Robotic crowd biology with Maholo LabDroids

To the Editor:
Concerns about the lack of reproducibility of experimental research\(^1\),\(^2\), the numerous labor-intensive tasks required for high-throughput research, and the dangers (and costs) associated with experiments involving pathogens and harmful reagents led us to set up a Robotic Biology Consortium. We believe that the use of humanoid robots (which we term ‘LabDroids’) to carry out life science research experiments has the potential to minimize the above problems.

In 2009, the first robot scientist capable of devising hypotheses and then testing them was reported. By integrating automation technologies and data analysis pipelines, the robot, named Adam, was able to find new (and subsequently validated) information in yeast functional genomics experiments\(^3\). More recently, a robotic system was developed to enable precise and dexterous experiments with the model insect Drosophila\(^4\). Today, several startups, including Transcriptic (Menlo Park, CA, USA) and Emerald Cloud Lab (S. San Francisco, CA, USA), offer researchers remote access to laboratory automation systems to carry out experiments\(^5\). However, current laboratory automation systems are fixed assemblies of job-specific modules and can enable only a limited suite of experiments.

To establish a versatile laboratory automation system, we developed a high-performance LabDroid system named ‘Maholo’ (Fig. 1a and Supplementary Video; technical specifications to be published elsewhere). Maholo has one torso pivot and two arms, each of which has seven rotational axes and can manipulate laboratory tools and instruments without robot-specific modifications. The automation of various laboratory operations was first simulated using a computer-aided design system (Fig. 1b) and calibrated in a real environment. Maholo can carry out most regular tasks involving liquid handling in test tubes, Petri dishes, and microplate wells with the same pipettes and aspirators that human researchers and technicians use. The automated workflows for these tasks include a cell-harvesting process that requires delicate sample handling (Fig. 1c). In this process Maholo collects a cell culture dish from a CO\(_2\) incubator and aspirates the culture medium before detaching the cells by trypsinization, then scrapes them free using a spatula with the correct pressure and speed, before collecting the cells in a tube. Unlike other laboratory automation systems, Maholo can reproduce human maneuvers without the assistance of action-specific jigs. Throughout cell culture harvesting, the left hand of Maholo serves as a jig to hold the culture dish, whereas the right hand performs several different tasks including dispensing, scraping, and transferring the cell suspension from dish to tube. This jig-free system enables greater flexibility in automating various laboratory protocols with a single robotic system. Force and vision sensors allow our LabDroid to manipulate other tools and devices, including a vortex mixer, sample mixers, tube rotors, incubators and refrigerators (Fig. 1d). For example, Maholo can open and shut a centrifuge door, press the front panel buttons and adjust the rotor angle with the aid of its vision system (Fig. 1e).

Maholo can load tubes in a centrifuge in properly balanced positions and can salvage samples from the rotor, stopping at a random angle (Fig. 1e).

In any experiment that involves manual handling of reagents, it is inevitable that data variation will arise owing to human error. This variability could be minimized by the consistent movements, operation timings, and spatial trajectories of a LabDroid. One could argue that non-humanoid automation systems, such as liquid handling robots that can manipulate microwell plates, could outperform LabDroids in precision and scalability for specific tasks. However, it is more challenging to automate complex workflows by combining such isolated job-specific automation systems, each of which is designed for human manipulation with minimal hardware and software engineering. Numerous tools in various combinations are used in the laboratory daily. Numerous efforts have already been devoted to optimizing these tools for human use. The cost of developing an integrated laboratory automation system with compatible modules to replace all of the experiments carried out in a typical laboratory would be prohibitively high. Instead, we propose that LabDroids, which can manipulate existing laboratory instruments, could form the basis of a versatile, scalable, and sustainable laboratory automation system that many laboratories might adopt.

The potential of LabDroids underpins our vision of robotic crowd biology, in which a crowd of LabDroids and an assortment of instruments in a large laboratory space are operated remotely online (Fig. 2a). LabDroids could be scaled to provide a versatile system comprising a team of droids that carry out
needs to be developed for describing experimental protocols, operating system assemblies, and recording results. Currently, Maholo’s proprietary software system and application program interface enables only Maholo to perform experimental tasks. Although robotic operation frameworks are also provided by several services, including Transcriptic, Emerald Cloud Lab, Aquarium (a product of Eric Klaven’s group at the University of Washington, Seattle) and Synthace’s (London) Antha, no practical framework has been proposed to transfer protocols among different laboratory automation systems or to freely integrate different tools and automation systems to automate complex experimental operations. We propose that a scalable laboratory automation should be split into two layers: first, a standard semantic layer, or process ontology layer, in which experimental workflows are described by connecting various job processes (‘process description’); and second, a translation layer, in which each job process described in the standard semantics is compiled into robotic operations for a given operation environment (‘process-to-operation mapping’). The first layer could be actualized from an open science community by harnessing previous efforts for process ontology for laboratory experiments. The second layer would require the manufacturing side to prepare its process-to-operation mapping for different job processes defined using the standard syntax.

At present, laboratory automation processes generally suffer from the ‘hard coding’ of systems and manual adjustments to sensitive environmental differences, which are usually not well documented. However, for LabDroids that have sensing systems and form an RCBL, robotic behaviors in a specified environment could be fed back to the central computing system and automatically optimized with the support of artificial intelligence. This would allow the ideal automated process-to-operation mapping or ‘real world programming of experiments’ (much like compiling a program script in a particular computational hardware environment).

Phase I of the Robotic Biology Consortium is to build a few small-scale RCBLs by early 2020. Each RCBL will be composed of multiple LabDroids, laboratory automation systems, and human-usable experimental tools and equipment. We plan to demonstrate fully remote operation of complex experiments in genomics, proteomics, and high-content cell screening, and to showcase the reproducibility of the experiments exchanged between different RCBLs.
Although substantial challenges remain, such as the establishment of widely agreed upon standard semantics, massively parallel operation of robotic crowds and instruments, and the implementation of artificial intelligence, robotic crowd biology using the LabDroid-centered system has the potential to scale current life science and laboratory automation in a robust and reproducible way.

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Note: Any Supplementary Information and Source Data files are available in the online version of the paper.

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AUTHOR CONTRIBUTIONS
N.Y. formulated the grand design of robotic crowd biology, prepared the figures, and wrote the manuscript. T.N. led the development of Maholo with the Robotic Biology Consortium and wrote the manuscript.

COMPETING FINANCIAL INTERESTS
The authors declare competing financial interests: details are available in the online version of the paper.

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With all due respect to Maholo, lab automation isn’t anthropomorphic

To the Editor:
Biosciences journals often require rigorous statistical evidence for the data presented because a substantial proportion of the biosciences literature is not reproducible1. In this issue, Yachie et al.2 propose that LabDroids could form part of a robotic infrastructure that might contribute to improved reproducibility. However, we argue that reproducible research can be enabled by existing (or new) automation technologies present in both individual research groups and centralized DNA foundries that can be accessed using cloud-based applications.

Most bioscience experiments move small amounts of liquid from one place to another in order to set up experiments and measure effects. Scientists use tools, such as adjustable micropipettes, first launched by Eppendorf (Hamburg, Germany) in 1961, to move liquids in the microliter range. Based on similar principles, automated technologies were developed to enable high-throughput processing. These technologies were mainly developed to screen large chemical libraries for drug leads in the pharmaceutical industry. The Beckman Coulter (Brea, CA, USA; then SmithKline Coulter) Biomek 1,000-tip-based liquid handler system was introduced in 1986,