PUBLISHED: 10 JANUARY 2017 | VOLUME: 1 | ARTICLE NUMBER: 0017

DIAGNOSTICS FOR GLOBAL HEALTH

Hand-spun centrifuge

A 20 cent centrifuge made of paper and string and operated by hand can separate plasma from blood in about 90 seconds.

Meaghan Bond and Rebecca Richards-Kortum

The majority of the world's population lives in low-income countries, yet most medical technologies are designed to be used in the developed world, where access to stable electrical power, clean water, consumable supplies and trained healthcare providers is taken for granted[1]. Reducing global-health inequities thus requires a concerted effort to design affordable and effective technologies that can be used in resource-poor settings. When available, low-cost tools to diagnose disease at the point of care (POC) can transform healthcare; for example, healthcare centres around the world use lateral-flow assays — simple devices for detecting the presence or absence of a target analyte — to rapidly detect human immunodeficiency virus (HIV) antibodies from a drop of whole blood, thus enabling providers to refer patients for treatment more effectively and to reduce loss to follow-up[2]. Such rapid HIV tests are so simple to implement that many low-income countries now train 'expert patients' to carry out POC HIV testing[2]. Yet designing assays that can be performed at the POC with a broad range of clinical samples such as blood, stool, urine and saliva remains a challenge. For example, assays to detect proteins, nucleic acids or even parasites in blood often require an initial step to separate the plasma fraction from it because the large number of red blood cells in whole blood interferes with the assays by restricting fluid flow, inhibiting the polymerase chain reaction or increasing background fluorescence[3]. Yet conventional sample-preparation technologies, such as centrifugation and filtration, are difficult to implement at the POC in low-resource settings because of the high cost, large size, and power and maintenance requirements of the necessary equipment (Fig. 1a,b).

Nevertheless, progress has been made in the development of low-cost, highly sensitive assays that can be used at the POC. A case in point is the use of paper, which can be cut, patterned with hydrophobic barriers or

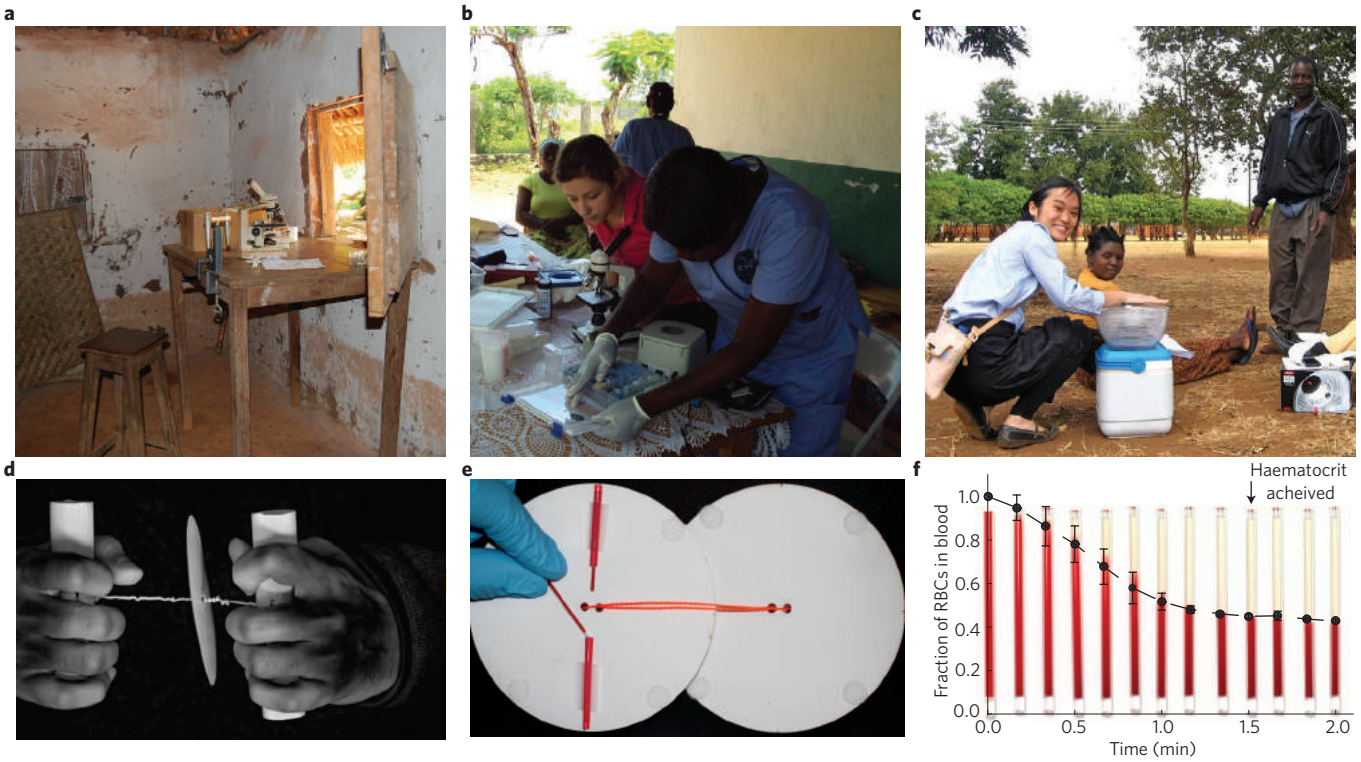

Figure 1 | Centrifuges for use in low-resource settings. **a**, Hand-crank centrifuge and microscope in a laboratory of a health centre in the Democratic Republic of the Congo[1]. **b**, Commercial centrifuge powered by a rechargeable laptop battery being used in Haiti. **c**, Salad-spinner centrifuge in use in Malawi. **d**, Hand-powered paper-and-string centrifuge[8]. **e**, Sealed straws allow the paper-and-string centrifuge to carry capillaries filled with whole blood. **f**, Fraction of red blood cells (RBCs) in blood, as a function of spinning time, separated by a 10-cm-diameter paper-and-string centrifuge. Stable haematocrit values are reached after about 90 seconds. Error bars represent the standard deviation of eight experiments carried out by two users. Figure reproduced with permission from: **a**, ref. [1], AAAS; **d**–**f**, ref. [8], Nature Publishing Group.

folded to form two- and three-dimensional structures that direct fluid flow past regions containing the pre-dried reagents needed to carry out multistep assays to detect a variety of analytes with clinically relevant sensitivity[4]. And commercially available blood-separation membranes using filtration aided by capillary force have been integrated with paper-based POC assays[5]. Paper and traditional microfluidic devices are however most appropriate for use with small sample volumes and are difficult to adapt for the large volumes that are often needed to achieve higher sensitivity or to process complex clinical samples. For this, cheap household items such as egg beaters[6] and salad spinners[7] (Fig. 1c) have been adapted to make hand-powered mechanical centrifuges capable of separating plasma from whole blood. However, these devices generate relatively low centrifugal forces (equivalent to ~30–300*g*, where *g* is the acceleration due to gravity) compared with a typical bench-top laboratory centrifuge used to measure haematocrit (~5,000*g*; ref. [7]). Inspired by an ancient whirligig (a buzzer toy), Manu Prakash and colleagues now describe in *Nature Biomedical Engineering* a 20 cent, hand-powered centrifuge that is capable of achieving centrifugal forces as high as 30,000*g* (ref. [8]).

Prakash and co-authors' whirligig is made from a disc with two holes on either side of its centre of gravity and a piece of string[8]. The string is passed through the holes and then held by hand at either end. When the string is initially wound up, tension applied by pulling at both ends causes the string to unwind and the disc to spin; when the tension is then released, the inertia of the disc causes the string to rewind in the opposite direction, drawing the hands back together. If one successively applies and releases tension at an appropriate rhythm, the process of winding and unwinding continues, producing a characteristic buzzing sound. The authors adapted the whirligig to serve as a low-cost centrifuge (Fig. 1d,e), optimizing it for high-speed operation by using two paper discs, fishing line and wooden handles. They demonstrate that it can be used to separate plasma from whole blood in less than two minutes, which is comparable to the time needed by a bench-top centrifuge.

Power for the paper-and-string centrifuge is supplied by the hands and dissipated by air drag and in the strings. Each of these components dominates the torque applied to the disc at different phases during the spinning cycle: torque resulting from the input force during the unwinding phase, from air drag as the string is winding and from the supercoiled string at the end of the winding phase[9]. The maximum rotational speed of the centrifuge was measured across a range of disc diameters and cycle frequencies. With a disc 10 mm in diameter, rotational speeds of up to 125,000 revolutions per minute (30,000*g*) could be achieved. By using a mathematical model of the centrifuge, Prakash and co-authors designed the paper-and-string centrifuge so that it would yield a centrifugal force of ~10,000*g* and could be used to separate blood cells from plasma. For this, two drinking straws (to hold sealed capillary tubes) were taped to a 10-cm-diameter paper disc, with the outer edge of each straw sealed shut. A second paper disc was secured in place over the straws using Velcro tabs. The authors show that in eight trials with two operators, variation in the red-blood-cell fraction of the centrifuged samples was small at the 1.5 minutes time point (Fig. 1f), resulting in haematocrit values that were in good agreement with those obtained using a US$700 commercial centrifuge. They also show that the plasma portions of the spun capillary tubes were free of cells. Notably, the centrifuge was also used to separate the buffy coat — the blood fraction that contains white blood cells and platelets — in 15 minutes. By using a standard quantitative buffy-coat test, malaria and other infectious diseases can be diagnosed by checking for the parasites via fluorescence microscopy. Moreover, the authors show that a wide variety of materials can be adapted to the whirligig format. In particular, they demonstrate centrifugation by using plastic discs made with a desktop 3D printer and the generation of centrifugal force in traditional lab-on-a-chip microfluidic systems and in microfluidic structures assembled from plastic film and double-sided adhesive tape.

The paper-and-string centrifuge of Prakash and co-authors is a significant step towards bringing the separation capability of clinical laboratory centrifuges to the POC. The authors demonstrated the use of the centrifuge to carry out simple diagnostics through the wall of sealed capillary tubes by viewing the haematocrit level or examining the blood for parasites using microscopy. Many other diagnostics, however, require safe transfer of plasma from the capillary tube to a paper or plastic device for subsequent analysis. And unlike many recent developments in paper microfluidics[4,10,11], the paper in the authors' centrifuge is used as a structural support for blood contained in a traditional capillary tube, rather than for containing or directing fluid flow. Also, assay designers will need to consider how to ensure that users correctly operate the device; for example, will operators reliably spin all blood samples for a full 90 seconds? Underspinning samples would lead to an overestimation of haematocrit. User safety during the high-speed rotation of potentially infectious fluids should be guaranteed. Yet, these considerations should not prevent the successful integration of Prakash and co-authors' centrifuge into the clinical workflow of more complex assays. Beyond its obvious clinical applications in the developing world, the paper-and-string centrifuge is poised to become an ingenious tool for science education. ❐

Meaghan Bond and Rebecca Richards-Kortum are in the Department of Bioengineering, Rice University, 6100 Main Street, Houston, Texas 77005, USA.
e-mail: rkortum@rice.edu

References

1. Richards-Kortum, R. & Oden, M. *Science* **342,** 1055–1057 (2013).
2. Reid, S. D., Fidler, S. J. & Cooke, G. S. *J. Clin. Epidemiol.* **5,** 387–396 (2013).
3. Cui, F., Rhee, M., Singh, A. & Tripathi, A. *Annu. Rev. Biomed. Eng.* **17,** 267–286 (2015).
4. Martinez, A. W., Phillips, S. T. & Whitesides, G. M. *Anal. Chem.* **82,** 3–10 (2010).
5. Tang, R. H. *et al. Crit. Rev. Biotech.* http://dx.doi.org/10.3109/07388551.2016.1164664 (2016).
6. Wong, A. P., Gupta, M., Shevkoplyas, S. S. & Whitesides, G. M. *Lab Chip* **8,** 2032–2037 (2008).
7. Brown, J. *et al. Am. J. Trop. Med. Hyg.* **85,** 327–332 (2011).
8. Bhamla, M. S. *et al. Nat. Biomed. Eng.* **1,** 0009 (2017).
9. Schlichting, H. J. & Suhr, W. *Eur. J. Phys.* **31,** 501–510 (2010).
10. Fu, E. *et al. Anal. Chem.* **84,** 4574–4579 (2012).
11. Rohrman, B. A. & Richards-Kortum, R. *Lab Chip* **12,** 3082–3088 (2012).