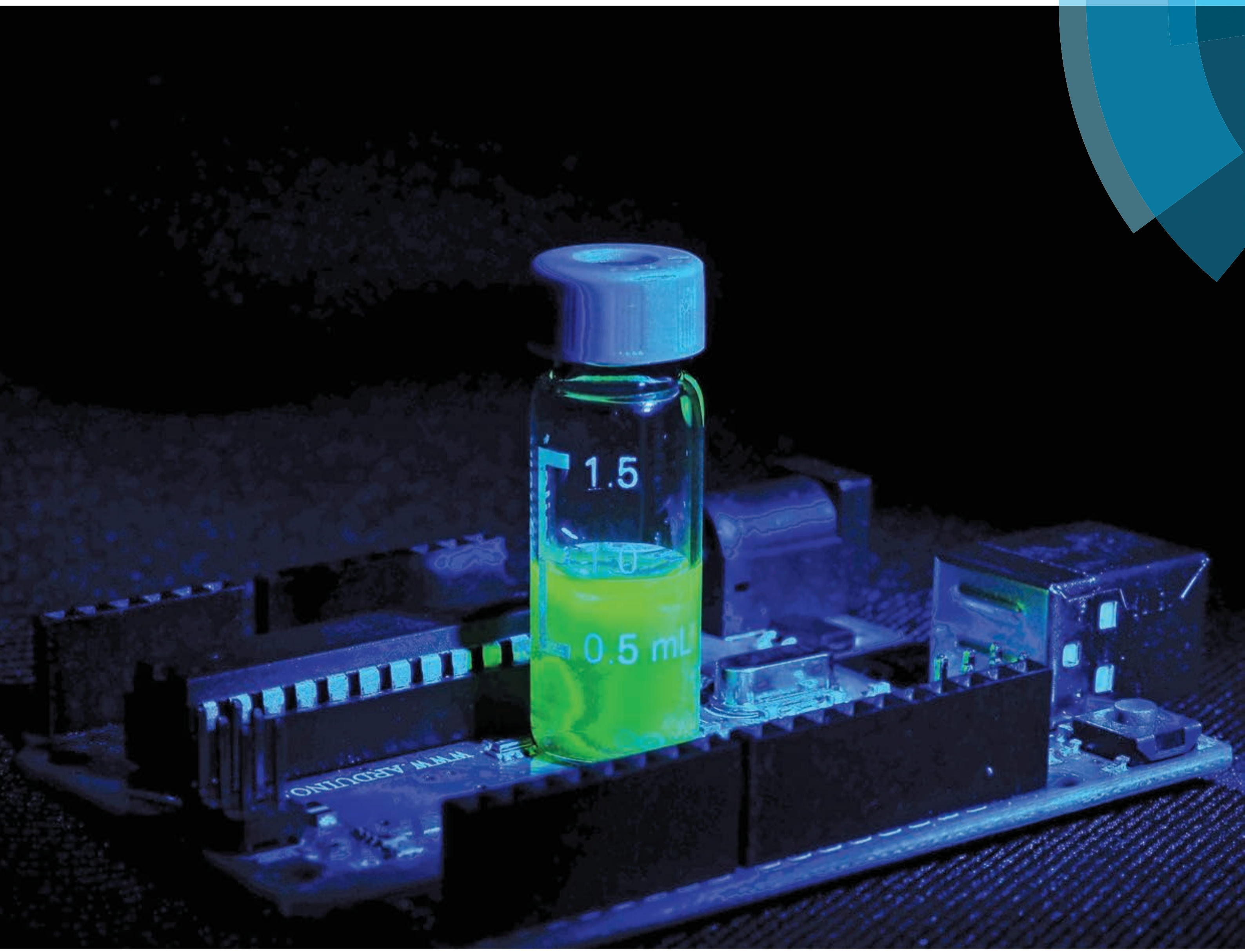
Volume 140 | Number 4 | 21 February 2015 | Pages 947–1360

Analyst

www.rsc.org/analyst



ISSN 0003-2654

ROYAL SOCIETY OF CHEMISTRY

MINIREVIEW
Pawel L. Urban
Universal electronics for miniature and automated chemical assays

Analyst

MINIREVIEW

View Article Online
View Journal | View Issue

Cite this: *Analyst*, 2015, **140**, 963

Universal electronics for miniature and automated chemical assays†

Pawel L. Urban[a,b]

Received 2nd November 2014, Accepted 8th December 2014

DOI: 10.1039/c4an02013h

www.rsc.org/analyst

This minireview discusses universal electronic modules (generic programmable units) and their use by analytical chemists to construct inexpensive, miniature or automated devices. Recently, open-source platforms have gained considerable popularity among tech-savvy chemists because their implementation often does not require expert knowledge and investment of funds. Thus, chemistry students and researchers can easily start implementing them after a few hours of reading tutorials and trial-and-error. Single-board microcontrollers and micro-computers such as Arduino, Teensy, Raspberry Pi or BeagleBone enable collecting experimental data with high precision as well as efficient control of electric potentials and actuation of mechanical systems. They are readily programmed using high-level languages, such as C, C++, JavaScript or Python. They can also be coupled with mobile consumer electronics, including smartphones as well as teleinformatic networks. More demanding analytical tasks require fast signal processing. Field-programmable gate arrays enable efficient and inexpensive prototyping of high-performance analytical platforms, thus becoming increasingly popular among analytical chemists. This minireview discusses the advantages and drawbacks of universal electronic modules, considering their application in prototyping and manufacture of intelligent analytical instrumentation.

1. Introduction

When I was a secondary school student, I felt lucky to get hold of a personal computer with a 486 DX2 processor running at 66 MHz in a sizeable white box proudly situated on my desktop. I soon started using it to conduct simple measurements in my "bedroom lab". During my academic training, I had a chance to apply science-grade electronic systems in graduate projects. After I launched my own research group, I quickly realised that I could get much of the performance of those quality electronic apparatuses by implementing much less expensive universal and open-source electronic modules. Indeed, with the introduction of the Intel Edison microcomputer in 2014,[1] one can get a lot more computing power than my 1994 machine in a volume smaller than a matchbox.

Universal electronic modules are generic units that can readily be adapted for specific applications. For example, they can facilitate the development of analytical instrumentation. Many of them are "open source", which means that their blueprints can be easily accessed. Various companies produce open-source electronic units; therefore, their prices are relatively low. While they are inexpensive, they can readily be adopted for recording data and controlling electromechanical components of analytical systems in fundamental and applied research. They differ from traditional equipment in that they are specifically designed for others to build and modify, and include extensive documentation and examples of software code. The design is simple and modular, and encourages the construction of integrated systems.[2] Interestingly, universal modules have already found applications in various areas of science,[3] including nanotechnology[4] and behavioural studies.[5]

[a]*Department of Applied Chemistry, National Chiao Tung University, Hsinchu 300, Taiwan*

[b]*Institute of Molecular Science, National Chiao Tung University, Hsinchu 300, Taiwan. Fax: +886-3-5723764*

†Electronic supplementary information (ESI) available: Additional tables (S1, S2). See DOI: 10.1039/c4an02013h

Pawel L. Urban

Pawel Urban obtained his education in the University of Warsaw (MSc) and in the University of York (PhD). His research training was supplemented with stays in the University of Alcala and ETH Zurich. He currently holds an academic position in the National Chiao Tung University. His research and teaching interests encompass biochemical analysis, development of analytical instrumentation, and engineering smart biosystems.

2. Hardware

A large portion of 21st century's analytical devices use electric currents. Therefore, the control of these devices, as well as data acquisition, is normally achieved by some kind of electric current modulation and recording. Analytical chemists developing instrumentation often face the problem of designing and building the electronic part of their systems. The implementation of integrated circuits (ICs) – pieces of silicon which incorporate nanoscale wiring and a multitude of nanosized electronic elements (*cf.* Table 1) – puts the prototypes of analytical devices closer to the final versions, which can be commercialised. However, few analytical chemists have formal training in electronic engineering. Therefore, the development of application-specific ICs for analytical tasks needs to be supported by collaborators with appropriate expertise and facilities. It is much easier to implement one of the available universal ICs with microcontroller functionality. Some of such ICs can readily be incorporated into simple analytical devices. They are still very small while offering a lot of flexibility. However, those who have little time to build much of the circuitry themselves, or are just experimenting with prototypes, may prefer to choose one of the available microcontroller prototyping boards which are extremely easy to use and are widely available. Such modules have an IC or several ICs soldered onto a larger polymer plate (a printed circuit board or PCB) along with other electronic elements. They possess numerous inputs and outputs for facile coupling with sensors and actuators. Various microcontroller boards provide several features which are particularly useful for analytical chemists, for example:

– digital inputs and outputs,
– analogue input,
– connectivity to computer (*e.g. via* USB port),
– programming in high-level languages.

Digitalised signals are received by digital inputs and sent out by digital outputs. They are transmitted in the form of pulses of low and high potentials. For example, in many cases, the potential 0 V signifies the binary 0 ("zero", "low" or "off" state) while the potential 5 V signifies the binary 1 ("one", "high" or "on" state). Thus, the digital inputs may directly receive information from switches with two states (on/off). Digital outputs may send out simple signals, for example to control the state of simple light sources (light on/off), relays (in this context defined as electromagnetically controlled switches), and other actuators. Thus, they can indirectly control pumps, valves, electromagnets, motors, and apply electric potentials. The speed of mechanic actuators (*e.g.* direct current motors) may be controlled by supplying pulses of current separated by pauses. The ratio of the duration of high and low signals (pause) can determine the speed of motion (*e.g.* revolutions per minute, in the case of a direct current motor). This kind of electric control of an actuator using digital pulses of electric current is called pulse-width modulation, and abbreviated PWM. The accuracy of PWMs can be different for different devices: for the common 8-bit PWM (*e.g.* Arduino Uno[6]), 256 discrete levels can be selected, while in the case of 12-bit PWM (*e.g.* Arduino Galileo Gen 2),[7] one can

Table 1 Various types of electronic modules available to analytical chemists, and typical features

Category	Pros	Cons
Application-specific integrated circuits (ASICs)	– High level of integration – Small – Optimised – No redundancy	– Expertise required – Design required – Fabrication required – Targeted application – Expensive
Universal integrated circuits	– Small – Versatile – Inexpensive	– Assembly of circuit required – Expertise required
Prototyping boards, microcontrollers	– Flexible – Medium performance – Easy to set up and program – Community support web pages, tutorials	– Larger than integrated circuits – Expensive
Single board computers	– Versatile – Medium performance – Compatible with Linux environment – Programmable in various high level languages	– More expensive than microcontrollers
Field-programmable gate arrays	– Fast – Flexible	– Expertise required – Relatively expensive
Research-grade electronic control and data acquisition systems	– Flexible – High performance – Intuitive user interface – Customer support	– Expensive – Bulky

Table 2 Selected representative examples of single-board microcontroller/microcomputer modules for prototyping. (The readers are advised to consult specification sheets provided by the manufacturers to obtain correct and up-to-date data)

Name	Type[a]	CPU (bits)	Speed (MHz)	Digital inputs	Analogue inputs
Arduino Uno	cont	8	16	14	6
Arduino Leonardo	cont	8	16	14 (20)	6 (12)
Arduino Yún	cont, comp	8, 32	16, 400	14 (20)	6 (12)
Arduino Duemilanove	cont	8	16	14	6
Arduino Due	cont	32	84	54	12
Arduino Mega 2560	cont	8	16	54	16
Arduino Mini	cont	8	16	14	8
Arduino Micro	cont	8	16	14 (20)	6 (12)
Arduino Nano	cont	8	16	14	8
Arduino Tre (Developer Edition)	cont, comp	8, 32	16, 1000	14, 23	6 (12)
Arduino Pro	cont	8	8 or 16	14	6
Arduino Fio	cont	8	8	14	8
RBBB	cont	8	16	14	6
Trinket	cont	8	8 or 16	5	3
Bluno	cont	8	16	14	6
Eleven	cont	8	16	14	6
EtherTen	cont	8	16	14 (22)	8
Teensy 3.0	cont	32	48	34	14
Espruino	cont	32	72	28 (44)	16
Spark	cont	32	72	8 (16)	8
chipKIT uC32	cont	32	80	30 (42)	12
Netduino 2	cont	32	120	14 (20)	6
Netduino plus 2	cont	32	168	14 (20)	6
Propeller Mini	cont	32	5	19	0
mbed LPC1768	cont	32	96	26	6
Intel Galileo Gen 2	cont, comp	32	400	14 (20)	6
Intel Edison (Arduino Breakout Kit)	cont, comp	32	100, 500	14 (20)	6
BeagleBone	comp	32	720	>60	7
BeagleBone Black	comp	32	1000	>60	7
Raspberry Pi B+	comp	32	700	26	0

[a] cont – microcontroller board; comp – microcomputer (single board).

access 4096 discrete levels, providing greater accuracy of control.

Analogue inputs are often used to measure electric potentials at the outputs of sensor circuits. For example, in a temperature sensor, the output signal can be related to temperature and fed to one of the analogue inputs of a microcontroller PCB (see section 3 for further discussion).

Examples of popular universal microcontroller prototyping platforms include: Arduino,[6] Basic Stamp,[8] Espruino,[9] mbed,[10] Netduino,[11] Propeller,[12] and Teensy[13] (Table 2). For instance, the Arduino family comprises over 10 PCBs, each with a multitude of analogue and digital inputs and outputs.[6] 5 V or 3.3 V digital logic options are the most common, making universal microcontrollers compatible with a large number of add-on shields – *e.g.* stackable PCBs with various additional peripherals (*e.g.* data converters, sensors, communications modules), which can be connected to the microcontroller PCBs without any soldering.

The performance of microcontroller modules depends on the characteristics of their central processing units (CPUs, components performing computing and supervising input/output operations), including the number of bits of information processed at a time, and clock speed. Most universal microcontrollers are equipped with CPUs with 8 up to 32-bit architectures, and operate at speeds below 200 MHz (Table 2). For example, the popular Arduino Uno and Mega boards run at the speed of 16 MHz, while Arduino Due runs at 84 MHz.[6] The increased computational speed increases the cost of hardware. If the CPU speed is important for a given application (*e.g.* extensive data pre-treatment), a single-board computer can be used instead of a microcontroller PCB. Popular platforms include (among others): Raspberry Pi,[14] BeagleBone,[15] and Intel Galileo.[7] For instance, the CPUs of Raspberry Pi B+ and BeagleBone Black run at the speeds of 700 MHz and 1 GHz, respectively. They also feature general-purpose input/output connectors with plurality of pins that can be utilised for communication with external devices.

Most universal microcontroller PCBs are programmed using the associated integrated development environment interfaces which are often available free of charge. The most popular programming language for many microcontrollers (including Arduino) is C.[6] It has been adapted for use with such microcontroller devices. An interesting example of close integration of computer programming and microcontroller programming is the implementation of .NET environment in the programming of some microcontrollers, for example Netduino.[11] In this case, the device can be programmed in one of the modern high-level languages: C#. Other programming languages are also used: for example, JavaScript in the case of Espruino.[9] In many cases, the program is loaded to the permanent memory of the microcontroller and retained even when the device is powered off. Therefore, the devices can function autonomously without the need for continued interaction with a personal computer. In the case of mbed microcontrollers,[10] the programming is realised *via* web-based integrated development environment, which exemplifies the application of cloud computing in prototyping electronic systems. The compiled program is transferred to the flash memory of the microcontroller *via* the USB cable, and loaded to the microcontroller. The collected data files can be directly downloaded from the flash memory of the device, which makes experimentation very easy. The single-board computers normally utilise Linux-based operating systems. Therefore, applications can be created using any of the popular languages, including C, C++, and Python.

Field-programmable gate arrays (FPGAs) can be defined as semiconductor devices based on a matrix of configurable logic blocks connected *via* programmable interconnects or "reprogrammable silicon chips".[16,17] While initially they might have to be considered as "glue logic chips", they can currently replace custom application-specific integrated circuits and processors.[17] Importantly, they can be programmed according to specific application needs. FPGAs are particularly useful under conditions which involve high frequencies and systems which can readily be described by circuits of logic gates. For example, they are often used to develop devices for processing digital signals.[18] FPGAs have found several applications in the development of analytical instrumentation, including: fast data acquisition, frequency counting, multiplexing, filtering, processing, control of auxiliary devices (pumps, valves, heaters, lasers, LEDs), synchronisation, interfacing with computers, recording, data storage, data transfer, peak analysis, feedback regulation, timing and signal generation (Table S1†). They have been used to build a variety of analytical instruments, including electrochemical sensors,[19–22] quartz crystal microbalances,[23–27] cell sorters,[28–32] mass spectrometry systems,[33–39] and nuclear magnetic resonance spectrometers.[40–43] While there is a growing interest in miniaturisation of NMR spectrometers,[44,45] FPGAs help to solve the engineering problems associated with the electronic circuitry to support the operation of such systems. Another interesting application of FPGA is in the construction of spectrophotometric detectors for liquid chromatographs incorporating LEDs as sources of monochromatic light.[46] In this case, FPGA controls the light-source LEDs and reads out the digitalised photocurrent signal of photodiodes. FPGAs also find applications in the design of robust microfluidic platforms: Although many electrical control systems use conventional logic which includes binary zeros and ones (signal off or on), automation of analytical methods often requires the implementation of the so-called fuzzy logic which assumes the existence of intermediate states to provide better control of real systems (*e.g.* microfluidic droplets). Gao *et al.*[47] introduced a strategy for fuzzy-enhanced feedback in digital microfluidics. In their design, an FPGA unit scans the capacitance of each electrode on the chip. The frequency information is transferred to the operation unit for real-time computation, providing electric feedback to the microchip.[47] This intelligent microfluidic system has the potential to provide reliable droplet manipulation, which is essential for applications in analytical chemistry. Stand-alone FPGA modules as well as expansion modules for research-grade platforms are available. The cost of some FPGA PCBs can be as low as ~50 USD, which can sometimes be smaller than using a conventional circuit board while keeping various advantages such as high speed, low power consumption, and small size.[48] While FPGAs provide excellent performance and flexibility, they are not a perfect solution for all applications. In fact, setting up FPGAs for specific applications in analytical chemistry requires a higher level of expertise, as compared with the other electronic modules described here. In particular, programming FPGAs is quite dissimilar to the procedural or object-oriented programming of microcontrollers; it requires the understanding of logic circuits. Therefore, FPGAs are certainly not the first choice for less experienced analytical scientists.

Many chemical assays published in the past three years implement smartphone cameras as sensors (Table S2†). These products can also provide a source of light for reflectometric and fluorometric measurements, enable communication with the analyst, assay control, data acquisition and treatment, and wireless transmission. For detailed overviews of the use of smartphones in analytical chemistry, the readers are directed to the specialised review articles published recently.[49–56] The book edited by Karlen[57] also provides a nice overview of the design and applications of mobile point-of-care diagnostic tools. One may speculate that smartphones will certainly play a significant role in the development of portable analytical devices in the near future. The success of smartphones in analytical chemistry is – in part – related to the fact that it is possible to convert RGB values obtained by a digital CMOS or CCD cameras into analytical data (for example, absorbance, reflectance, fluorescence intensity, *etc.*). Apart from smartphones, other consumer electronic products find applications in analytical chemistry. For example, a set consisting of a computer screen and an inexpensive digital photographic camera was recently used to conduct spectral and temporal imaging of non-linear chemical reactions.[58] However, a drawback of using consumer cameras (*e.g.* those in smartphones) for the acquisition of analytical data is that many such devices do not provide direct pixel intensity values. The image treatment algorithms often affect the dynamic range and/or resolution of the exported images. Switching off the automatic adjustment of white balance, exposure time, or saturation can be challenging. Thus, the difficulty of exporting raw data and controlling data treatment compromises the reliability of the analytical assays based on consumer electronics.

Certainly, the inexpensive universal electronic modules have limitations and often lower specifications than the research-grade electronic control and data acquisition systems. As opposed to many inexpensive electronic modules, the high-end systems possess an intuitive user interface, are highly flexible, and can be expanded with high performance digital units, while customer support is normally available.

3. Analogue-to-digital conversion

Many sensors used in analytical science provide signals that have an analogue nature. That is, they change over a certain range of scale (*e.g.* electric potential). Such signals need to be binned into discrete intervals within that range in order to be handled by digital signal processing units. The number of the bin corresponding to a measured signal can then be transferred into the binary form, and further processed digitally. Many microcontroller PCBs provide several analogue inputs enabled by the on-board analogue/digital converters (ADC; *cf.* Table 2). Common applications of analogue inputs include the measurement of light intensity, temperature, or electrode potential. Connecting a photosensor, such as photodiode to an analogue input is straightforward.[59]

The three important parameters of the analogue inputs are: resolution, speed, and impedance (opposition that an electronic component, circuit, or system offers to alternating and/or direct electric current[60]).

The resolution of an analogue input is directly related to the type of the ADC used. For example, many Arduinos are equipped with ADCs with the specified resolution of 10 bits, which gives 1024 discrete levels of potential that can be distinguished by the device (~5 mV at the reference potential of 5 V). Considering the priorities of analytical chemists, the resolution of the ADC is closely linked with the so-called quantisation error (rounding error of the input voltage). While this error can affect signal noise, and – to some extent – the accuracy of the conducted measurements, the quality of the final analytical output will also depend on the proper calibration of the detection system as well as the existence of various biases related to the chemical assay, hardware, and data treatment algorithm.

Another factor is the voltage range of the ADC. Many boards can measure positive voltages within the range 0–5 V. However, the upper limit can be lowered by supplying a specific (lower) reference potential. This way, the quantisation error of measurements can be reduced. For example, the width of bins decreases from ~5 mV at the reference potential of 5 V to ~3 mV at the reference potential of 3.3 V (when using a 10-bit ADC). While 10-bit resolution is typical for many of the on-board ADCs, some microcontroller boards have slightly better performance with respect to this parameter. For example, Arduino Due[6] has a 12-bit analogue input while Teensy 3.0 has a 16-bit analogue input (according to the specification tables).[13] It is also possible to use an external off-board ADC. Such accessory PCBs are readily available in a variety of sources at low cost. If the resolution of the ADC conversion is the priority, one may need to implement a conventional research-grade platform, which can provide outstanding resolutions at a higher cost.

Where timing of data acquisition is important, it is also necessary to realise the speed of the analogue-to-digital conversion. This parameter is limited by the IC's ADC clock (*e.g.* 16 MHz in Arduino Uno), which limits sampling rate. Ways to improve the sampling rate from the software level are described in online forums, and can be tested by analysts constructing prototypes of their devices.[61] Most boards enable millisecond temporal resolutions by default. However, in some cases, micro-second or sub-micro-second resolutions can be achieved. Increasing temporal resolution can open the door to exciting applications of these inexpensive platforms, for example, time-resolved measurements. If an application relies on the resolution of time base (*e.g.* collecting absorbance data in time domain), attention must be paid to the clock jitter[62] since it may influence the quality of the logged data.

The common ways of connecting sensors to analogue inputs include: voltage divider, Wheatstone bridge, and the use of operational amplifiers. When doing so, care must be taken to match the impedance of analogue inputs and the external sensor circuits. If the impedance of a sensor circuit to be connected to ADC is too high, an operational amplifier is normally used. Operational amplifiers can also increase the sensitivity of the measurements of electric potentials. Examples of simple electronic circuits, which can readily be coupled with microcontroller boards can be found in tutorial books[63] and on-line.[64]

4. Applications in analytical chemistry

For early-stage experimenters, it is common to demonstrate the application of Arduino in photometric measurements. Examples of such devices have been described in chemical education literature.[65,66] However, using the same boards, high accuracy measurements can be conducted.[67] Several dozen applications of universal electronic modules (including ICs, microcontroller PCBs and single-board computers) in the development of analytical instrumentation have been documented (Table 3). This section provides examples of possible applications of universal electronic modules in the construction of small and automated analytical instruments.

In one study, Mitchell *et al.*[68] demonstrated an *in situ* pathogen detection system for detecting and quantifying an *Escherichia coli* gene (Fig. 1). It relies on hybridisation of target DNA with quantum dot-labelled magnetic beads. In this device, the authors used an Arduino Uno to control the magnet positioner extension and the flow rates of pumps. A smooth control of these parameters was possible thanks to the pulse-width modulation enabled by some of the digital output pins available on the Arduino board.[68] Certainly, Arduino Uno is an inexpensive entry level microcontroller PCB, and is equipped with 6 PWM output pins.[6] As outlined above, PWM is very useful for controlling electromechanic actuators. Therefore, it should be considered for prototyping analytical systems by less experienced experimenters. Please note that,

Table 3 Application of universal electronic modules in analytical chemistry (examples)

Application	Platform(s)	Features used	Ref.
Plasmonic thermocycler	Arduino	Operation of optical shutter and cooling fan	Roche *et al.*[85]
Automated target capture, mixing, controlled target release in a microfluidic channel	Arduino	Control of a motor	Verbarg *et al.*[86]
Automated solid-phase extraction inductively coupled plasma mass spectrometry	Arduino	Synchronisation of the transfer of samples and rinsing	Charlton *et al.*[87]
Sequential injection analysis using peristaltic pump and electrochemical detection	Arduino	Control of peristaltic pump	Kongkedsuk *et al.*[88]
Imaging of oxygen and pH	Arduino	Trigger source	Ehgartner *et al.*[89]
Portable bacteria pre-concentrating microfluidic sensor and impedance sensing system	Arduino	Control of operation Communication Sending signals	Jiang *et al.*[73]
Electrochemical biosensor array for quantitative polymerase chain reaction	Arduino	Interfacing heaters	Tseng *et al.*[90]
Reproducible electrochemical etching of sharp STM probes	Arduino Uno	Interfacing etching control circuit	Jobbins *et al.*[91]
Capacitively coupled contactless conductivity detection	Arduino Uno	Confirmation of electrical continuity of electrode circuit	Gaudry *et al.*[92]
Control of light-sheet microscopes	Arduino Uno	Image acquisition and analysis	Gualda *et al.*[93]
Hydrogen gas sensor	Arduino Uno	Data acquisition Control of signal	Hassan *et al.*[94]
High-performance liquid chromatography with fluorescence detection	Arduino Uno	Operation of sampler	Alcaráz *et al.*[95]
Single chip detector for capillary electrophoresis	Arduino Uno	Collection and transmission of data	Drevinskas *et al.*[96]
Trapping volatile organic compounds	Arduino Uno	Control of valve actuation, plunger movement, application of electric current, communication with GC	Ghosh *et al.*[97]
Dispenser for particles and cells	Arduino Uno	Control of a DVD drive unit	Kasukurti *et al.*[98]
Photometry	Arduino Uno	Absorbance measurement	McClain,[65] Urban[66]
In situ pathogen detection system	Arduino Uno	Control of the magnet positioner extension and the flow rates of the pumps	Mitchell *et al.*[68]
Bioimpedance-based 2-dimensional imaging system for detection and localisation of pathological epithelial tissues	Arduino Uno	Control Signal processing	Ching and Chen[99]
Solid-phase microextraction, two-dimensional gas chromatography	Arduino Duemilanove	Control of solenoid valves	Bogusz *et al.*[100]
Electrochemical biosensor	Arduino Duemilanove	Scanning potentiostat circuit	Loncaric *et al.*[101]
Nanoliter-scale open chemical reactor	Arduino Duemilanove	Valve actuation	Galas *et al.*[102]
Comprehensive two-dimensional gas chromatography	Arduino Duemilanove	Control of two-stage cryogenic modulator	Hantao *et al.*[103]
3D-printed sensing platform	Arduino Due	Control of temperature Interfacing photodiode	Chudobova *et al.*[104]
Spectrophotometric assessment of blood hemoglobin concentration	Arduino Nano	Data acquisition	Bond *et al.*[105]
Portable capillary electrophoresis system	Arduino Nano	Automated injection	Mai *et al.*[76]
Determination of nitrogen mustard degradation products in water samples	Arduino Nano	Control of portable capillary electrophoresis system	Sáiz *et al.*[106]
Raman system for point-of-care detection of arthropathic crystals in the synovial fluid	Arduino Nano	Control of servo motor	Li *et al.*[107]
Fluorescence measurement	Arduino Pro Mini	Control of LEDs used for excitation	Awqatty *et al.*[108]
Oxygen optical sensors	Arduino Mega	Control of sensor	Badocco *et al.*[109,110]
Control of gap height for digital microfluidics	Arduino Mega	Distribution of signals	Yafia and Najjaran[111]
Automated digital microfluidic platform	Arduino Mega	High-voltage switching	Choi *et al.*[112] Fobel *et al.*[113]
Colorimetric bioassay	Arduino Mega	Control of component devices, data collection and processing	Duy *et al.*[114]
Automated preparation of microscale samples for mass spectrometry	Arduino Mega	Digital output pins for controlling relays (connected to pump, solenoid actuator, DC motor) Operating stepper motor Interfacing with touch screen Triggering MS analysis	Hu *et al.*[79]
Determination of oxygen with a light emission based optical sensor	Arduino Mega	Control of sensor parts	Mondin *et al.*[115]

Table 3 *(Contd.)*

Application	Platform(s)	Features used	Ref.
Automated extraction system	Arduino Mega	Control of syringe pump Control of multi-position valve Control of high-voltage module Trigger of LC	See and Hauser[78]
Cost-effective fabrication of transparent microfluidic chips	Arduino Mega	Control of 3D printer for fabricating microchips	Shallan *et al.*[116]
Reverse transcription polymerase chain reaction	Arduino Duemilanove Arduino Mega	Temperature monitoring Control of motors	You *et al.*[117]
Wire-guided droplet manipulation	Arduino Mega Arduino Uno	Operating three motors Proportional-integrative-derivative controller	Harshman *et al.*[118]
Portable low-cost long-term live-cell imaging platform	Arduino Mega Arduino Uno	Interfacing sensors (thermistors) Control of heating elements	Walzik *et al.*[119]
Optical sensing system	MSP430	Control of paired emitter detector diode device	Czugala *et al.*[120]
Wearable micro-fluidic platform	Arduino Fio Arduino Lilypad Arduino Pro	Motion control Control of LEDs Collecting data	Curto *et al.*[121]
Robotics-assisted mass spectrometry assay	Arduino Fio Arduino Mega (×2), Arduino Uno, Arduino Leonardo	Interfacing sensors Controlling servos of a robotic arm Triggering MS measurement Reading digital and analogue signals from sensors	Chiu and Urban[80]
Unmanned platform for long-range remote analysis of volatile compounds	Teensy 2.0	Control of head, driver, electrophoresis module, and detection system	da Costa *et al.*[122]
Simple module to control a series of PDMS-based valves	Teensy 2.0	Controlling solenoid actuators	da Costa *et al.*[123]
Electrochemical detection on a mobile phone	Teensy 2.0	Interfacing mobile phone, data transmission	Lillehoj *et al.*[72]
Capillary microfluidic immunoassays	Teensy 3.0	Voltage measurement *via* 16-bit ADC	Novo *et al.*[124]
Microfluidic system for dried blood spot analysis	RBBB Arduino	Control of a digital microfluidic device	Shih *et al.*[77]
Droplet-to-digital microfluidic device	RBBB Arduino	Feedback control system Control of Peltier cooler	Shih *et al.*[125]
Smartphone accessory for detection of Kaposi's sarcoma	IOIO	Communication with the smartphone	Mancuso *et al.*[69]
Point of care genetic testing	LPC2378	Controlling the temperature of the chip Triggering the LEDs Acquiring voltage readings from the photodiode Sending data to a Wi-Fi module	Stedtfeld *et al.*[126]
Electronic nose for aroma detection	mbed (LPC1768)	Control of the operation Data storage Communication with the user	Macías *et al.*[81]
On-line interface of dynamic samples with GC-MS	Raspberry Pi	Digital output pins for controlling relays (connected to peristaltic pump and solenoid valves) Convenient interaction with the user Triggering GC-MS analysis	Ting *et al.*[83]
Low-cost miniaturised potentiostat	BeagleBone	Cyclic voltammetry measurements on three-electrode systems Data storage	Diaz Cruz *et al.*[82]
Compact high-resolution capacitively coupled contactless conductivity detector	ATmega168	Data acquisition	Mendonça Francisco and do Lago[127]
Solvent replenishment system for digital microfluidics	PICAXE	Temperature control	Jebrail *et al.*[128]
Smartphone controlled handheld microfluidic liquid handling system	ATMega328p (×2)	Receiving commands from smartphone Receiving data from sensor Controlling pump and valves Adjusting pressure levels	Li *et al.*[71]

normally, PWM pins are not connected to any actuator directly but *via* a power transistor. This is because the current drawn from an output pin in this PCB is limited to 40 mA.

In another work, Mancuso *et al.*[69] developed a smartphone accessory capable of detecting Kaposi's sarcoma-associated herpes virus nucleic acids down to the concentration of 1 nM. Their device was based on an IOIO microcontroller board which enabled simple communication with the smartphone.[69] In fact, the IOIO microcontroller is specifically designed for Android devices; therefore, it is very suitable for the development of miniature analytical systems with smartphone interfaces.[70] Along these lines, Li *et al.*[71] disclosed the design

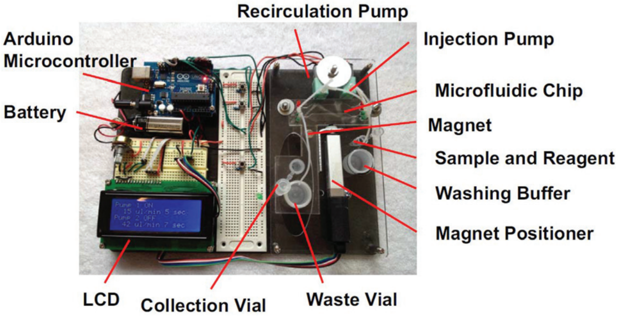


Fig. 1 *In situ* pathogen detection system. The illustration of the Gen1-IPDS showing the labelled hardware.[68] Reprinted from K. A. Mitchell, B. Chua, A. Son, Development of first generation *in-situ* pathogen detection system (Gen1-IPDS) based on NanoGene assay for near real time *E. coli* O157:H7 detection, *Biosens. Bioelectron.*, **54**, 229–236, Copyright (2014), with permission from Elsevier.

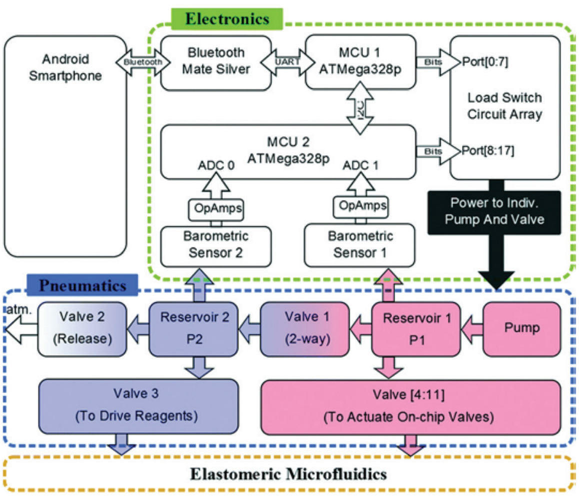


Fig. 2 Smartphone controlled handheld microfluidic liquid handling system. Block diagram of the system. The system consists of an Android smartphone, an electronic PCB with microcontrollers and Bluetooth module, and a pneumatic system capable of generating two different pressure output. Valve 1 is a two-way normally-closed solenoid valve and valves 2 to 11 are three-way solenoid valves. Reproduced from ref. 71 with permission of The Royal Society of Chemistry.

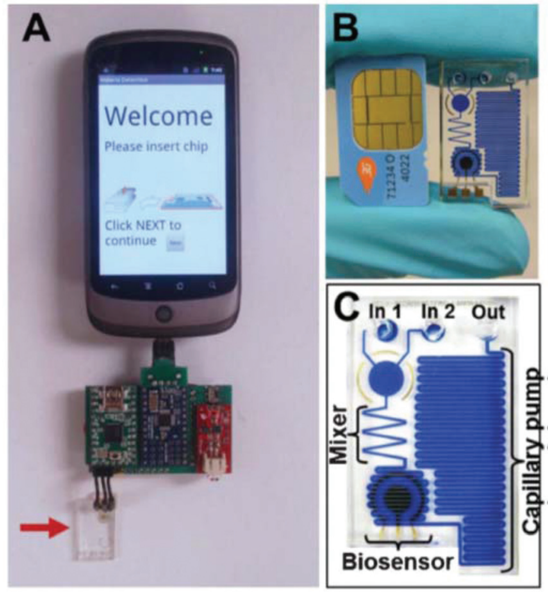


Fig. 3 Rapid electrochemical detection on a mobile phone. (A) Photograph of the assembled prototype device. The arrow indicates the microfluidic chip. (B) Photograph of the chip and a mobile phone SIM card for comparison. (C) An enlarged image of the chip with labelled components. The channels are filled with dye for improved visualisation of the fluidic network. Reproduced from ref. 72 with permission of The Royal Society of Chemistry.

of a handheld automated microfluidic liquid manipulation system controlled by a smartphone. Their device incorporates elastomeric on-chip valves and a small pneumatic actuation system (Fig. 2). The control unit was elegantly arranged using two ATMega328p 8-bit microcontrollers which have different tasks. The first chip takes care of receiving commands from smartphones *via* Bluetooth, sending commands to the second chip, requesting real-time barometric data, and sending it to the smartphone, as well as controlling pump and solenoid valve operation. The second chip controls the status of other electromechanical components, monitoring the barometric sensor data, adjusting pressure levels in the two pressure reservoirs, and sending barometric data to the first chip when required.[71] This study exemplifies the possibility of constructing modular – yet miniature – analytical sensor systems composed of multiple electronic control units. Various tasks are delegated to different microcontroller ICs while the size of the device is small. However, using bare ICs may require a substantial amount of wiring and/or soldering; therefore, this solution is recommended to experimenters with some experience in the assembly in electronic circuits on prototyping breadboards, perfboards or PCBs.

Lillehoj *et al.*[72] presented a compact mobile phone platform for the electrochemical detection of biomolecules which can potentially be applied in point-of-care diagnostics (Fig. 3). The control circuit is connected to the smartphone *via* USB port. The miniature microcontroller (Teensy 2.0) processes the received data, and feeds data back to the phone in real time. However, certain modifications had to be implemented in order to ensure compatibility with the USB port of the smartphone operated with the Android operating system. Although the Teensy 2.0 module used in this work, is a PCB, it is still very small compared to the popular prototyping microcontroller PCBs (*e.g.* Arduino Uno, Arduino Mega). In fact, the size of this PCB is comparable with the size of the microfluidic chip implemented for sample processing and detection. Thus, Teensy – along with Basic Stamp, Trinket, Arduino Micro, Arduino Nano, and Spark – is particularly useful in the construction of miniature analytical devices.

Jiang *et al.*[73] demonstrated a low-cost miniature sensor of bacteria (Fig. 4). It is based on electrical impedance spectroscopy. The interface of this device comprises an Android cell phone, a Bluetooth shield, a microcontroller (Arduino), a chip

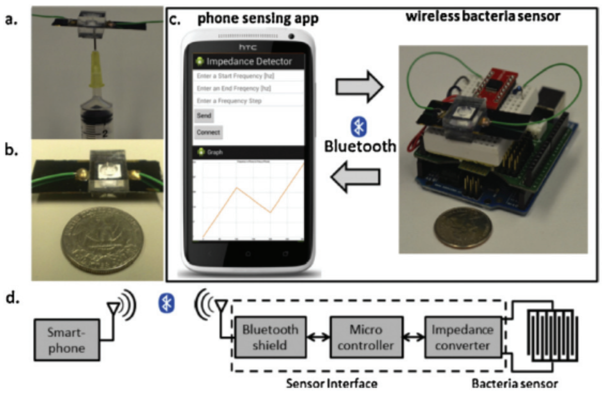


Fig. 4 Wireless mobile phone bacteria sensing system. (a) Picture showing syringe injection of testing liquid into the sensor package; (b) close view of the EIS bacteria sensor package; (c) picture showing communication scheme between smartphone sensing app and wireless bacteria sensor; (d) diagram of wireless sensing system.[73] Reprinted from J. Jiang, X. Wang, R. Chao, Y. Ren, C. Hu, Z. Xu, G. L. Liu, Smartphone based portable bacteria pre-concentrating microfluidic sensor and impedance sensing system, *Sens. Actuators, B*, **193**, 653–659, Copyright (2014), with permission from Elsevier.

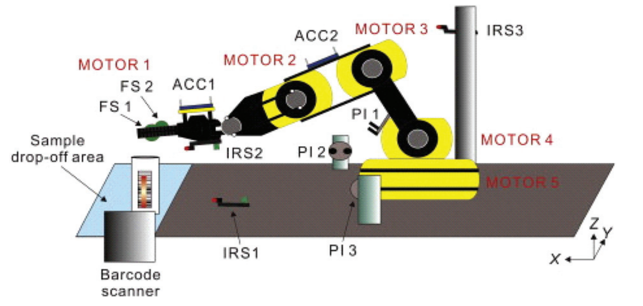


Fig. 5 Abundance of sensors and actuators connected to an open-source electronic control system in the Robotics-Assisted Mass Spectrometry Assay (RAMSAY-1). Abbreviations: FS, force sensor; ACC, accelerometer; IRS, infrared sensor; PI, photointerrupter.[80] Reprinted from S.-H. Chiu, P. L. Urban, Robotics-assisted mass spectrometry assay platform enabled by open-source electronics, *Biosens. Bioelectron.*, **64**, 260–268, Copyright (2015), with permission from Elsevier.

for impedance converter network analyser, and the sensor.[73] The Bluetooth shield enables wireless communication between the sensor device and the smartphone over short distances. However, using an Arduino along with a shield does not let one miniaturise the device beyond certain limit. It is interesting to note that some microcontroller PCBs integrate wireless connectivity (including antennae) – for example: Bluno[74] for Bluetooth and Spark[75] for local wireless networks. Wireless communication is also enabled by single-board microcomputers such as the Intel Edison,[1] facilitating the construction of miniature analytical devices with wireless connectivity.

Although microcontrollers handle low-voltage signals (typically, ≤5 V), they can be used to develop apparatuses that involve high voltages. In these cases, appropriate interfaces (for example, relays) are implemented to bridge low-voltage microcontroller circuits with the high-voltage circuits used in the analytical procedures. For example, Mai *et al.*[76] developed a portable capillary electrophoresis system controlled by the miniature microcontroller PCB – Arduino Nano. Shih *et al.*[77] applied RBBB Arduino to control a digital microfluidic system for dried blood spot analysis. In most cases, the digital microfluidic systems based on the electrowetting-on-dielectric phenomenon require application of electric potentials to the electrodes "printed" on the microchip. This requirement can be addressed by coupling digital outputs of one of the available microcontrollers (*cf.* Table 2) with inputs of a relay extension board (a PCB with multiple relays, an interface circuit, and connectors). In this case, the digital outputs provide low-direct-current low-voltage signals that trigger the corresponding relays. The relays then direct the electric current from a dedicated power source to the electrodes on the microchip. The characteristics of that current (direct *vs.* alternating current, amplitude, frequency) can be optimised independently of the microcontroller.

Microcontrollers also assist the development of instruments for preparation of complex samples and their delivery to highly selective detectors (*e.g.* mass spectrometers). Using Arduino Mega, See and Hauser[78] devised an automated extraction system. The microcontroller took care of switching syringe pumps, multi-position valves, high-voltage modules, and triggering liquid chromatograph. Arduino Mega was also at the heart of a system for automated preparation of microscale samples for mass spectrometry.[79] It enabled timing and control of all the main operations of the device, including peristaltic pumps, solenoid actuators, direct current motors, stepper motors, interfacing with touch screen, and triggering data acquisition. In our recent work,[80] we devised a robotics-assisted mass spectrometry assay (RAMSAY) platform which takes advantage of flexible and inexpensive open-source electronic modules (Fig. 5). The robotic arm is equipped with many sensors that provide feedback information to the control unit. They include: force sensors, accelerometers, infrared proximity sensors, and photointerrupters. The control device comprises four Arduino boards: Mega ×2, Uno, and Leonardo; which communicate with one another. One Arduino Mega board guides the movements of the robotic arm. The other takes care of communication with the user *via* a touch-screen panel. The Arduino Uno PCB interfaces RAMSAY with the internet (displaying sample number of the associated website) while the Arduino Leonardo PCB processes information about the sample.[80] Here, the use of multiple microcontroller PCBs facilitated the development of the first prototype by adding new modules along with the associated sensors. Various functions of the system could be programmed separately, which greatly simplified drafting the code. At the same time, malfunction of the system could easily be diagnosed and rectified.

Microcontroller PCBs also support the development of electronic noses. For example, an electronic nose for aroma detection was recently disclosed.[81] In this case, an mbed (LPC1768) microcontroller enabled control of the device operation, data storage, and communication with the user. While many reports discuss implementation of microcontroller PCBs, some demonstrate the usefulness of single-board computers in conducting chemical measurements. In one study, Diaz Cruz *et al.*[82] developed a low-cost miniaturised potentiostat based on the BeagleBone board. The apparatus carries out cyclic voltammetry measurements on three-electrode systems, and stores the data. Our group recently proposed an on-line interface for transferring dynamic samples to GC-MS apparatus operated by the popular Raspberry Pi microcomputer.[83] This single-board computer controls peristaltic pump and solenoid valves, and triggers GC-MS analysis. It also facilitates interaction with the user. In this case, the use of the microcomputer was optional, and the unit could readily be built with one of many microcontroller PCBs listed in Table 2. However, using modules with higher performance gives the advantage of flexible prototyping. As the prototype is developed, new functions can readily be incorporated without the need to upgrade the platform. The recently introduced Intel Edison[1] and the upcoming Arduino Tre[6] will certainly give rise to exciting developments in the area of chemical assay automation and miniaturisation.

Overall, considering the large number of microcontrollers and microcomputers available (Table 2), it may not be a trivial task for a chemist to decide upfront which module is best for their analytical system. Fortunately, many applications can be served by various modules without substantial loss of performance. However, there are a few questions which one needs to ask at the start – for example:

– How many digital output pins do we need?
– How many digital output pins should enable PWM?
– How many digital input pins do we need?
– How many analogue input pins do we need?
– What is the required resolution of ADC?
– Is the size of the device important?
– How much computing power do we need?
– Do we require high-speed control or data processing?
– Which programming language do we prefer to use?

For instance, if we design a digital microfluidic system with many electrodes to which potentials need to be supplied at specific times, we may decide to use a microcontroller with a large number of digital outputs (*e.g.* Arduino Mega or Due) that can be coupled with a multi-relay board. If we are interested in voltage measurements with low quantisation error, we may opt for a device with a high-resolution ADC (*e.g.* Teensy 3.0). If we design a miniature sensing device, we may need to consider the size of the PCB, and choose one of the smallest units (*e.g.* Arduino Micro, Arduino Nano, and Spark, Teensy, Trinket). If our device has to transmit data by radio waves, we can select a module with wireless connectivity (*e.g.* Arduino Yún, Bluno, Spark). If we already have a basic module (*e.g.* Arduino Uno) but still want to use a higher resolution ADC or transmit data wirelessly, we can simply incorporate an appropriate extension board into our system, which will increase its functionality. If we require extra computing power, or just prefer to program the device using one of the compilers available in the Linux environment, we can choose a single-board computer (*e.g.* Intel Galileo, BeagleBone, or Raspberry Pi).

5. Conclusions

Open-source and other universal electronic modules have already entered the analytical chemistry field, enabling the development of inexpensive instrumentation. They have a number of advantages: flexibility, good performance, small size, and low cost. Examples of applications include: sample disruption, extraction, real-time analysis by mass spectrometry, robotic sample handling, monitoring of biocatalytic processes, detection of disease biomarkers, and communication with smartphones. As automation and computerisation of chemistry procedures is gaining importance,[84] the availability of universal electronic modules (microcontrollers, microcomputers) can help to achieve the projected goals. It is predicted that the abundance of universal electronic modules and simplification of programming and device assembly will further inspire analytical scientists to construct innovative automated and miniaturised systems for various applications. Certainly, in a number of applications, the conventional research-grade electronic platforms still outperform the inexpensive PCBs. They excel in some important parameters (*e.g.* temporal resolution, analogue data logging resolution), and in reliability, intuitive user interfaces, expandability, and support. However, they come at a higher cost and normally occupy a larger amount of space, which renders them less suitable for the development of miniature analytical assays.

Acknowledgements

I would like to thank the Ministry of Science and Technology of Taiwan (formerly, National Science Council; grant no. NSC 102-2113-M-009-004-MY2) for the financial support. I am also grateful to the anonymous Reviewers for useful suggestions.

Notes and references

1 Intel Edison, http://www.intel.com/content/www/us/en/do-it-yourself/edison.html (viewed on 27/10/2014).
2 T. Nawy, *Methagora*, http://blogs.nature.com/methagora/2013/06/promoting-shared-hardware-design.html, (posted on 27/06/2013; viewed on 10/10/2014).
3 Open-source Lab, http://www.appropedia.org/Open-source_Lab (viewed on 01/11/2014).
4 J. M. Pearce, *Nature*, 2012, **491**, 519–521.
5 O. Pineño, *Behav. Res. Methods*, 2014, **46**, 196–205.
6 Arduino, http://www.arduino.cc/ (viewed on 27/10/2014).
7 Intel Galileo Gen 2, http://www.intel.com/content/www/us/en/do-it-yourself/galileo-maker-quark-board.html (viewed on 24/11/2014).

8 Parallax – Basic Stamp, http://www.parallax.com/catalog/microcontrollers/basic-stamp (viewed on 02/11/2014).

9 Espruino, http://www.espruino.com/ (viewed on 27/10/2014).

10 ARM mbed platforms, http://developer.mbed.org/platforms/ (viewed on 27/10/2014).

11 Netduino, http://netduino.com/ (viewed on 27/10/2014).

12 Parallax – Propeller, http://www.parallax.com/catalog/microcontrollers/propeller (viewed on 02/11/2014).

13 Teensy, https://www.pjrc.com/teensy/ (viewed on 27/10/2014).

14 Raspberry Pi, http://www.raspberrypi.org/ (viewed on 27/10/2014).

15 BeagleBone, http://beagleboard.org/bone (viewed on 27/10/2014).

16 Xilinx – Field Programmable Gate Array (FPGA), http://www.xilinx.com/training/fpga/fpga-field-programmable-gate-array.htm (viewed on 01/11/2014).

17 National Instruments – Introduction to FPGA Technology: Top 5 Benefits, http://www.ni.com/white-paper/6984/en/ (viewed on 24/11/2014).

18 R. Woods, J. McAllister, G. Lightbody and Y. Yi, *FPGA-based Implementation of Signal Processing Systems*, Wiley, Chichester, 2008.

19 Y. Takahashi, H. Shiku, T. Murata, T. Yasukawa and T. Matsue, *Anal. Chem.*, 2009, **81**, 9674–9681.

20 K. McKelvey, M. A. Edwards and P. R. Unwin, *Anal. Chem.*, 2010, **82**, 6334–6337.

21 M. E. Snowden, A. G. Güell, S. C. S. Lai, K. McKelvey, N. Ebejer, M. A. O'Connell, A. W. Colburn and P. R. Unwin, *Anal. Chem.*, 2012, **84**, 2483–2491.

22 J. Rothe, O. Frey, A. Stettler, Y. Chen and A. Hierlemann, *Anal. Chem.*, 2014, **86**, 6425–6432.

23 T. Nakamoto, Y. Isaka, T. Ishige and T. Moriizumi, *Sens. Actuators, B*, 2000, **69**, 58–62.

24 N. Nimsuk and T. Nakamoto, *Sens. Actuators, B*, 2007, **127**, 491–496.

25 N. Nimsuk and T. Nakamoto, *Sens. Actuators, B*, 2008, **134**, 252–257.

26 E. Zampetti, S. Pantalei, A. Macagnano, E. Proietti, C. Di Natale and A. D'Amico, *Sens. Actuators, B*, 2008, **131**, 159–166.

27 F. N. Dultsev and E. A. Kolosovsky, *Anal. Chim. Acta*, 2011, **687**, 75–81.

28 S. H. Cho, C. H. Chen, F. S. Tsai, J. M. Godin and Y.-H. Lo, *Lab Chip*, 2010, **10**, 1567–1573.

29 C. H. Chen, S. H. Cho, H.-I. Chiang, F. Tsai, K. Zhang and Y.-H. Lo, *Anal. Chem.*, 2011, **83**, 7269–7275.

30 T.-H. Wu, Y. Chen, S.-Y. Park, J. Hong, T. Teslaa, J. F. Zhong, D. Di Carlo, M. A. Teitell and P.-Y. Chiou, *Lab Chip*, 2012, **12**, 1378–1383.

31 Y. Chen, T.-H. Wu, Y.-C. Kung, M. A. Teitell and P.-Y. Chiou, *Analyst*, 2013, **138**, 7308–7315.

32 M. Zhao, W. C. Nelson, B. Wei, P. G. Shiro, B. M. Hakimi, E. S. Johnson, R. K. Anand, G. S. Gyurkey, L. M. White, S. H. Whiting, A. L. Coveler and D. T. Chiu, *Anal. Chem.*, 2013, **85**, 9671–9677.

33 P. F. DeCarlo, J. R. Kimmel, A. Trimborn, M. J. Northway, J. T. Jayne, A. C. Aiken, M. Gonin, K. Fuhrer, T. Horvath, K. S. Docherty, D. R. Worsnop and J. L. Jimenez, *Anal. Chem.*, 2006, **78**, 8281–8289.

34 G. D. Schilling, F. J. Andrade, J. H. Barnes IV, R. P. Sperline, M. B. Denton, C. J. Barinaga, D. W. Koppenaal and G. M. Hieftje, *Anal. Chem.*, 2006, **78**, 4319–4325.

35 S. J. Hanna, P. Campuzano-Jost, E. A. Simpson, I. Burak, M. W. Blades, J. W. Hepburn and A. L. Bertram, *Phys. Chem. Chem. Phys.*, 2009, **11**, 7963–7975.

36 P. Somboon, M. Kinoshita, B. Wyszynski and T. Nakamoto, *Sens. Actuators, B*, 2009, **141**, 141–146.

37 G. Churchill, K. Putyera, V. Weinstein, X. Wang and E. B. M. Steers, *J. Anal. At. Spectrom.*, 2011, **26**, 2263–2273.

38 A. A. Sysoev, D. M. Chernyshev, S. S. Poteshin, A. V. Karpov, O. I. Fomin and A. A. Sysoev, *Anal. Chem.*, 2013, **85**, 9003–9012.

39 P. I. Hendricks, J. K. Dalgleish, J. T. Shelley, M. A. Kirleis, M. T. McNicholas, L. Li, T.-C. Chen, C.-H. Chen, J. S. Duncan, F. Boudreau, R. J. Noll, J. P. Denton, T. A. Roach, Z. Ouyang and R. G. Cooks, *Anal. Chem.*, 2014, **86**, 2900–2908.

40 K. Takeda, *Rev. Sci. Instrum.*, 2007, **78**, 033103.

41 K. Takeda, *J. Magn. Reson.*, 2008, **192**, 218–229.

42 X. Liang and W. Weimin, *Rev. Sci. Instrum.*, 2009, **80**, 124703.

43 M. K. Sørensen, M. S. Vinding, O. N. Bakharev, T. Nesgaard, O. Jensen and N. C. Nielsen, *Anal. Chem.*, 2014, **86**, 7205–7208.

44 C. M. Castro, A. A. Ghazani, J. Chung, H. Shao, D. Issadore, T.-J. Yoon, R. Weissleder and H. Lee, *Lab Chip*, 2014, **14**, 14–23.

45 S. S. Zalesskiy, E. Danieli, B. Blümich and V. P. Ananikov, *Chem. Rev.*, 2014, **114**, 5641–5694.

46 K. G. Kraiczek, R. Bonjour, Y. Salvadé and R. Zengerle, *Anal. Chem.*, 2014, **86**, 1146–1152.

47 J. Gao, X. Liu, T. Chen, P.-I. Mak, Y. Du, M.-I. Vai, B. Lin and R. P. Martins, *Lab Chip*, 2013, **13**, 443–451.

48 J. M. Emory, Z. Peng, B. Young, M. L. Hupert, A. Rousselet, D. Patterson, B. Ellison and S. A. Soper, *Analyst*, 2012, **137**, 87–97.

49 D. Mark, F. von Stetten and R. Zengerle, *Lab Chip*, 2012, **12**, 2464–2468.

50 A. K. Yetisen, M. S. Akram and C. R. Lowe, *Lab Chip*, 2013, **13**, 2210–2251.

51 D. Erickson, D. O'Dell, L. Jiang, V. Oncescu, A. Gumus, S. Lee, M. Mancuso and S. Mehta, *Lab Chip*, 2014, **14**, 3159–3164.

52 S. C. B. Gopinath, T.-H. Tang, Y. Chen, M. Citartan and T. Lakshmipriya, *Biosens. Bioelectron.*, 2014, **60**, 332–342.

53 A. Ozcan, *Lab Chip*, 2014, **14**, 3187–3194.

54 W. Weaver, H. Kittur, M. Dhar and D. Di Carlo, *Lab Chip*, 2014, **14**, 1962–1965.

55 C. F. Woolley and M. A. Hayes, *Analyst*, 2014, **139**, 2277–2288.
56 A. K. Yetisen, J. L. Martinez-Hurtado, F. da Cruz Vasconcellos, M. C. Emre Simsekler, M. S. Akram and C. R. Lowe, *Lab Chip*, 2014, **14**, 833–840.
57 *Mobile Point-of-Care Monitors and Diagnostic Device Design (Devices, Circuits, and Systems)*, ed. W. Karlen, CRC Press, Boca Raton, 2014.
58 K.-T. Hsieh and P. L. Urban, *RSC Adv.*, 2014, **4**, 31094–31100.
59 D. A. Bui and P. C. Hauser, *Anal. Chim. Acta*, 2015, **853**, 46–58.
60 TechTarget – Impedance, http://whatis.techtarget.com/definition/impedance (viewed on 24/11/2014).
61 Arduino Forum – Faster Analog Read?, http://forum.arduino.cc/index.php?topic=6549.0 (viewed on 24/11/2014).
62 Arduino Forum – Clock, http://forum.arduino.cc/index.php?topic=62964.0 (viewed on 24/11/2014).
63 S. Monk, *Hacking Electronics: An Illustrated DIY Guide for Makers and Hobbyists*, McGraw-Hill, New York, 2013.
64 Adafruit – Learn, https://learn.adafruit.com/ (viewed on 02/11/2014).
65 R. L. McClain, *J. Chem. Educ.*, 2014, **91**, 747–750.
66 P. L. Urban, *J. Chem. Educ.*, 2014, **91**, 751–752.
67 A. D'Ausilio, *Behav. Res. Methods*, 2012, **44**, 305–313.
68 K. A. Mitchell, B. Chua and A. Son, *Biosens. Bioelectron.*, 2014, **54**, 229–236.
69 M. Mancuso, E. Cesarman and D. Erickson, *Lab Chip*, 2014, **14**, 3809–3816.
70 SparkFun – IOIO for Android, https://www.sparkfun.com/products/retired/10748 (viewed on 24/11/2014).
71 B. Li, L. Li, A. Guan, Q. Dong, K. Ruan, R. Hu and Z. Li, *Lab Chip*, 2014, **14**, 4085–4092.
72 P. B. Lillehoj, M.-C. Huang, N. Truong and C.-M. Ho, *Lab Chip*, 2013, **13**, 2950–2955.
73 J. Jiang, X. Wang, R. Chao, Y. Ren, C. Hu, Z. Xu and G. L. Liu, *Sens. Actuators, B*, 2014, **193**, 653–659.
74 Bluno, http://www.dfrobot.com/index.php?route=product/product&product_id=1044 (viewed on 24/11/2014).
75 Spark, http://www.spark.io/ (viewed on 24/11/2014).
76 T. D. Mai, T. T. T. Pham, H. V. Pham, J. Sáiz, C. García Ruiz and P. C. Hauser, *Anal. Chem.*, 2013, **85**, 2333–2339.
77 S. C. C. Shih, H. Yang, M. J. Jebrail, R. Fobel, N. McIntosh, O. Y. Al-Dirbashi, P. Chakraborty and A. R. Wheeler, *Anal. Chem.*, 2012, **84**, 3731–3738.
78 H. H. See and P. C. Hauser, *Anal. Chem.*, 2014, **86**, 8665–8670.
79 J.-B. Hu, S.-Y. Chen, J.-T. Wu, Y.-C. Chen and P. L. Urban, *RSC Adv.*, 2014, **4**, 10693–10701.
80 S.-H. Chiu and P. L. Urban, *Biosens. Bioelectron.*, 2015, **64**, 260–268.
81 M. Macías Macías, J. E. Agudo, A. García Manso, C. J. García Orellana, H. M. González Velasco and R. Gallardo Caballero, *Sensors*, 2013, **13**, 5528–5541.
82 A. F. Diaz Cruz, N. Norena, A. Kaushik and S. Bhansali, *Biosens. Bioelectron.*, 2014, **62**, 249–254.
83 H. Ting, J.-B. Hu, K.-T. Hsieh and P. L. Urban, *Anal. Methods*, 2014, **6**, 4652–4660.
84 E. C. Hayden, *Nature*, 2014, **516**, 131–132.
85 P. J. R. Roche, L. K. Beitel, R. Khan, R. Lumbroso, M. Najih, M. C.-K. Cheung, J. Thiemann, V. Veerasubramanian, M. Trifiro, V. P. Chodavarapu and A. G. Kirk, *Analyst*, 2012, **137**, 4475–4481.
86 J. Verbarg, K. Kamgar-Parsi, A. R. Shields, P. B. Howell Jr. and F. S. Ligler, *Lab Chip*, 2012, **12**, 1793–1799.
87 J. J. Charlton, M. J. Sepaniak, A. K. Sides, T. G. Schaaff, D. K. Mann and J. A. Bradshaw, *J. Anal. At. Spectrom.*, 2013, **28**, 711–718.
88 J. Kongkedsuk, A. Hongwitayakorn, W. Bootnapang, N. Boonto and R. Chaisuksant, *Chiang Mai J. Sci.*, 2013, **40**, 224–231.
89 J. Ehgartner, H. Wiltsche, S. M. Borisov and T. Mayr, *Analyst*, 2014, **139**, 4924–4933.
90 H.-Y. Tseng, V. Adamik, J. Parsons, S.-S. Lan, S. Malfesi, J. Lum, L. Shannon and B. Gray, *Sens. Actuators, B*, 2014, **204**, 459–466.
91 M. M. Jobbins, A. F. Raigoza and S. A. Kandel, *Rev. Sci. Instrum.*, 2012, **83**, 036105.
92 A. J. Gaudry, M. C. Breadmore and R. M. Guijt, *Electrophoresis*, 2013, **34**, 2980–2987.
93 E. J. Gualda, T. Vale, P. Almada, J. A. Feijó, G. G. Martins and N. Moreno, *Nat. Methods*, 2013, **10**, 599–600.
94 J. J. Hassan, M. A. Mahdi, C. W. Chin, H. Abu-Hassan and Z. Hassan, *Sens. Actuators, B*, 2013, **176**, 360–367.
95 M. R. Alcaráz, G. G. Siano, M. J. Culzoni, A. Muñoz de la Peña and H. C. Goicoechea, *Anal. Chim. Acta*, 2014, **809**, 37–46.
96 T. Drevinskas, M. Kaljurand and A. Maruška, *Electrophoresis*, 2014, **35**, 2401–2407.
97 A. Ghosh, S. K. Seeley and J. V. Seeley, *Anal. Chem.*, 2014, **86**, 6993–7000.
98 A. Kasukurti, C. D. Eggleton, S. A. Desai, D. I. Disharoon and D. W. M. Marr, *Lab Chip*, 2014, **14**, 4673–4679.
99 C. T.-S. Ching and J.-H. Chen, *Sens. Actuators, B*, 2015, **206**, 319–326.
100 S. Bogusz Jr., L. Wang Hantao, S. C. G. Neves Braga, V. de Cássia Rodrigues de Matos, M. F. da Costa, R. D. Hamer, D. F. Ventura and F. Augusto, *J. Sep. Sci.*, 2012, **35**, 2438–2444.
101 C. Loncaric, Y. Tang, C. Ho, M. A. Parameswaran and H.-Z. Yu, *Sens. Actuators, B*, 2012, **161**, 908–913.
102 J.-C. Galas, A.-M. Haghiri-Gosnet and A. Estévez-Torres, *Lab Chip*, 2013, **13**, 415–423.
103 L. Wang Hantao, H. G. Aleme, M. M. Passador, E. L. Furtado, F. A. de Lima Ribeiro, R. J. Poppi and F. Augusto, *J. Chromatogr., A*, 2013, **1279**, 86–91.
104 D. Chudobova, K. Cihalova, S. Skalickova, J. Zitka, M. A. Merlos Rodrigo, V. Milosavljevic, D. Hynek, P. Kopel, R. Vesely, V. Adam and R. Kizek, *Electrophoresis*, 2014, DOI: 10.1002/elps.201400321.

105 M. Bond, C. Elguea, J. S. Yan, M. Pawlowski, J. Williams, A. Wahed, M. Oden, T. S. Tkaczyk and R. Richards-Kortum, *Lab Chip*, 2013, **13**, 2381–2388.

106 J. Sáiz, T. D. Mai, P. C. Hauser and C. García-Ruiz, *Electrophoresis*, 2013, **34**, 2078–2084.

107 B. Li, S. Yang and O. Akkus, *Analyst*, 2014, **139**, 823–830.

108 B. Awqatty, S. Samaddar, K. J. Cash, H. A. Clark and J. M. Dubach, *Analyst*, 2014, **139**, 5230–5238.

109 D. Badocco, A. Mondin and P. Pastore, *Sens. Actuators, B*, 2013, **181**, 943–948.

110 D. Badocco, A. Mondin and P. Pastore, *Sens. Actuators, B*, 2013, **181**, 949–954.

111 M. Yafia and H. Najjaran, *Sens. Actuators, B*, 2013, **186**, 343–352.

112 K. Choi, A. H. C. Ng, R. Fobel, D. A. Chang-Yen, L. E. Yarnell, E. L. Pearson, C. M. Oleksak, A. T. Fischer, R. P. Luoma, J. M. Robinson, J. Audet and A. R. Wheeler, *Anal. Chem.*, 2013, **85**, 9638–9646.

113 R. Fobel, C. Fobel and A. R. Wheeler, *Appl. Phys. Lett.*, 2013, **102**, 193513.

114 J. Duy, R. L. Smith, S. D. Collins and L. B. Connell, *Biosens. Bioelectron.*, 2014, **52**, 433–437.

115 A. Mondin, D. Badocco and P. Pastore, *Sens. Actuators, B*, 2014, **190**, 775–781.

116 A. I. Shallan, P. Smejkal, M. Corban, R. M. Guijt and M. C. Breadmore, *Anal. Chem.*, 2014, **86**, 3124–3130.

117 D. J. You, P. L. Tran, H.-J. Kwon, D. Patel and J.-Y. Yoon, *Faraday Discuss.*, 2011, **149**, 159–170.

118 D. K. Harshman, R. Reyes, T. S. Park, D. J. You, J.-Y. Song and J.-Y. Yoon, *Biosens. Bioelectron.*, 2014, **53**, 167–174.

119 M. P. Walzik, V. Vollmar, T. Lachnit, H. Dietz, S. Haug, H. Bachmann, M. Fath, D. Aschenbrenner, S. A. Mofrad, O. Friedrich and D. F. Gilbert, *Biosens. Bioelectron.*, 2015, **64**, 639–649.

120 M. Czugala, R. Gorkin III, T. Phelan, J. Gaughran, V. F. Curto, J. Ducrée, D. Diamond and F. Benito-Lopez, *Lab Chip*, 2012, **12**, 5069–5078.

121 V. F. Curto, S. Coyle, R. Byrne, N. Angelov, D. Diamond and F. Benito-Lopez, *Sens. Actuators, B*, 2012, **175**, 263–270.

122 E. T. da Costa, C. A. Neves, G. M. Hotta, D. T. R. Vidal, M. F. Barros, A. A. Ayong, C. D. Garcia and C. L. do Lago, *Electrophoresis*, 2012, **33**, 2650–2659.

123 E. T. da Costa, M. F. Mora, P. A. Willis, C. L. do Lago, H. Jiao and C. D. Garcia, *Electrophoresis*, 2014, **35**, 2370–2377.

124 P. Novo, V. Chu and J. P. Conde, *Biosens. Bioelectron.*, 2014, **57**, 284–291.

125 S. C. C. Shih, P. C. Gach, J. Sustarich, B. A. Simmons, P. D. Adams, S. Singh and A. K. Singh, *Lab Chip*, 2015, **15**, 225–236.

126 R. D. Stedtfeld, D. M. Tourlousse, G. Seyrig, T. M. Stedtfeld, M. Kronlein, S. Price, F. Ahmad, E. Gulari, J. M. Tiedje and S. A. Hashsham, *Lab Chip*, 2012, **12**, 1454–1462.

127 K. J. Mendonça Francisco and C. L. do Lago, *Electrophoresis*, 2009, **30**, 3458–3464.

128 M. J. Jebrail, R. F. Renzi, A. Sinha, J. Van De Vreugde, C. Gondhalekar, C. Ambriz, R. J. Meagher and S. S. Branda, *Lab Chip*, 2015, **15**, 151–158.