Nanopore Detector Feedback Control Using Cheminformatics Methods Integrated with Labview/Labwindows Tools

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NANOPORE DETECTOR FEEDBACK CONTROL USING CHEMINFORMATICS METHODS INTEGRATED WITH LABVIEW / LABWINDOWS TOOLS

A Thesis

Submitted to the Graduate Faculty of the University of New Orleans in partial fulfillment of the requirements for the degree of Master of Science in Computer Science

by

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B.E. Annamalai University

August 2006
ACKNOWLEDGEMENTS

I take this opportunity to thank my thesis advisor Dr. Stephen Winters-Hilt. I thank him for giving me the freedom to explore the various possibilities in this fast growing field. I would also like to take this opportunity to thank my thesis committee members, Dr. Yixin Chen and Dr. Bin Fu. I also thank Dr. Shengru Tu, graduate coordinator, Department of Computer Science, UNO for guiding me all through my Master’s program. I would also like to thank Dr. Mahdi Abdelguerfi, Chairman, Department of Computer Science, University of New Orleans, for his support. I would also like to express my gratitude to all the other professors in the department.

I would also like to express my appreciation to all my colleagues at Children’s Hospital, New Orleans who helped me a lot understanding the chemistry behind the experiment. I also thank the software team at UNO who helped me with the interfacing of external code.

Finally, my parents and friends for their overwhelming support all the way.
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ABSTRACT

Single biopolymers (DNA, RNA, or polypeptide) can be examined using an alpha-hemolysin channel detector. When a biopolymer is present in an alpha-hemolysin channel it can produce a highly structured ionic current blockade pattern, where the lifetimes at various sub-blockade levels reveal information about the kinetics of the biopolymer. Here we describe integration of LabVIEW/LabWindows automation capabilities with the "in-house" Channel Current Cheminformatics (CCC) software. Data acquired with LabVIEW/LabWindows is passed to the CCC software, on a streaming real time basis, for analysis and classification. The classification results are then quickly returned to the LabVIEW/LabWindows automation software for experimental feedback control. The prototype signal processing architecture is designed to rapidly extract useful information from noisy blockade signals. A fast, specially designed, generic Hidden Markov Model can be used for the channel current feature extraction. Classification of feature vectors obtained by the HMM can then be done by Support Vector Machines.
1. INTRODUCTION

LabVIEW is a powerful, graphical programming development system which is ideally suited for data acquisition, storage, analysis, and presentation. LabVIEW is one of the best known data acquisition and instrument control tool. It has rich libraries consisting of Input / Output, Analysis and display. LabVIEW has development tools that include Control block diagrams, State diagram, User interface programming. The control block diagrams can be used for designing linear, nonlinear, discrete, and continuous control systems. A State diagram can be used for defining multiple states and transition logic between them using a graphical state diagram representation. While a User interface programming can be used for managing very complex user interfaces.

In the nanopore detector LabVIEW is used to control the instrument settings in an on-line feedback manner that is informed by LabVIEW passing information in and out of its software environment into the CCC (Channel Current Cheminformatics) software environment. LabVIEW can be used to control the voltage switching, temperatures changes, or laser modulations. This provides bandwidth broadening capabilities to the nanopore instrument. LabVIEW is not limited to the only controls stated above. Instead it can also be used to drive a Pico pump or to perfuse a nanopore detector, to provide automated perfusion of the device all that is needed is a stepper motor that can be controlled by LabVIEW. Moreover the integration capabilities of external code to LabVIEW broadens the application of LabVIEW in the nanopore detector as it becomes possible to integrate the in-house software developed at UNO’s Biomedical Informatics and Bioinformatics (BIB) Lab.
2. BACKGROUND

2.1 The highly stable, nanometer-scale, α-hemolysin protein channel

The α-hemolysin channel is a protein heptamer, formed by seven identical 33 kD protein molecules secreted by Staphylococcus aureus. The total channel length is 10 nm and is comprised of a 5 nm trans-membrane domain and a 5 nm vestibule that protrudes into the aqueous cis compartment (Song et al., 1996). The narrowest segment of the pore is a 1.5 nm-diameter aperture (Song et al., 1996), see Fig. 1a. By comparison, a single strand of DNA is about 1.3 nm in diameter. Given that water molecules are 0.15 nm in diameter; this means that one hydration layer separates ssDNA from the amino acids in the limiting aperture. This places the charged phosphodiester backbone, hydrogen bond donors and acceptors, and apolar rings of the DNA bases within one Debye length (3 Å in 1 M KCl) of the pore wall. Not surprisingly, DNA and RNA strongly interact with the α-hemolysin channel during translocation. Although dsDNA is too large to translocate, about ten base-pairs at one end can still be drawn into the large cis-side vestibule. This actually permits the most sensitive experiments to date, as the ends of “captured” dsDNA molecules can be observed for as long as desired to resolve features (Winters-Hilt, 2004;
Winters-Hilt and Akeson, 2004; Winters-Hilt et al., 2003; Winters-Hilt, 2003; Vercoutere et al., 2003). For ssDNA translocation under normal operating conditions (Kasianowicz et al., 1996; Akeson et al., 1999; Meller et al. 2000; Meller et al. 2001; Vercoutere, et al., 2001; Bezrukov, 2000; Bezrukov et al., 1994), approximately one nucleotide passes the limiting aperture of the channel every microsecond, and a vigorous effort is underway to find ways to slow down and control this translocation process (Meller et al. 2001).

LabVIEW is used for acquiring the signal and LabVIEW makes use of its automation capabilities with Channel Current Cheminformatics (CCC) software developed at UNO’s Biomedical Informatics and Bioinformatics (BIB) Lab. Different tools are employed at each stage of the signal analysis (as shown in Fig. 1b) in order to realize the most robust (and noise resistant) tools for knowledge discovery, information extraction, and classification. Statistical methods for signal rejection using SVMs are also employed in order to reject extremely noisy signals. Since the automated signal processing is based on a variety of machine-learning methods, it is highly adaptable to any type of channel blockade signal. This enables a new type of informatics (cheminformatics) based on channel current measurements, regardless of whether those measurements derive from biologically based or a semiconductor based channels.

LabVIEW is capable of running voltage driven experiments, which requires the switching of voltages at a very high frequency. It is also used to modulate the temperature and the perfusion of the nanopore detector can also be automated as soon as a channel is formed. The automation of the perfusion device requires the use of a stepper motor which is controlled by LabVIEW. Some of the other instruments that can be controlled by LabVIEW include an optical chopper and a laser lamp. All the control equipment is driven by feedback originating from the nanopore detector as shown in Figure 2.2 of the overall architecture of LabVIEW/LabWindows data acquisition system.
Support Vector Machines can also be integrated to LabVIEW/LabWindows using the integration capabilities of LabVIEW. The SVM discriminators are trained by solving their KKT relations using the Sequential Minimal Optimization (SMO) procedure (Platt, 1998). A chunking (Osuna et al., 1997; Joachims, 1998) variant of SMO also is employed to manage the large training task at each SVM node. The multi-class SVM training generally involves thousands of blockade signatures for each signal class. The data cleaning needed on the training data is accomplished by an extra SVM training round.
2.2 Noise in acquired signal

Noise can be defined as the addition of external factors to the signal. It is a disturbance that affects the signal and it also distorts the information carried by the signal. Noise sources limit the resolution of the nanopore detector, a lot of times noise serves as a signal that tells where the noise is originating from. There are numerous sources of noise and there are also a variety of them. The types of noises are many, one of them is AF noise emanating during moving, vibrating or colliding of molecules in the pore. The nanopore detector itself is very sensitive to AF noise. The main noise encountered in the nanopore detector is Gaussian Noise. Gaussian noise can be explained further by white noise and thermal noise.

2.2.1 White noise

A White noise is a random signal with a flat power spectral density. The signal's power spectral density has equal power in any band, at any centre frequency, having a given bandwidth. An infinite-bandwidth white noise signal is a theoretical construct. By having power at all frequencies, the total power of such a signal is infinite. In practice, a signal can be "white" with a flat spectrum over a defined frequency band.

A Gaussian white noise is a good approximation of many real-world situations and it generates mathematically tractable models. The values of a Gaussian white noise are independent.

2.2.2 Thermal noise

Thermal noise is an unwanted current or a voltage that is produced that is produced in electronic equipment due to the agitation of electrons by heat. Thermal noise is also known as Johnson noise, it has its roots in thermodynamics. Thermal noise is associated with the random movement of free particles in the nanopore. Even though the random movements average to zero, there are fluctuations about the average that constitute the thermal noise.

2.2.3 Membrane Noise

The fluctuations that are inherent in the biological membrane constitute the membrane noise. This is caused by the excited membrane and the fluctuations in current or voltage are caused due
to the random opening and closing of ion channels, that is the opening and closing of the mouth of the nanopore due to the translocation causes the lipid bilayer membrane to go to a state of excitation.

2.2.4 Device Noise

Electrical distortions are introduced in the system due to the electrical components that are used in the experiment. For example an inductance is caused when two charged wires are close together.

2.2.5 Nanopore Noise Sources

Noise cannot be eliminated altogether but it can be reduced by using appropriate compensation circuits and there are various compensation systems which can be used to make the conditions favorable to the user.

The accessible detector bandwidth is delimited by noise resulting from 1/f (flicker) noise, Johnson noise, Shot noise, and membrane capacitance noise. Shown below is a 500ms Sample of a 9GC hairpin capture, as illustrated in Figure 2.3 there are four current spectral densities. We have the bi-layer at 0 pA and we see a sharp rise in current to 120 pA which is a signature of the open channel. The toggles seen in Figure 2.3 occurs when the molecule blocks the channel and when there is no motion of the molecule the toggles are absent, we then say that the molecule is stuck in the channel. For 1.0 M KCl at 23C, the α-hemolysin
channel conducts 120 pA under an applied potential of 120 mV. The thermal noise contribution at the 1 GΩ channel resistance has an RMS noise current of 0.4 pA. Shot noise is the result of current flow based on discrete charge transport. During nanopore operation with 120 pA current (with 10KHz bandwidth) there is, similarly, about 0.6 pA noise due to the discreteness of the charge flow. As with Johnson noise, the Shot noise spectrum is white. The power spectra for the various current spectral densities is shown in the figure below.

![Power Spectra](image)

**Figure 2.4: Power Spectra**

It can be seen in the above power spectra plots that our accessible band width is limited by 1/f noise. The complex toggling with stationary statistics (due to the stationarity of the physically observed kinetics), tends to have a 1/f power spectrum at low frequencies. This is exhibited in the power spectra plot of a toggle. A two-state Markovian toggling system has $1/f^2$ power spectrum, we seek signals with power spectra $f^{-z}$ with $0.5 \leq z \leq 2.5$ over a significant range.
2.3 Choice of Aperture

The specific capacitance of a lipid bilayer is approximately 0.8 μF/cm², and the specific conductance is approximately 10⁻⁶ Ω⁻¹cm⁻². In order for bilayer conductance to produce less RMS noise current than fundamental noise sources, the leakage current must be a fraction of a pA. This problem is solved by reducing to less than a 500μm² bilayer area, for which less than 0.6 pA leakage current results and for which total bilayer capacitance is at most 4pF. This indicates that a decrease in bilayer area by another magnitude is about as far as this type of noise reduction can go. Hence the aperture ranges in size between 1 micron in diameter and 100 microns in diameter, where smaller apertures are used in the single channel experiments and larger apertures in the multi-channel experiments.

2.4 Data Acquisition System

The data acquisition (DAQ) system is a combination of tools and processes that are used to gather analyze and record information about the phenomena in the nanopore device. The hardware setup consists of a computer, data acquisition card and a break out box, a break out box gives the user easy access to all the pins of the card. The card is connected to the breakout box using a noise shielding cable.

![Figure 2.5 Hardware Setup](image)

A Data acquisition system can be divided into two general categories: hardware and software.
2.4.1 Hardware

The hardware consists of an Analog to Digital converter which forms the core component of the data acquisition system. The data acquisition card used in the experiment is manufactured by National Instruments and it has an on board buffer which can store 512 samples. The card also has two 12-bit analog outputs; 8 digital I/O lines; and two 24-bit counters. The card can sample at a maximum of 500,000 samples per second.

2.4.2 Software

Data acquisition software is needed to communicate with the card and perform other operations. The software chosen for this application was LabVIEW and LabWindows. The software serves a lot of purposes some of them include, specifying a particular sampling rate, stream data to and from disk, perform I/O operations, store, analyze and present data.

The data acquisition software involves three levels of processing: (shown in Figure 2.5) the device driver level, the diagnostic level for measurement and automation setup, and the LabVIEW user interface level to the Nanopore Detector Channel Current Cheminformatics (CCC) software.

The DAQ is the data acquisition device which is manufactured by National Instruments, Measurement & Automation explorer is a software interface to communicate with the Data Acquisition device and it also serves to configure the data acquisition card. LabVIEW communicates with the hardware and performs signal acquisition and also drives the feed back control.
Figure 2.6: Levels of processing in LabVIEW

2.5 LabVIEW

LabVIEW is a software tool for designing test, measurement, and control systems. LabVIEW can be used to interface with real-world signals, analyze data for meaningful information, and share results. Because LabVIEW has the flexibility of a programming language combined with built-in tools designed specifically for test, measurement, and control, it is possible to create applications that range from simple temperature monitoring to sophisticated simulation and control systems.

LabVIEW has the performance, flexibility, and compatibility of a traditional programming language such as C or BASIC. LabVIEW programming language has the same constructs that traditional languages have -- variables, data types, looping, and sequencing structures as well as error handling. And, with LabVIEW, it is possible to reuse legacy code packaged as DLLs or shared libraries and integrate with other software using ActiveX, TCP, and other standard technologies.

LabVIEW programs are known as Virtual Instruments because they imitate real instruments only that they are Virtual Instruments. The LabVIEW program has three parts front panel, block diagram and the icon/connector. A front panel consists of controls while the block diagram
consists of functions for the controls in the front panel. The icon/connector is used to link the various functions of the control in the block diagram.

LabVIEW software is used manage the flow of data into the computer and to provide feedback to the experimental instrumentation. The various tasks that can be accomplished by LabVIEW are shown in Figure 2.2 of the overall architecture of the data acquisition system.

2.6 LabWindows/CVI

LabWindows/CVI is a proven ANSI C integrated development environment that provides a comprehensive set of programming tools for creating test and control applications. The main advantage of using LabWindows is efficiency and maintainability, apart from the ease of integrating external code without the hassles of a Dynamic Link Library. It is for the reason that C is behind LabWindows, it makes it easy to write applications as fast as in LabVIEW, moreover the choices are numerous when an application is programmed in C.

LabWindows/CVI applications include the following elements:

- User interface
- Data acquisition
- Data analysis
- Program control

The relationship between the various program elements is shown in Figure 2.6. In LabWindows/CVI control elements receive input from the user interface, data acquisition, and data analysis elements.

Each element has various components in them for example one can use LabWindows/CVI to create user interfaces that contain graphs, menus etc. A user interface editor can be used to create these items interactively. It is also possible to create these elements programmatically.
In LabWindows/CVI, the user interface that is created can be used to control the data acquisition (DAQ) device. The user interface also displays the acquired data. After the data is acquired, the next phase involves the analysis of the acquired data. The analysis of the acquired data is performed by the in house software (Channel Current Cheminformatics tools are used). Initially the time domain finite state automaton is used to detect the start and end of a blockade and the CCC software tools which are used later involves a variety of machine learning algorithms, each chosen to provide robust noise-resistant signal analysis at various stages of the signal analysis.

![Figure 2.7: Program elements in LabWindows/CVI](image)

The program control portion of the program coordinates the user interface, data acquisition, and data analysis. The program control contains the logic for managing the flow of program execution and user defined functions.

The callback functions help to control the flow of applications. They enable the program to execute the code in response to the user’s action.
3. METHODS

3.1 LabVIEW architecture

Initially LabVIEW was used as the main tool to acquire and process data, but later on due to certain difficulties discussed below a change in the environment was adopted. The basic design of the system was modeled on a state machine with a producer consumer loop.

![Producer Consumer Loop](image)

**Figure 3.1: Producer Consumer Loop**

In the above design, data is read continuously from a circular buffer and the producer loop performs the I/O operation, while the consumer loop performs the plotting and other operations like data processing and control applications.

3.1.1 Circular Buffer

Data is acquired continuously via a circular buffer that is implemented by the LabVIEW hardware/software. When the data acquisition starts, the hardware buffer starts to fill with data and this is periodically shifted to the LabVIEW buffer for processing. The buffer can hold up to 512 samples. LabVIEW is only used as an intermediary in the signal processing, however, as specialized CCC tools used for this purpose instead. So LabVIEW’s task initially is just DataStream management that links to on-line signal processing using the in-house software (written in C and Perl). LabVIEW’s role is crucial on managing the instrumentation, however, particularly the instrumentation feedback upon blockade signal classification or weak-signal rejection.
3.1.2 LabVIEW prototype design

LabVIEW is a convenient environment for managing the experimental automation and the critical feedback that is needed once it is informed by the CCC software. One example of this is the easily designed virtual instrument interface. A prototype is shown in Figure 3.3 below. The goal is to increase the sophistication of the interface to account for the feedback controls and API to the CCC software.
LabVIEW is used to control the instrument settings in an on-line feedback manner that is informed by LabVIEW passing information in and out of its software environment into the CCC software environment. CCC identification of particular blockade analytes, or a given analytes blockade state (there can be many) can then be used with LabVIEW controls to drive voltage switching, temperatures changes, or laser modulations. This can provide bandwidth broadening capabilities to the nanopore instrument. The advantage in using LabVIEW is the possibility of creating a nice visualization tool in minutes; it has a very good data-flow user interface and it is very convenient for creating data acquisition applications.

3.1.3 Disadvantages

There are a few disadvantages with LabVIEW also, which demands the use of another package, LabWindows developed by the same company National Instruments. The major disadvantages of using LabVIEW are the Data-flow paradigms that can be clumsy to use for state-based systems
(e.g. finite state machines). It is not particularly easy to integrate with conventional programming (e.g. C, C++, and PERL). There are only two known approaches for integrating external code with LabVIEW. One of them involves making Dynamic Link Libraries, which are hard to debug and the other one makes use of their built-in functions which involves changing the code drastically to suit the platform needs and more over only code written in C can be interfaced. The block diagram for the prototype shown in Figure 3.4 is shown below. It can be seen here that it is in fact hard to program Data-flow paradigms.

Figure 3.4: Block Diagram of the LabVIEW prototype

3.2 LabWindows Architecture

After weighing all the pros and cons of LabVIEW, it was decided that LabWindows environment would be favorable to integrate the in house software and also build the data acquisition system in the same package. The LabWindows architecture makes use two methods; it involves multi threading and it also sends the data packets to another computer using the Transmission Control Protocol. The ground level architecture implemented in LabWindows is the same as that of
LabVIEW. LabWindows also makes use of a circular buffer as explained for LabVIEW; LabWindows uses the circular buffer to store the acquired samples.

The TCP protocol is used to send the acquired samples to another computer that is capable of performing the computation tasks. Designing the architecture this way has numerous advantages and it is explained in the methods concerning to LabWindows.

3.2.1 Multithreading

In Microsoft Windows multithreading extends the idea of multitasking into applications, so that specific operations within a single application can be subdivided into individual threads, each of which can theoretically run in parallel.

![Figure 3.5: Multithreading application](image)

Hence the operating system can divide processing time not only among different applications, but also among each thread within an application. In the nanopore data acquisition system the data is acquired on the server and sent as packets to the client. The client runs a multi threaded LabWindows application; two threads are used in the data acquisition system. One thread is used for file Input / Output operations while another thread performs computation tasks on the acquired data. A $\tau$ - finite state automaton is an example of a computation task which is
integrated to the data acquisition system. The finite state automaton is used to detect the start and the end of a particular blockade.

3.2.2 Transmission Control Protocol

The transmission control protocol (TCP) serves to manage the data transfer between the server and the client. TCP is a reliable, connection-based protocol. It provides error detection and ensures that data arrives in order and without any duplication.

Data is acquired continuously using a circular buffer, as the data is retrieved from the buffer it is plotted and it also sends the data to the client in parallels. The server sends 50,000 samples per second to the client to ensure that there is a timely feed back from the client.

![TCP diagram](image)

**Figure 3.6: TCP diagram**

The client here serves as a “think tank”; the client will later be made into an information rich source capable of taking decisions and the client can also suggest the server about the feed back control like voltage switching or automatic perfusion of the nanopore device or the client can even instruct the server to eject a molecule etc. The client will be able to set flags on the server for this purpose. Multithreading is made use in the client, two threads are used in the client and as stated before, as soon as the client receives the data from the server one thread performs the I/O operations while another thread executes the $\tau$ - Finite State Automaton.
3.2.3 Prototype design of the Server

The server and the client run on two independent AMD Opteron machines. The prototype of the server has various options which can be seen in the screen shot below.

![LabWindows Server Screen Shot](image)

**Figure 3.7: LabWindows Server Screen Shot**

The Figure 3.7 which is a screen capture of the prototype with a 9GC hairpin molecule, As far as customizing the controls the user has the option of selecting which channel to use, timing parameters etc. To perform computational tasks such as the Finite State Automaton the client should also be running, so the data can be passed to the client for analysis. The server indicates whether the client is connected and the data sent to the client can also be stopped manually. When a toggle is detected, the client sets a flag on the server which turns on the indicator “FSA passed” indicating the presence of toggles.
3.2.4 Prototype design of the Client

The client connects to the server using the intranet; there is an option to specify the server address etc. The client records the data and as well runs the finite state automaton as a multithreaded application. The standard I/O window shown in the above screen capture displays the length of the toggle in terms of samples, the average and the standard deviation. Client capture is that of a 9GC hairpin molecule. It is evident from the screen shot that the toggle shown in the Figure 3.8 passes the FSA.

3.3 $\tau$ - Finite state automaton

A specially designed $\tau$ - finite state automaton is used to detect the blockades in the acquired signal. The acquired signal is sent sequentially to the finite state automaton, the signal is stored in an array and it is scanned using a moving window of 100 samples. A proper blockade would
have a baseline of around 120 pA and the average of the previous samples are recorded. This average is used to quantize the signal. As soon as a molecule enters the alpha hemolysin channel, a sharp drop in the current is visible, as soon as this drop is visible it indicates the start of a blockade and the signal is recorded from this point until there is a sharp downward spike which is an indication of the end of blockade, this signifies the absence of the molecule in the channel as shown in Figure 3.9.

Figure 3.9: Sampling protocol

If a blockade does not last for long enough or does not confirm to the range of approx lower level average then the blockade is discarded. The entire finite state automaton is described in the flowchart shown in figure 3.10
The finite state automaton has six states they are

- Reset Begin
- Reset End
- Signal Active
- Signal Complete
- Bad eLevel
- Acquire Signal

The various states in the Finite State Automaton can be explained with Figure 3.11
3.3.1 Reset Begin

In this state the acquired signal is scanned for a proper baseline, it has a counter that scans for a particular number of samples that satisfies the baseline. When the sample scanned satisfies the baseline requirement, it decrements the counter baseline-to-reset until it becomes zero. When it becomes zero, it enters the next state.

3.3.2 Reset End

If the baseline–to-reset is zero then it enters the state reset end, In this state the sample are checked whether they are between the start-drop value and start drop limit. If the samples
scanned do not satisfy this condition then it remains in this state until the conditions are satisfied.

### 3.3.3 Signal Active

In the signal active state it checks for the end-level-value and the end-level-range. If the end-level-range and the end-level-value are below a particular threshold then it updates the signal_end and the signal_length. After this it checks whether the open channel average is above a particular threshold. If so it enters the Signal Complete state, if not it checks whether it is less than the max_length and if max_length is less than the threshold it goes into the state Bad eLevel. Where as, if it is a bad end level it goes into the state Bad eLevel.

### 3.3.4 Bad eLevel

In Bad eLevel it checks for a series of conditions like the max_internal, min_internal, end_level_range etc., and if any set of conditions do not satisfy then it enters the reset end state. In this state a few values like signal_max and signal_min are updated.

### 3.3.5 Signal End

In the Signal End state the samples are checked whether it is greater than the minimum length and it is also less than the max_min internal. If so it enters the state Acquire Signal otherwise it goes to the initial state Reset Begin.
4. RESULTS

A complete data acquisition system was built in LabVIEW and LabWindows using the above stated methods. The real time system is optimized by implementing various computational methods in the data acquisition system.

LabVIEW is a graphical programming language, and due to lack of flexibility in LabVIEW, LabWindows is used. LabVIEW relies on hefty runtime libraries that may slow the performance. Moreover coding large projects in LabVIEW becomes difficult. The code for the initial data acquisition system is shown in Figure 4.1

![Figure 4.1: LabVIEW code](Image)

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LabWindows data acquisition system which is based on TCP and Multithreading architecture is a very powerful system which facilitates the integration of external code very easily.

The real time data acquisition system built on LabWindows was tested on a 9GC hairpin molecule as shown in the screen shot below.

![Figure 4.2: 9GC hairpin molecule screen shot in LabWindows](image)
The LabWindows data acquisition system has a $\tau$ - Finite State Automaton integrated to it, once the FSA detects a blockade it passes the signal data to another subroutine to calculate the length of the blockade average and the standard duration. The results for a 9GC hairpin data is tabulated below

<table>
<thead>
<tr>
<th>Number of Samples</th>
<th>Average</th>
<th>Standard Deviation</th>
<th>Time (ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5000</td>
<td>35</td>
<td>2.2</td>
<td>100.0</td>
</tr>
<tr>
<td>280</td>
<td>50.3</td>
<td>13.1</td>
<td>5.6</td>
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Figure 4.3: 9GC Hairpin data results
5. CONCLUSION

A successful real-time data acquisition system was implemented using LabWindows. The τ-FSA coupled with LabVIEW/LabWindows serves as a powerful tool to analyze data obtained in the nanopore detector. The main advantage of this approach is the integration of the in-house software, which can be tailored as per the needs of the experiment. Since the data is obtained on a streaming real-time basis and the processing of data is also done online, the results can decide the control and the feedback for the detector. The CCC software developed at UNO’s Biomedical Informatics and Bioinformatics (BIB) Lab consists of HMM’s and SVM’s, which when integrated with the data acquisition application can help classify a particular molecule.

Filtering and cleaning of data can also be done online thus shedding more light on the molecule under investigation. The entire system can be programmed into a FPGA, allowing it to perform high speed sequencing experiments and data applications.

One of the most promising uses for automated feedback control of the alpha hemolysin nanopore detector is in its application to immunological screening. It has been observed by our lab that single antibodies can be captured in the nanopore detector to form a nanopore/antibody detector. Binding of antigen can then be observed as a change in the blockade current for the composite antibody-antigen blockade. From observation of the on-off binding kinetics between antigen and antibody, screening for antibody with high affinity to target antigen (essential to developing a vaccine) can then be pursued.

Automation of the nanopore detector, with feedback, promises to greatly enhance the potential of this device technology.
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VITA

Srikanth Sendamangalam was born in Madras, India and received his B.E. degree in Electronics and Instrumentation Engineering from Annamalai University. He completed his undergraduate final project on Control of Dish Alignment using Artificial Neural Networks. He was admitted to the graduate school of University of New Orleans, New Orleans in January 2004 in the Department of Electrical Engineering. Then he transferred to the Department of Computer Science, UNO and worked under the guidance of Dr Stephen Winters – Hilt.

All throughout his studies in the Computer Science department he was working as a Research Assistant for the Children’s Hospital, New Orleans and also for the Department of Computer Science, UNO. His graduate studies were concentrated on Artificial intelligence.