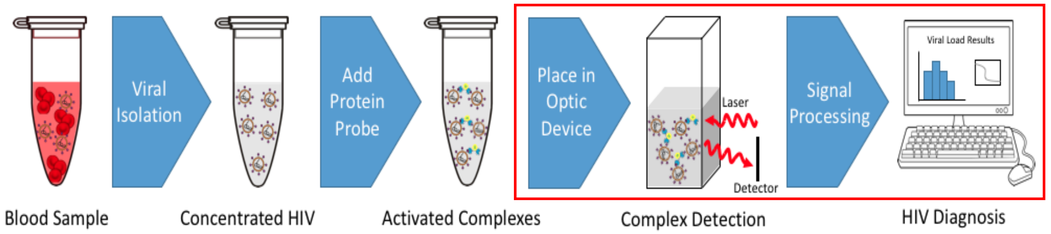
Above: Dynamic light scattering concept. Laser projected into sample scatters off of nanoparticles, which is detected with optics and a photon detector. Image courtesy of LSInstruments

Data Processing Requirements

Goals	Target	Solution
Speed: Needs to be fast enough to prevent data loss	UART @ 6 MBaud, each data point is 2 16-bit ints, additional 2 control bits per int, means max speed = 1 data point every 7 µs. Speed sufficient currently unknown.	Data collection @ 4.05kHz / 1 data point per 250 µs Autocorrelation @ 2.63MHz / 1 data point per 0.38 µs Combined collection and processing @ 4.05kHz / 1 data point per 250 µs
Cross-platform: Needs to be capable of operating on multiple devices and operating systems	Capable of running on Windows and Mac OS, with acceptable speeds on at least 3 devices.	Java 8 platform chosen, separate drivers for different OSs. Undergoing tests for cross-device compatibility.

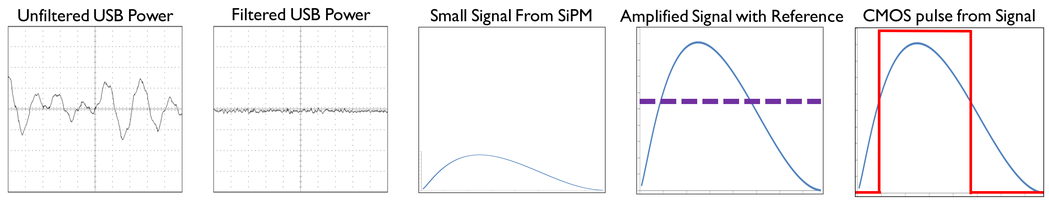
Diagnostic Strategy

The following Diagnostic Strategy has been proposed for HIV viral load Determination:



Complex detection involves dynamic light scattering (DLS). A fiber optic output from DLS is fed into signal processing circuitry, converting photon events into time stamps to be processed by a computer. A real-time autocorrelation function provides a measure of viral aggregates, allowing medical professionals to get an immediate HIV viral load count determination.

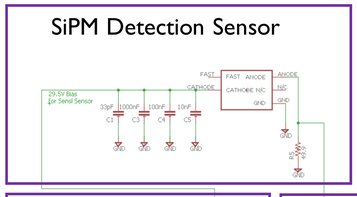
Detection Circuitry and Processing

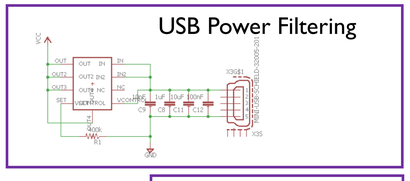


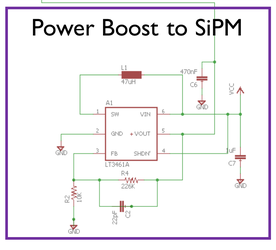
For convenience of use, the detector is powered via USB, allowing a computer or portable battery to run the detection system. USB voltage often has a noisy output, and for high frequency applications this must be filtered out to provide consistent power to each component.

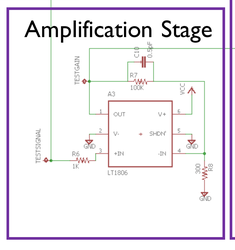
DLS to Data Collection:

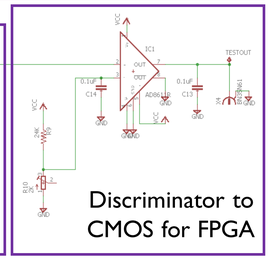
- Photomultiplier chip senses photon events from DLS fiber optic
- Signal is amplified x100
- Discriminator compares amplitude of signal to threshold voltage
- If signal < threshold: Low
  If signal > threshold: High
- CMOS output sent to FPGA for data acquisition



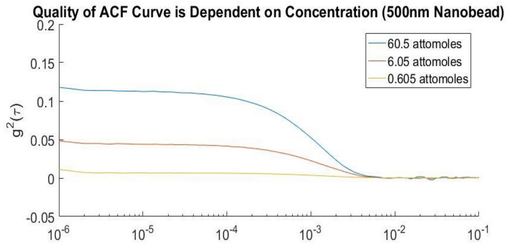




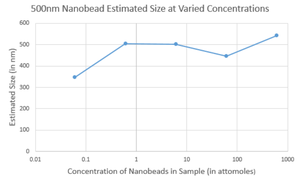




Results

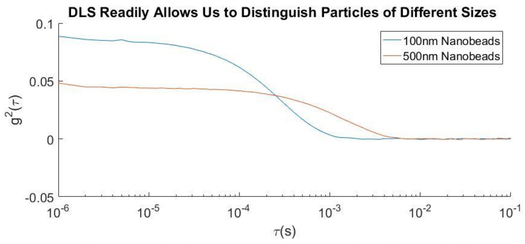


- Quality of the ACF curve is dependent on concentration of particles in solution.
- Too high of a concentration does not allow for functional light scattering.



Concentration (in attomoles)	Estimated Size (in nm)
604.6	543.5699
60.46	446.202
6.046	502.6991
0.6046	504.887
0.06046	347.19

- Too low of a concentration produces a weak scattering signal.
- Low concentration limit can be improved by better alignment of detection optics



- At optimized concentrations we observed a distinct difference in the ACF curve for a 100nm (representative of HIV size) and 500nm (representative of HIV aggregates) Nano beads.

- A difference in the decay time can be seen in the 100nm and 500nm ACF curves above.
- The ACF curve distinguishes the size of a particle using the decay time, the difference in amplitudes of the curve does not influence the particle size estimation.

Future Work

- Improve DLS detection efficiency by more precise coupling of signal into fiber optic cable.
- Printed circuit board will be manufactured according to initial design and will be tested to validate CMOS output timing as well as noise-protection for SiPM signal.
- Optomechanical coupling must be designed to attach the fiber optic output from the DLS technique to the detection circuitry.
- Improved speed of data computation.

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