A Smartphone Controlled Handheld Microfluidic Liquid Handling System

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Electronic Supplementary Information (ESI)

Electronic Supplementary Information (ESI) Available: Explanation and implementation details of selected hardware and software design.

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Working Principle of Pressure Releasing in Reservoir 2 by Controlled Volume Expansion

To achieve pressure control in Reservoir 2, we initially used a 3-way solenoid valve to release possible excessive pressure in it. However, the time it takes for the pressure in Reservoir 2 to reach atmospheric pressure is almost negligible, because the size of the common port of a solenoid valve is relatively large. In this project, we used a solenoid valve with a sealed common port to perform pressure release in a stepwise fashion. The working principle is described below:
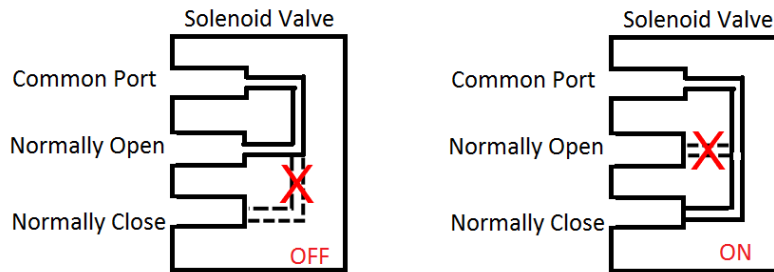

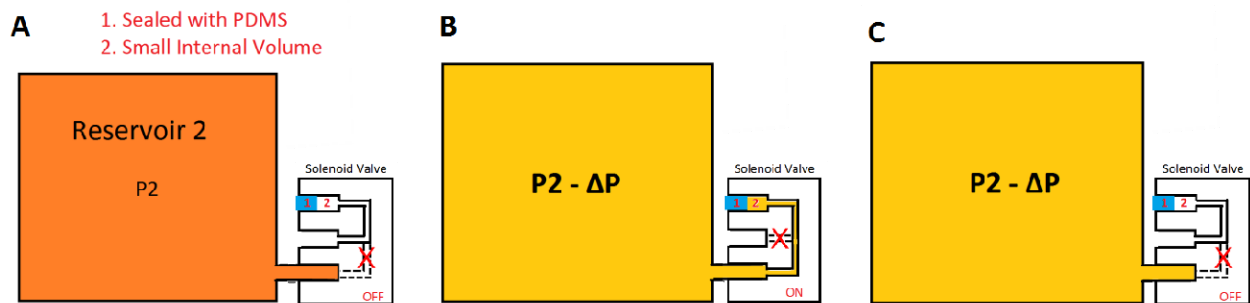**Fig. S1** Simplified cross section of a solenoid valve. [1]

Fig. S2 Design and working principle of pressure releasing by controlled volume expansion. (A) Design of releasing solenoid valve with reservoir. (B) When the solenoid valve is on, the volume of Reservoir 2 is expanded by a small amount due to the small internal volume of the valve (Valve 2). (C) When the solenoid valve is turned off, the pressure in the small internal volume of the valve is released. .

When the solenoid valve is on, the effective volume of Reservoir 2 is expanded (Fig. S2B), and hence, the pressure in Reservoir 2 drops by a small amount. Afterwards, when we turn off the solenoid valve, the pressure in the small internal volume of the solenoid valve will be released (Fig. S2C).

It takes about 10ms for a solenoid valve (Pneumadyne, S10MM-30-12-3) to be opened or closed completely, so the maximum frequency of the stepwise pressure releasing is 50Hz.

Estimation of the Small Internal Volume of Valve 2

As described in the previous section, the resolution of pressure release is determined by the ratio of the volume of Reservoir 2 and the small internal volume of Valve 2. This allows us to estimate the small internal volume according to the Ideal Gas Law: $PV = nRT$.

Let the volume of Reservoir 2 is V_1, and the small internal volume of Valve 2 is V_2.

Compared to the volume of Reservoir 2 (16.2 mL), the small internal volume is relatively small. So, we ignore the number of molecules inside the small internal volume. Assume that temperature T is constant during our experiments, for every stepwise pressure release, we have: $P_1V_1 = P_2(V_1+V_2)$. Given that the initial pressure in Reservoir 2 is P_0; we can derive an exponential function:

Table S1 Stepwise pressure values

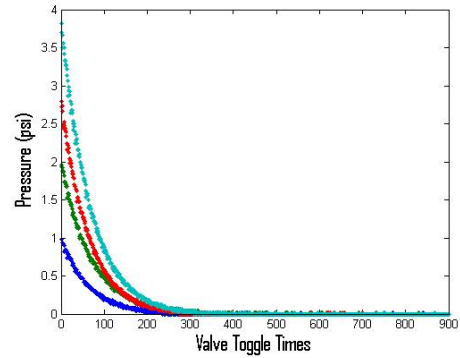| Valve Toggle Times	Pressure in Reservoir 2
0	P_0
1	$P_1 = P_0(\dfrac{V_1}{V_1 + V_2})$
2	$P_2 = P_1(\dfrac{V_1}{V_1 + V_2}) = P_0(\dfrac{V_1}{V_1 + V_2})^2$
3	$P_3 = P_0(\dfrac{V_1}{V_1 + V_2})^3$
…	…
x	$P(x) = P_0(\dfrac{V_1}{V_1 + V_2})^x$
…	…

Fig. S3 Pressure release test.

Take the logarithm of P(x), we have:

$$\log P(x) = \log P_0 + x \log \frac{V_1}{V_1 + V_2}$$

Since we have the stepwise pressure release data (Fig. S3), it is now possible to plot these data in semi-log graph and estimate the volume by straight line fitting (Fig. S4).

Table S2 Estimated Values of V_2

Data Series	Slope of Fitted Lines	Estimated V_2 (mL)
1	-0.015508	0.2532
2	-0.01427	0.2328
3	-0.016023	0.2617
4	-0.015104	0.2465
Average		0.2486

Therefore, the estimated small internal volume of Valve 2 is:

$$V_2 \approx 250 \ \mu L.$$

Note: Systematic error may be included by substituting

absolute pressure with gauge pressure.

Fig. S4 Pressure release test (log-scale)

Barometric Sensors Calibration

Two barometric sensors are used to monitor the pressure levels in Reservoir 1 and 2. In our design, the resolution of digitized pressure reading is 0.02psi (ADC reading of 1), while the maximum pressure of the system is 14psi (ADC reading of 700). To calibrate the barometric sensors, we used a regulated pressure source (generated by a gas tank, a pressure regulator, and a dial pressure gauge) following the steps given below:

1. Open the gas tank, and tune the pressure regulator to supply both barometric sensors with 14psi air pressure.

2. Adjust both gain resistors of the instrumentation amplifiers to make both ADC readings to 700.

3. After 20s of recording, decrease the pressure supply by 1psi by adjusting the pressure regulator.

4. Repeat step 3 until the pressure supply reaches 0 (excluding 1psi, limited by the dial pressure gauge).

5. Export the recorded data to a computer, and process with MATLAB

   a. take 10s of recording from each segment of data of different pressure levels

   b. plot the average value of each segment of extracted data vs. the pressure levels (Fig. S7)

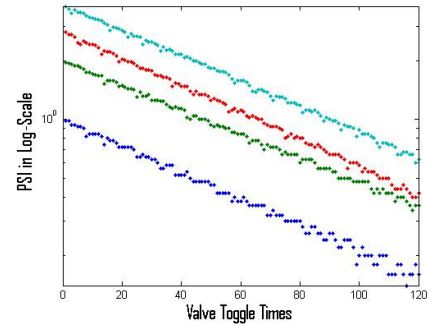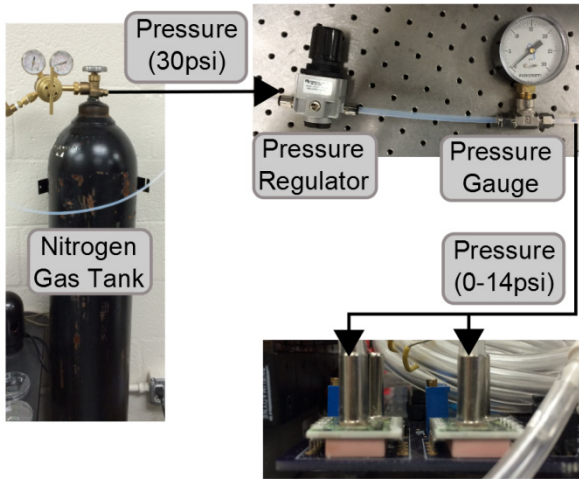   c. find the calibration curve by fitting the data points with a straight line

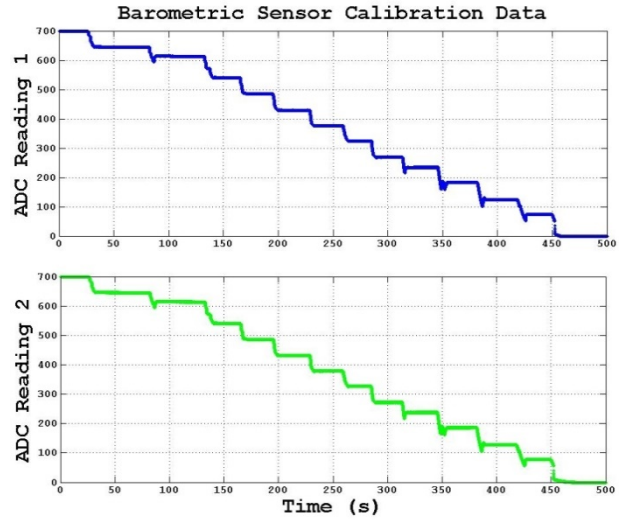**Fig. S5** Barometric sensors calibration setup.

Fig. S6 Recorded data of ADC readings for calibration.
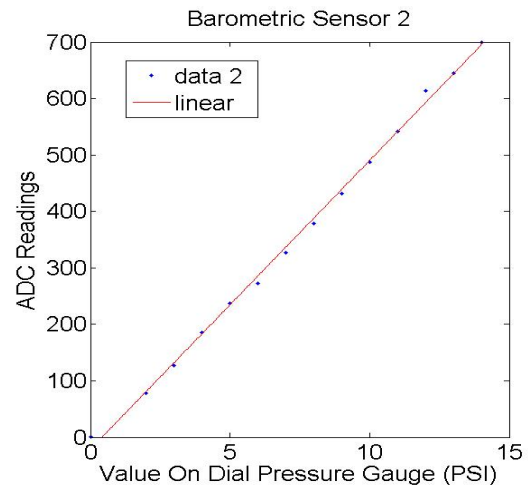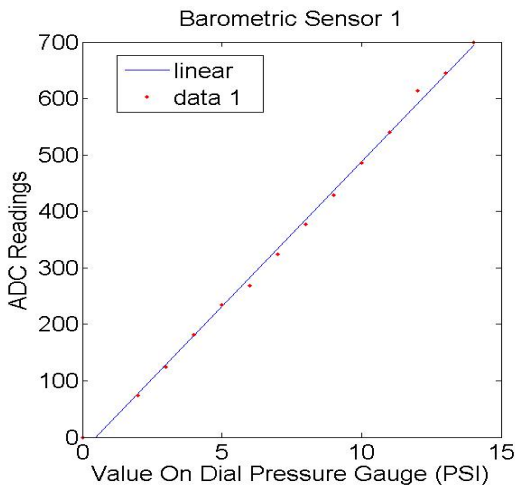

Fig. S7 Calibration curve of Barometric Sensor 1 and Barometric Sensor 2.

The fitted calibration curves are:

$$\begin{cases} ADC_1 = 51.347 \cdot P_1 - 24.443 \\ ADC_2 = 51.133 \cdot P_2 - 20.833 \end{cases}$$

Hence, we can program these two functions into the microcontrollers to identify the calibrated ADC values according to the given pressure values. With better instruments (pressure regulator and gauge), it is feasible to obtain more accurate calibration curves in the future.

Fabrication of Liquid Reagent Containers

We used a miniaturized container, modified from a microcentrifuge tube, to hold the liquid samples and reagents in our system. Fabrication details are described below:
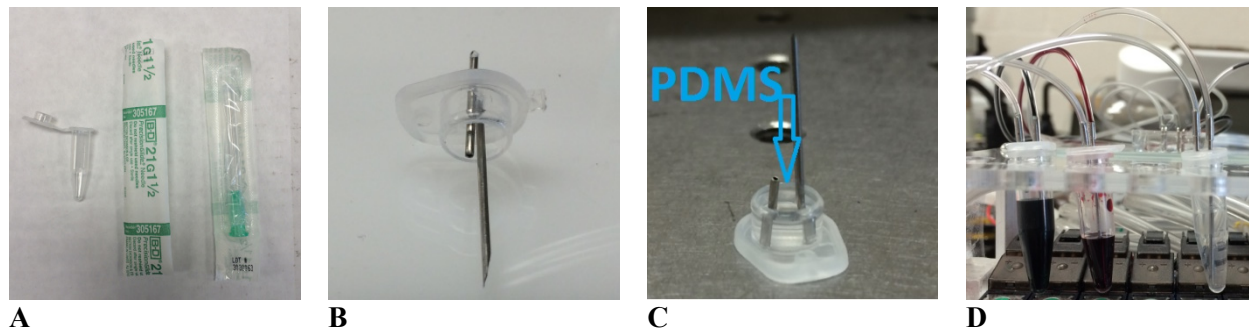

A **B** **C** **D**

Fig. S8 Fabrication of Liquid Reagent Containers.

1. Prepare one microcentrifuge tube with lid, and two 21 gauge needles (Fig. S8A).

2. Penetrate through the lid with two needles, one longer (reaching the bottom of the tube) and the other shorter (above the liquid) (Fig. S8B).

3. Seal the lid with PDMS to prevent air leakage (Fig. S8C).

4. Fill liquid reagent or sample into the tube, and connect the tube to the system with Tygon tubing (Fig. S8D).

Design of Software Architecture
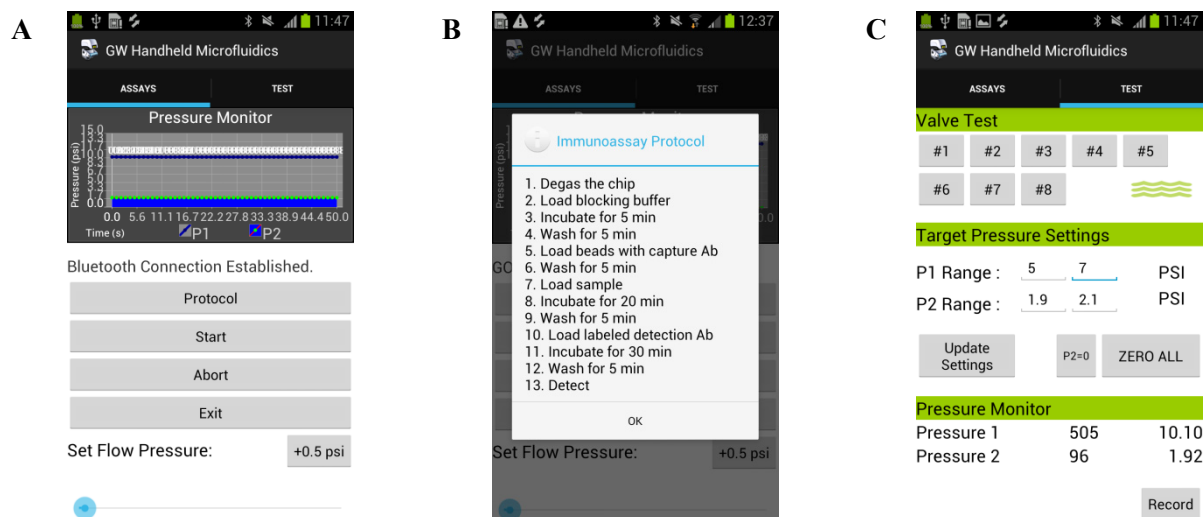

A

B

C

Fig. S9 GUI Layout of the Android smartphone app.

The Android application we developed has two tabs: one for running a simulated immunoassay protocol; and, the other for testing and calibrating each individual function of the system. It has the following functions (Fig. S9):

(a) When a user starts to run the Android application after the system is powered up, the program automatically searches for target Bluetooth device and establishes connection. After the connection is set up, the program will command the system to increase the target pressure of Reservoir 1 (for on-chip valve actuation) to a range of 10 to 14 psi; and set the pressure of Reservoir 2 (for liquid driving) to 0 psi. The user can adjust the progress bar at the bottom to change the target pressure of Reservoir 2. Real-time data from the barometric sensors is collected from the system at a sampling rate of 50Hz, and plotted in the figure at the top using Androidplot 0.6.0 library [2].

One can press the start button to run the simulated immunoassay protocol. During experiments, the abort or exit button could be used to terminate the immunoassay process.

(b) Once the protocol button is pressed, the immunoassay protocol will be displayed. This protocol is programmed in the smartphone application, and explained in a message box. A user can modify the program to adapt to different applications.

(c) When the TEST tab is selected, the window for testing individual function shows up. It is grouped into three sections. Buttons in the first section are for controlling the ON/OFF status of the output valves. The second section is for setting the target pressures of the two reservoirs. The last section displays the readings and calculated pressure values (in PSI). The record button at the bottom is to save collected data to a text file, which could be used for calibration and other purposes.

(d) Communication between the android app and microcontrollers are realized by a customized software application protocol, which uses one ASCII character to represent a specific instruction. This application protocol has three fundamental functions: (1) change the state of an output port (solenoid valve or pump), (2) set target pressure ranges of P1 and P2, and (3) acquire real-time barometric sensor data from the microcontrollers. Detailed design is listed in Table S3.

Table S3 Detailed Design of Software Application Protocol

Command	Explanation	Command	Explanation
Uppercase A to R	Activate load switch circuit 1-18	**Lowercase a to r**	Deactivate load switch circuit 1-18
Y / y	Enable/disable acquiring barometric sensor data from the microcontrollers	**Z / z**	Reset the system
!_ _ _ _	Set the target pressure range of Barometric Sensor 1	**@_ _ _ _**	Set the target pressure range of Barometric Sensor 2
	These two commands, '!' and '@', should be followed by a sequence of four character. Every two chars are representing the lower and upper part of a short value, respectively. Four characters will be converted into two short values in the microcontrollers, which specify the lower bound and upper bound of the target pressure level (ADC readings).		
	For example:		

	[Android App]
	    send !AABB
	
	    [Microcontrollers on receive !AABB]
	    Lower Bound of Barometric Sensor 1 = 16705 // AA
	    Upper Bound of Barometric Sensor 1 = 16962 // BB		
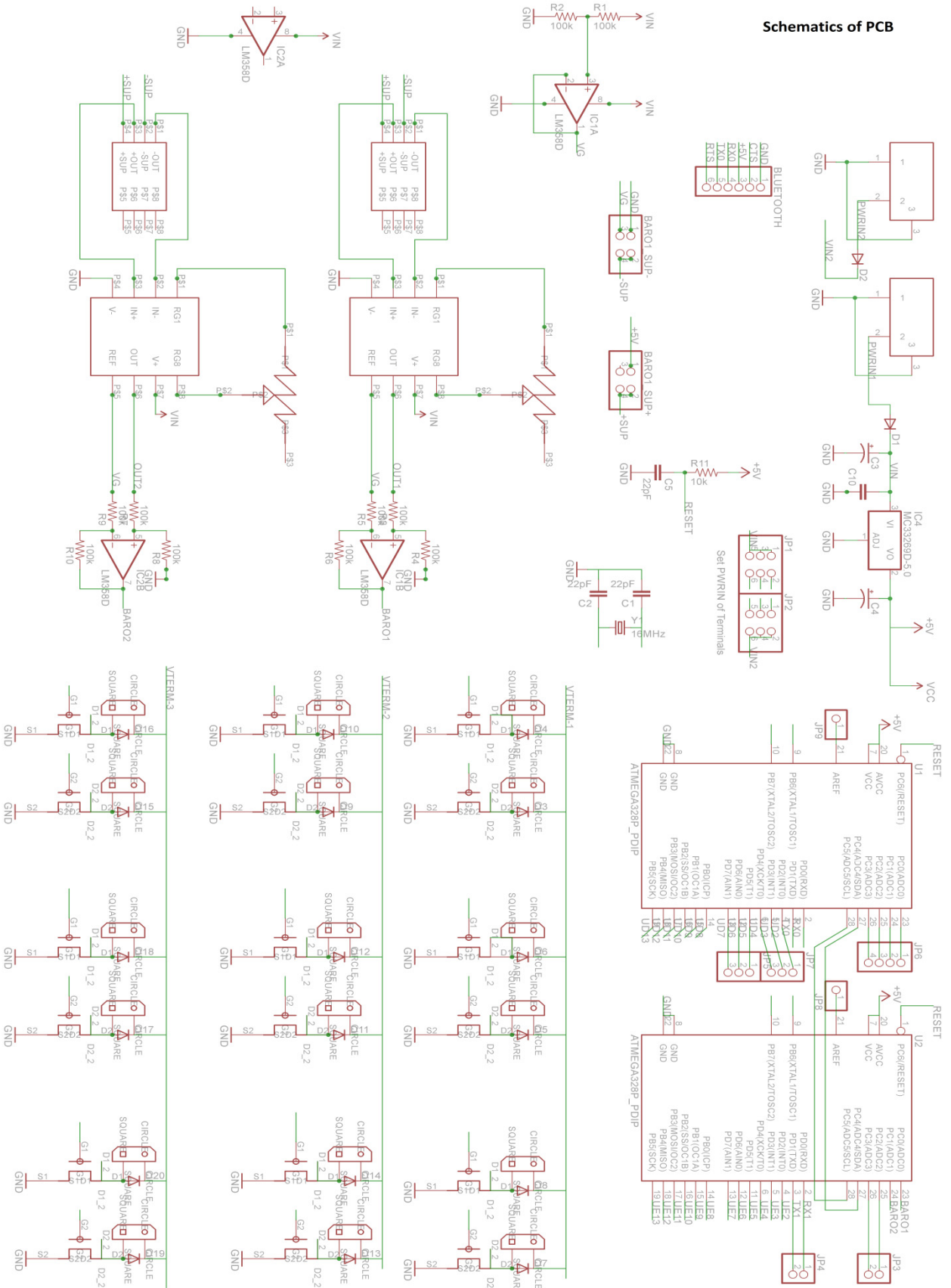
Supplementary References:

[1] Pneumadyne Catalog, http://www.pneumadyne.com/documents/PDFs/Solenoid_Valves.pdf,

(accessed Feb. 2014).

[2] Androidplot, http://androidplot.com/docs/dynamically-plotting-sensor-data/, (accessed Feb. 2014).