The LEGO® brick road to Open Science and Biotechnology

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Abstract

LEGO® is a brand of toys that, for decades, have entertained generations of children. Beyond amusement, LEGO® bricks also constitute a building ecosystem of their own that creators from the general public, as well as scientists and engineers, can use to design and assemble devices for all purposes, including scientific research and biotechnology.

Here, we describe several of these constructions to highlight LEGO® building properties, their advantages, caveats, and impact in biotechnology. We also discuss how this emerging trend in LEGO® building pairs with a growing interest in open-access and frugal science, which aims to provide access to technology to all scientists regardless of financial wealth and technological prowess.

LEGO® bricks: from the toy box to the lab bench

"I loved to play with LEGO®," recalled the 2001 Physics Nobel Laureate Wolfgang Ketterle during his lecture at the 69th Lindau Nobel Laureate Meeting. "In my days, LEGO® was just a box of bricks and you had to use your imagination to build very very complicated things out of very few building blocks" [1]. Many scientists and engineers carry the same nostalgia from their youth and the same passion for LEGO® constructions today. In many cases, LEGO® bricks have fueled their curiosity and creativity early on and motivated their appeal to science and research later. In fact, there are many similarities between a child playing with LEGO® bricks and a scientist planning an experiment: both with a limited number of resources and their imagination need to find an optimal way to build or experiment. Therefore, it is not surprising that many scientists who played with LEGO® bricks as kids are now interested to use them to create tools and biotechnology devices, effectively turning LEGO® bricks into a powerful building ecosystem.

As it turns out, LEGO®-based systems abolish the boundaries between expensive technological tools and financially constrained investigators, between experimental requirements and their practical realization. Here, we will attempt to review the variety of systems that have been developed with LEGO® parts both in the general public and in Science. We will identify the benefits and limitations of building with LEGO® parts and show how these can be used to design inexpensive, robust and professional-grade tools or experimental strategies. Finally, we will discuss how this new trend questions some of the recent science evolutions and promotes Open Science.

Building, creating and inventing with LEGO® bricks

Traditionally, LEGO® bricks have been widely publicized as toys for kids (see Box 1). However, over time, a group of dedicated and independent builders (AFOL for Adults Fans Of LEGO®, see Glossary) have started to consider them unique building units that can be used to assemble diverse objects, very much in the spirit of the original Automatic Binding Brick (ABB), and not necessarily only toys. This concept has now been explored to establish design and assembly principles summarized in a seminal book [2]. Although initially not officially endorsed or commercially promoted by The LEGO Group, this emerging prospect has somehow become tacitly acknowledged. In recent years, The LEGO Group has endorsed several professional AFOLs as LEGO® Certified Professionals (21 individuals as of 2021, https://www.lego.com/fr-fr/aboutus/lego-certified-professionals/). The LEGO Group has also progressively released several sets and collections that support this DIY approach, such as the LEGO® Architecture Studio set (#21050) and the LEGO® Ideas series. In this section, focused on the general public, we will highlight a few examples of these constructions and their creators to establish that LEGO® bricks are unique building units that can help achieve craftsman's creativity at all performance levels .

Some creations are only designed for entertainment (see Box 2) and to showcase the mechanical prowess achieved with simple LEGO® bricks. Automatons and mechanical constructions have been developed by independent creators such as JK Brickworks with its LEGO® Ideas set "the Maze" (#21305) or its "Hoberman Sphere" (Fig. 1A). Other creators rather specialize in LEGO® Technic building, which provides electric- or pneumatic-powered capabilities and more intricate building options. For instance, these include Wolf Zipp and his re-creation of the SLJ900 bridge girder erection machine, a masterpiece of LEGO® Technic engineering (https://www.youtube.com/channel/UC2vjCc0CiaxF8bHHaOPQUXw). Besides these relatively simple entertaining creations, others stand out by their unexpected level of performance and refinement, suggesting that professional-grade quality devices could be achieved from LEGO® parts. This is the case of Cubestormer 3, an automated Rubik's Cube solver, created by David Gilday and Mike Dobson, that temporarily held the world record for fastest solving a Rubik's Cube by a robotic system at 3.253s. Cubestormer 3 was almost solely based on LEGO® parts, including a LEGO® Mindstorms system and a Samsung Galaxy S4 for video input. Also, as a testimony to the precision and mechanical reliability of LEGO® parts, the air-powered LEGO® car designed by Raul Oaida and Steve Sammartino is the first life-sized functioning car assembled from LEGO® parts, except tires, which is powered up to 30 km/h by an engine built from LEGO® pneumatic motors. Over the years, similar cars were assembled by The LEGO Group, including a replica of the most potent road car of its time, the iconic Bugatti Chiron.

Finally, it turns out that some systems combine both professional-grade built and real-life use, such as the Braigo Braille printer designed and assembled by Shubham Banerjee with 350 USD worth of LEGO® parts, which compares to the price of conventional Braille printers in the 2000 USD range. This highlights that besides their quality, LEGO® creations may be built at a fraction of the cost of commercially available systems.

All these creations, which fall under the general public scope, are a testimony to the level of performance and reliability that can be achieved by combining LEGO® parts and one's creativity. This fueled researchers and creators from different fields to consider LEGO® parts as building units to design and assemble simple to complex scientific tools and systems for scientific research and biotechnology.

David Aguilar, aka "Hand Solo", is an inspiring example of a creator bridging these two worlds. David, who was born without a right forearm, has designed and assembled his series of fully functional LEGO®-based prosthetic arms, which he named MK after the armor suits of Iron Man from the Marvel® Universe (Fig. 1B). His creativity resounded in the media and David, now a bioengineering student, recently engineered a simple and light LEGO® prosthetic arm for a young Kazakh boy.

Biotechnology research and education with LEGO®

Owing to their extreme versatility, reliability and performance, LEGO® parts have emerged as particularly relevant building units for designing systems and tools for research, education, and science. Indeed, over the past decade, scientists have designed, characterized, and reported many systems from all fields (Table 2). These systems range from very simple, almost simplistic [3,4] to complex and intricate [5]. In all cases, they turn out to be very effective at what they were designed for and bear a low cost to efficiency ratio. Here, we briefly review some of these systems to highlight the unifying principles guiding their design and assembly, the advantages, and the caveats. For clarity's sake, we will discuss them field by field below and in Box 3 for scientific fields beyond biological research and Biotechnology.

Education/STEM

Besides building curiosity and critical thinking, a paramount role of education is to introduce students to fundamental concepts and principles, to essential knowledge and experimental techniques, all of which can be achieved or contributed to, using LEGO® parts.

Concepts and principles are often abstract and figuring out a mental projection of these can be challenging for students. Sometimes, physical representation and manipulation can help. This educational strategy can be implemented with LEGO® bricks to showcase simple scientific tools such as a colorimeter [6] or a liquid handling robot [7]. It can also be used to explain concepts such as the evolution and variability of the viral genome of influenza associated with antigenic drift using LEGO® bricks that represent swappable blocks of genetic material [8]. Similarly, historical concepts and techniques can be presented more figuratively. For instance, DNA sequencing and associated bioinformatics resources can be introduced using the brickopore system, which replaces nucleotides with LEGO® bricks (www.brickopore.co.uk). Finally, the scientific principles behind the operation of complex scientific systems can be explained using a device based on LEGO® such as the 'conceptual AFM', for example, a fully functional LEGO® AFM replica [9]. For advanced students, professional-grade LEGO® systems are also an educational opportunity to learn design and assembly principles in addition to scientific principles. Such educational projects include LEGO®-based microscopes such as MicroscoPy, for instance, a LEGO®- and 3D-printed parts-based open source transmitted light microscope that can introduce students to both design, LEGO® building, electronics assembly, and programming (Table 2). LEGOLish is another fully functional microscope that brings the concept to a yet unsurpassed level as a LEGO®-based light-sheet microscope equipped with a smartphone as a camera that can scan real biological samples to demonstrate the properties of that type of microscopy (www.legolish.org).

Altogether, LEGO® parts provide instructors with various tools to illustrate concepts, principles and provide a framework for their application.

Instrumentation

In an appeal to the more technical aspects of LEGO® parts, creative researchers have engineered several pieces of general lab equipment of all levels of complexity to address specific needs or provide alternatives for cheaper equipment. Some of those are relatively simple, yet effective, such as the peristaltic pump engineered by Martin Haase (https://www.youtube.com/watch?v=N0Cj0D3M-9E) or the spectrophotometer from Pereira and Hosker [10]. Others are frankly complex, such as the automated LEGO® Mindstorms fraction collector [11]. In all cases, they provide highly reliable equipment, inexpensive to purchase and maintain.

Besides these very generic pieces of equipment, more specialized instrumentation is directly designed or inspired by LEGO® building. For example, microfluidics have been inspired by the assembly properties and versatility of LEGO® bricks and developed some LEGO®-like building systems on a microfluidics scale. µOrgano is a LEGO®-like plug-and-play system to create modular multi-organ chips [12]. This system, much like LEGO® systems, is based on the assembly of building modules, master-organ-chips, and plug-and-play connectors. Similarly, Morgan et al developed a modular LEGO®-based microfluidics system with an FDM 3D printer illustrating the power of the combination of LEGO® building and 3D printing. Ma et al brought the concept of modular assembly to another level and scale by generating reversible supramolecular LEGO®-like bonds to assemble hydrogels [13]. This system has not been showcased in any experimental application yet but explores the possibility to use a modular brick design at the molecular scale to assemble microfluidics compatible parts.

Biological research

It is in biological research that LEGO® parts display the prime of their versatility, contributing to systems and tools in fields ranging from entomology to plant sciences to cell biology.

Traditionally, in entomology and natural history collections, insect specimens were dry pinned for conservation and documentation. This resulted in extensive, delicate, and space-consuming collections such as the 27 million pinned insect specimens at the Natural History Museum of London. Now, in the digital era, specimen digitization constitutes a means to archive them and prevent their manipulation. This requires specimen holding tools not always readily available to researchers. To address this matter, Dupont et al created the Insect specimen manipulator (Imp) from LEGO® Technic parts [14], a versatile and customizable holding system to perform observation or digital acquisition.

In a completely different setting, in plant science, studying plant growth requires live monitoring of the organism in a controlled environment. To this end, Lind et al imagined using transparent LEGO® walls to assemble cubes in which gel-like growth medium can be poured and plant growth monitored over time [15]. Here, the key features of LEGO® parts were their flexibility and versatility in terms of assembly and combination, as well as the possibility to sterilize and reuse them. These are examples of straightforward tools designed to fulfil a specific need while incorporating the ingredients to an excellent DIY recipe: design flexibility and versatility, affordability and wide availability of LEGO® parts.

LEGO® parts proved useful to design and assemble stretching systems. The Féral lab engineered a uniaxial cyclic stretcher for cells in tissue culture [3,4] which applies uniaxial cyclic stretch to a monolayer of cells cultivated on a PDMS plate. Besides the PDMS plate, the system is assembled only from LEGO® parts. While this system cannot provide all the range of stimulations of commercial systems, within its range, it does provide consistent and reliable stimulation at a fraction of the cost of these systems. This turns out to be a general property of such DIY systems: they may not necessarily provide the same refinements as high-end systems, which, incidentally, the user does not always need but offer reliability and consistency at a fraction of the cost. A radically different, the LEGO® stretcher designed by Teemu Ihalainen, named Brick Strex, provides similar features with the noticeable improvement to perform simultaneous cell stretching and live-cell imaging [18].

By following the same philosophy, the Henriques lab developed a robotized fluidic system that could control the liquid environment of a biological sample while observed under a microscope [5]. This fluidic system was named NanoJ-Fluidics but nicknamed Pumpy McPumpface by the authors. Pumpy corresponds to a set of LEGO®-based syringe pump units that can assemble into an array. Each unit is responsible for injecting a chemical agent into an imaging chamber. An Arduino board stacked with a motor control shield drives all the DC motors and interfaces with custom automation software. Pumpy is driven by micromanager [19] and NanoJ [20], which presents an interface that allows users to automate complex reagent exchange protocols synchronized with image acquisition in a microscope. Pumpy can carry out event-driven experiments, where a visual cue on the sample will trigger a fluidic protocol. This allows the microscope to capture both live-cell temporal data up to fixation, and fixed-cell data for the same field-of-view, generally with a large number of molecular types labelled. The authors also carried out similar experiments with super-resolution imaging within the same field of view showing the ability to switch from live cell SRRF [21] imaging of a single fluorophore to fixed cell nanoscale resolution imaging of 5 different fluorophores through STORM [22] and DNA-PAINT [23].

One step further in technological complexity, LEMOLish (www.legolish.org/lemolish) is the scientific professional -grade version of the educational lightsheet microscope LEGOLish. Built into a fully automated lightsheet system, the LEGO® assembly (1400 bricks!) enables to image optically cleared samples with unexpected sample-size-to-resolution performance, to achieve mesoscopic imaging of organs and organisms from millimeters to centimeters in size with cellular resolution. Following a strict DIY and cost-efficient philosophy, the authors hacked the LEGO® EV3 module, or “intelligent brick”, to synchronize lasers, sample movement and camera trigger, in a final layout that automatically acquires 3D stacks at the action of one button. The authors report 3D images of mouse -embryos, -tumors, -brains, -vasculature or full chicken embryos exceeding 4cm in size, and advocate for LEMOLISH to become a benchtop entry point into lightsheet imaging, and an affordable (2-orders of magnitude below commercial systems) companion for laboratories aiming to start with the complex task of tissue-clearing protocols. While lightsheet microscopy has revolutionized several life science disciplines such as developmental biology or neuroscience, the access to research-grade equipment is still an economical leap for a majority of laboratories, thus demonstrating again the potential of LEGO®-based inventions to democratize high-end technology with acceptable scientific performance.

LEGO® design in Science:

Aside from the joy and fun of building scientific tools with LEGO® bricks, one may wonder the rationale, benefits, and relevance of using kids' toys to assemble scientific equipment. The reasons to build with LEGO® bricks range from the nature of the LEGO® brick and the LEGO® brick system themselves to the ethical beliefs and principles of the creators.

At the core of every LEGO® creation are the LEGO® bricks and the LEGO® building system, which harbor several specific properties and associated benefits. One exciting feature of LEGO® parts for biotechnology is their compatibility with the assembly of mechanical systems for biology. As mentioned earlier, LEGO® parts are made from ABS, a thermoplastic used in injection molding. ABS and its derivatives are routinely used in household appliances, consumer goods and anecdotally constituted the bodywork of the iconic Citroen Méhari. ABS is also the mainstream material for FFF (also known as FDM®) 3D printing and is generally considered a biocompatible material. In general, ABS properties allow LEGO® parts to withstand high mechanical loads and resist high impacts, relative to the scale of the creations. This resistance to breakage and wear is an essential factor in mechanical systems, particularly in gearboxes exposed to high mechanical loads and repetitive motion. In contrast, the high production standards of LEGO® parts limit gearwheel wobbling and backlash. In addition, ABS can be easily decontaminated and sanitized, which is critical in cell biology.

Another substantial benefit for creators is the wide range of parts constituting the LEGO® collection and their combinatorial possibilities. As of 2011, there were at least 2350 different LEGO® parts officially listed which combined to user-designed 3d printed parts gives a glimpse of the almost infinite combinations offered from such parts.

Beyond the specific properties of each LEGO® part, the LEGO® brick system is a unique building framework with its principles and metrics, including the clutch power and the LEGO® stud metric system. This provides a building space with its geometry and metrics that have been explored and conceptualized [2]. As we show in Figure 3, the design of LEGO® scientific instruments often relies on a very simple core mechanical function (pushing, pulling, translating, rotating, …) achieved with very few gears, axles and one or more stepper motors, while the bulk of the other bricks merely serves to position or stabilize the elements to be actuated upon (here, a substrate, a syringe or a cuvette). Noteworthy, taken apart known backlash issues that can be compensated, such basic assemblies can reach surprising micron or microliter precisions (Fig. 2). Moreover, the LEGO® Mindstorms and Power Function collections add automation and computing power to the LEGO® ecosystem, motorization and remote control. Altogether, the technical features of LEGO® parts and the ecosystem they provide constitute an ideal environment to design and assemble mechanical systems.

Concluding remarks and future perspectives

The use of LEGO® parts to design scientific systems provides practical tools and strategies that can be used to address curiosity-driven scientific questions. These systems do not necessarily offer all the refinements of commercial systems, but they provide scientifically robust, open-access, and customizable tools. The rationale for designing and assembling LEGO® systems for science was generally based on specific requirements from their creators that were not fulfilled by any commercial systems.

There are an estimated 2350 different official LEGO® parts available today, which provide almost endless design possibilities and questions what systems could not be, at least in part, assembled from LEGO® parts. For instance, systems as complex as the LEMOlish light sheet microscope have been assembled. With the emergence of LEGO® part design software and 3D printing, we foresee that any custom LEGO® compatible brick could be designed and produced [25], further expanding the design possibilities.

Besides The LEGO Group, which commercializes individual bricks, it is hard to imagine how any company could financially and logistically support the large-scale commercial implementation of these systems. At the core of these systems, the LEGO® bricks design is patented, and they are only produced by The LEGO Group. Furthermore, the cost of these systems, which constitute one of their main interests for individual researchers, makes them much less profitable for companies, especially if they cannot produce LEGO® bricks. The LEGO Group has historically been very open to creators and their alternative use of LEGO® bricks, without actively supporting them through any institutionalized program though. While we do not necessarily call upon The LEGO Group to actively support this trend, we cannot help wondering how the association of such intellectual creativity with the industrial and designing prowess of The LEGO Group would propel this field forward and benefit science as a whole, much in the spirit of the LEGO® Ideas collection.

Beyond their diversity, these LEGO® systems are characterized by mutual features, including customization, affordability, and open access. Interestingly, these characteristics constitute the core values of an emerging trend that aims to promote DIY science and open access. These core values underlie an ideology that implicitly questions recent developments and evolution in science (see Outstanding Questions). This also very much relates to the movement of frugality in science as presented by George Whitesides [26] and Martin Kaltenbrunner [27]. They argue, and we second them, that there is a rush towards expensive and complex technology in research, and we could add in society, which is a luxury of western countries that low-income nations or financially constrained institutions cannot afford. In the western world, this escalating trend is likely fueled, and possibly plagued, by the unfounded belief that expensive equipment is a prerequisite for good science, that compelling amounts of data and uttermost precision are safeguards for quality. As recently addressed by Nobel prize recipient Sir Paul Nurse [28], many scientists now challenge this belief and promote a curiosity-driven and concept-based science that would use proportionate and appropriate technological tools to address scientific problems. Proportionate and appropriate use of technology can also be extended to technology-based applications in society. While the benefits of technological advance for scientific research and for the society are not debated, once again, the human behaviors, beliefs and practices surrounding these progresses may hamper their benefits for mankind and create drawbacks.

For instance, the temptation and competitive pressure to use the most cutting-edge technology to publish in the most prestigious journals, de facto exclude or impede financially and technologically constrained researchers from voicing their conceptual and experimental contributions to science to similar levels as wealthy researchers. Similarly, some cutting-edge biotechnological applications remain exclusive to the western world while they would greatly benefit developing countries and their population such as the SARS-CoV-2 vaccines in the wake of the current COVID-19 pandemic. In response, some researchers have taken it upon themselves to develop practical and affordable alternatives to some technological tools [29,30]. In times of recent economic meltdown and financial constraints, it may also be particularly relevant to address and implement a fair and reasoned use of limited financial resources provided either by the taxpayer or by donations in the case of charities. Indeed, this reasoning may apply to all resources, and as mentioned by Whitesides and Kaltenbrunner, less is more; resources, of all kinds, are generally limited, and proportionate use of these resources should allow us to do more not at the cost of quality, now, and potentially tomorrow as these resources may wane.

These really are two sides of the same coin with technological progress benefitting scientific research and society on one side while human bias and behavior generate limitations and malpractice, on the other. We also feel that frugal science and LEGO® building, for instance, may constitute a balanced position trying to reconcile technological needs with practical benefits and fair use of resources. These two views of science are not exclusive and may be complementary, constituting the edge of this two-sided coin. For instance, the worldwide COVID-19 crisis pushed the development of cutting-edge technology such as the RNA vaccines in parallel to the individual or collective initiatives to develop and provide PPE, ventilators and diagnostic tests in times of restrictions, ultimately showing that these two visions of Science may coexist.

Much as barefoot stepping on a LEGO® brick has become a universal meme, LEGO® building in open science and Biotechnology has all the ingredients and spice to become a universal ecosystem to design and assemble innovative, robust and inexpensive systems available for the whole scientific community.

Text Boxes

Box 1 – Historical perspective

LEGO® is a brand of toys founded by Ole Kirk Kristiansen back in 1932, which belongs to The LEGO Group, a Danish company based in Billund, DK. Ole Kirk Kristiansen (1891-1958) was a Danish master carpenter who originally bought a carpentry factory in Billund, DK, in 1916. Following the 1929 stock market crash and the ensuing Great Recession, Kristiansen was almost forced out of business and had to adjust his production to include easily saleable products such as kid toys. By 1934, Kristiansen had decided to focus his production on toys and decided to name the company LEGO®, based on the contraction of the two Danish words Leg Godt which mean « play well ». From the beginning, one of the obsessions of Kristiansen was the utmost quality of his productions, a legacy that stands to this day as attested by The LEGO Group motto, «only the best is good enough » (det bedste er ikke for godt). In June 1946, upon the demonstration of an injection molding machine, he converted his production to plastic, first with cellulose acetate, then using ABS. Around the same time, he witnessed a demonstration of the brick item that Hilary Fisher Page had invented at his company Kiddicraft. This sparked the creation of the Automatic Binding Brick (ABB), the ancestor of the LEGO® brick as we know it today. A pivotal moment came in January 1958 when The LEGO Group submitted a patent application for a « toy building element » which described the stud and tube design which replaced the structurally unstable hollow design of the ABB and introduced the concept of clutch power as well as the new interlocking principle of LEGO® bricks. This design provides stability and almost endless possibilities for combining bricks: six 2x4 bricks can combine in up to 915103765 different ways. Ever since, The LEGO Group has expanded at all levels, employing thousands of people across several countries and shipping billions of bricks around the world. Following Kristiansen’s footstep, The LEGO Group has had a long-lasting interest in science, especially engineering, programming, and space. Indeed, over time, The LEGO Group has introduced several different LEGO® collections appealing to science and engineering including the LEGO® Technic collection in 1977 and the LEGO® Mindstorms collection developed through collaboration and partnership with MIT in 1998. They also contributed to the promotion of science and STEM in education with the LEGO® education program.

Box 2 - LEGO® bricks Artwork

Despite being once denied the status of Art [31], LEGO® bricks are indeed elements that can be used to create pieces of Art. Arguably, the artwork nature of individual bricks may be discussed, since these are building units much like other materials such as paint, clay, bronze, or wood. However, this view could be challenged, as their design itself is a reflection of the human mind and creativity. However, inarguably they can be assembled into pieces that express one’s creative mind and emotions. In fact, several creators or artists have used LEGO® bricks to create artefacts of all nature (Table Box 2). For instance, John Muntean has combined LEGO® brick into abstract sculptures called Magic Angle Sculptures© which, upon lighting and rotation, can project a variety of different artistic shadows (https://www.jvmuntean.com) (Figure Box2). The concept behind these sculptures is that our 'interpretation of Nature depends on our point of view' and that 'perspective matters'. Another creator, Nathan Sawaya, assembles LEGO® bricks into monumental sculptures and reproduces classical paintings which have been displayed in his world-touring exhibition *The Art of the Brick* (https://www.brickartist.com). Contemporary urban artist Jan Vormann found another artistic use of LEGO® bricks which ironically recalls to their fundamental nature, filling wall holes of historic constructions with multicolor assemblies (https://www.janvormann.com). LEGO® mosaics are also widespread: for instance, Eric Harshbarger creates reproductions of classical paintings as well as original pieces while the late Arthur Gugick contributed with the assembly of stunning lenticular mosaics. Altogether, these creators have also indirectly inspired, by their design, the creation of LEGO®-like artworks such as the sculptures of Antony Gormley, for instance. Jeff Sanders’ brickbending artworks defy geometric rules by assembling straight LEGO® parts into bended creations which testifies of the mechanical resistance of individual

LEGO® bricks. Beside those renowned artists, anonymous individuals also engage in LEGO® art creation under various forms including LEGO® mosaics or stop-motion movies for instance. The LEGO Group itself now supports and promotes LEGO® artwork as it just announced the release of the LEGO® Art collection and the LEGO® Brick Sketches™, hybrid constructions between paintings and puzzles.

Box 3 – LEGO® bricks in other scientific fields

Behavioral Sciences

LEGO® bricks and behavioral sciences may seem like an odd association. In this field, it is not necessarily the technical and mechanical aspects of LEGO® parts that appealed to researchers but also the behavioral consequences of using LEGO® bricks.

For instance, LEGO® has been used in cognitive psychology in the context of choice reaching task (CRT) which may provide insights into underlying cognitive processes (Table box 3). This behavior has been extensively investigated, and a LEGO® robotic system that implements the model has been assembled to investigate the implications and predictions of the model [32,33].

Slightly apart from behavioral sciences, LEGO® bricks have also been used to address autistic spectrum disorders and associated social interactions. Dr Daniel LeGoff, a pediatric neuropsychologist, invented the LEGO® Therapy aimed at improving the social skills of children with autism spectrum disorder [32,33].

Physics

Much like in other fields, the physicists' primary interest in LEGO® parts has stemmed from the possibility to create custom tools and systems for scientific research. For instance, LEGO® bricks have been instrumental in the creation of two alike tensile testers [16,17]. Conceptually, it is interesting to note that these two systems have independently evolved into a very similar design. Celli and Gonella have reported a straightforward yet versatile experimental platform for investigating phononic phenomena in metamaterial architecture [37].

Prestigious institutions also fancy LEGO® constructions: besides building a miniature LEGO® LHC for the LEGO® Ideas series, researchers at CERN have used LEGO® parts to prototype and include a LEGO® device to the NA61/SHINE experiment (https://home.cern/news/news/experiments/using-lego-study-building-blocks-universe). Experimenting with LEGO® bricks has also yielded unexpected discoveries about their properties. Chawner et al. report that LEGO® bricks are in fact particularly potent thermal insulators [38]. This is an exciting feature for quantum computing which relies on isolated low temperatures, providing cheaper alternatives to expensive materials currently in use in the field.

Chemistry

In contrast to physicists, chemists have scarcely relied on LEGO® bricks to generate experimental systems. This is not surprising since their activity does not depend so heavily on mechanical systems. However, in some cases, LEGO® bricks were helpful in the design of systems with unusual specifications. For instance, LEGO® bricks and plates were used to assemble a dark box able to handle 96-well plates in a field-deployable spectrofluorometric system aimed at detecting nerve gas [39]. In this case, the use of LEGO® parts provides specific properties to the system that were the central requirements of the creators.

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Figure Legends

Figure 1 – LEGO® creations in the general public and arts. (A) LEGO® prosthetic arm creator David Aguilar (with permission from David Aguilar, Jose Sanchez – Estudi la Seu d'Urgell). (B) The "Hoberman Sphere" in motion or motionless from creators JK Brickworks (with permission from Jason Alleman).

Figure 2 – The uniaxial cell stretcher (top), the Pumpy microfluidics system (center) and LEMOLISH (bottom). In each box, the left part shows the few core mechanical elements that drive the main function (blue text) of the instrument shown to the right, with indicators of performance. Common to all, one stepper motor converts (“Drive” with red arrows) a large rotation angle into final high-precision movements (blue arrows) by means of suitable gear reduction ratios.

Table 1 – List of LEGO® creations from the general public

Table 2 – List of LEGO® creations in Biotechnology and biological research.

Figure Box 2 – LEGO® artwork. (A) Creator Jeff Sanders and Brickbending creation Spiral Annulus. (B) Extreme Brickbending creation the Rhombicuboctahedron (with permission from Jeff Sanders). (C) and (D) LEGO® artwork the Knight Mermaid Pirate-ship Magic Angle Sculpture and creator John V. Muntean (with permission from John V. Muntean).

Table Box 2 – List of LEGO® artwork creators

Table Box 3 – List of LEGO® creations in Science

Glossary

ABB: Automatic Binding Brick, the ancestor of the regular LEGO® brick as we know it today without the stud and tube design and therefore with much less clutch power and stability.

ABS: Acrylonitrile Butadiene Styrene, a thermoplastic polymer which transition temperature is around 104°C, widely used for injection molding in various industries

AFM: Atomic Force Microscopy is a type of scanning probe microscopy that uses a cantilever and a probe to scan the surface of a sample in order to generate a topographic map or assess its mechanical properties by indentation.

AFOL: Adults Fan Of LEGO®, adults, by opposition to kids who are the original targeted audience of LEGO® toys, that engage in LEGO® building of all sorts and create a community with gatherings, etc. They have now also become a major market since they can afford more expensive models.

Clutch power: the interlocking assembly of LEGO® bricks which is based on the stud and tube design creates a high "clutch power" that hold individual bricks together in multimeric assemblies.

DIY: Do It Yourself, this is the process of generating parts or performing repairs/modifications on a system without intervention of commercial/industrial counterparts.

FFF: Fused filament fabrication, widely referred to as FDM® (Fused Deposition Modeling) which is trademarked by Stratasys, is a 3D printing process that uses a melted thermoplastic filament to deposit material.

Frugal science: it is a trend that promotes cost-conscious research-based and application-driven science in order to include and engage all qualified individuals in research and benefit all publics.

LCP: LEGO® Certified Professional are professional creators and LEGO®-related business owners officially endorsed and supported by The LEGO Group. There are a handful number of LCP positions that are country specific for professionals fulfilling specific criteria.

PDMS: PolyDiMethylSiloxane is a silicone-based organic polymer which has many uses in science and in the industry. Notably, it is used as an optically clear elastomer for microfluidics devices.

Highlights

LEGO® bricks constitute a building ecosystem that can be used by the general public, science researchers and engineers to design and assemble systems of all kinds.

The variety of LEGO® creations from the general public, spanning from artwork to automated systems, demonstrate the versatility and quality of LEGO® systems.

In parallel, an increasing number of custom LEGO® systems for science are designed to fulfil the specific requirements of experimental scientists from all fields.

The development of LEGO® building in science and biotechnology constitutes an emerging trend that aims to provide widely available professional-grade tools and systems to all researchers regardless of financial and technological constraints.

Outstanding Questions Box

What are the technological or creative limits of LEGO® building? What can be designed and built using LEGO® parts?

How will the LEGO® building accommodate the emergence of 3D printing? Will 3D printing provide a platform to design and produce new innovative parts for LEGO® building, or will it provide an alternative to LEGO® building that may surpass it at some point? Will 3D printing help in bypassing the aforementioned LEGO® building limits?

How will this open-access trend in developing LEGO® systems merge with other open-access trends in software development, microscopy?

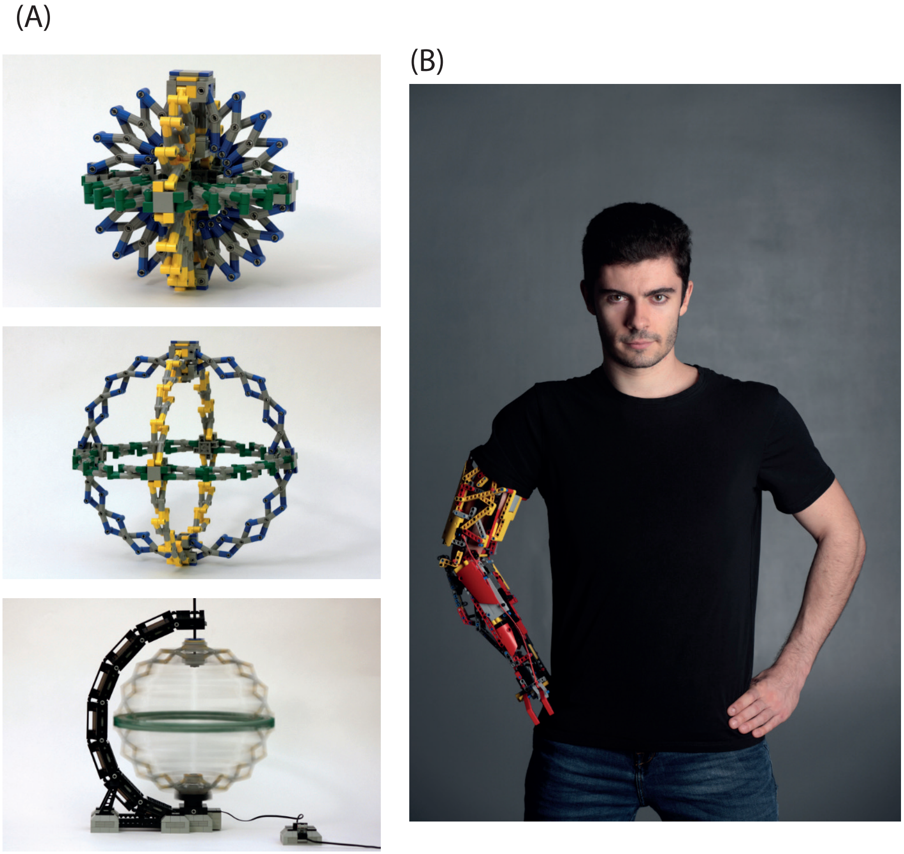
Will there be any commercial endeavor to scale up this trend to industrial levels? Will any company take it upon itself to promote and distribute these tools? In particular, will The LEGO Group support this trend?

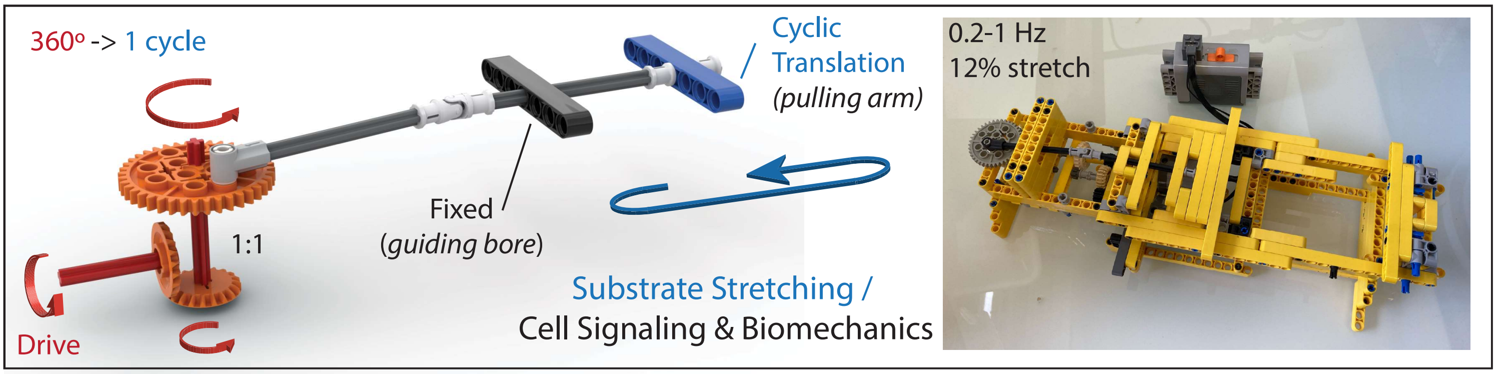
Related to the previous point, will creators keep providing their systems as open-access, or will they start patenting them? How would this patenting process cope with The LEGO Group, which has historically been very protective of its patents?

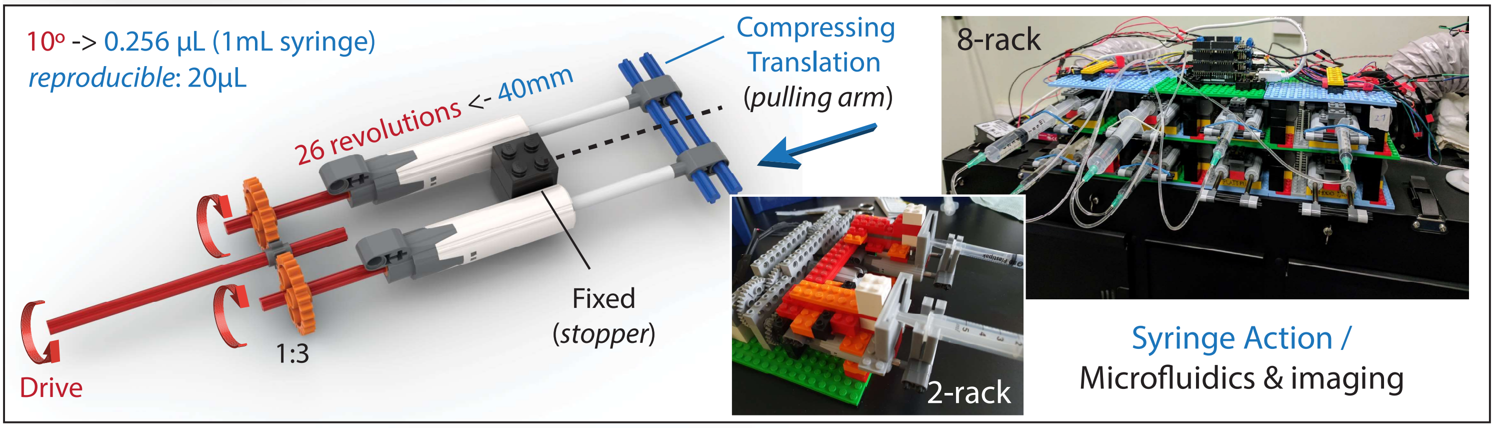
Along this line, what will the position of The LEGO Group regarding this alternative use of LEGO® parts? Will they actively support it by creating a LEGO® science collection, supporting a select number of Certified Science Professional Builders, for instance, or setting up a support program (financially supported grant program or free access to LEGO® parts)? Alternatively, will they tacitly acknowledge it without providing incentives?

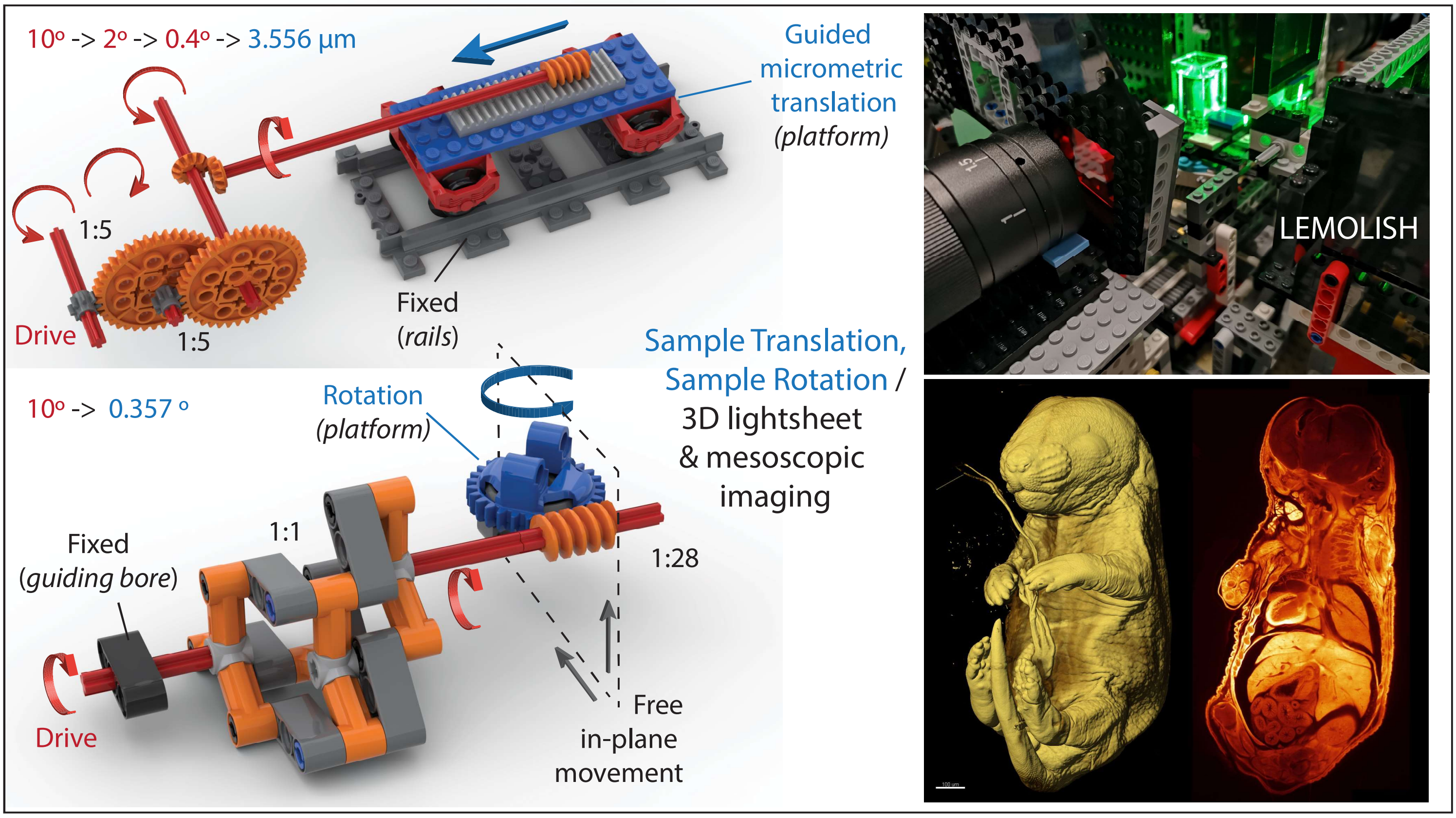
The rationale for LEGO® building calls out for bigger and more fundamental questions in science. There obviously is an escalating trend towards highly refined technologies and devices which are associated with substantially increasing financial costs. To what extent this trend is financially and humanly sustainable? What is the balance between the benefits from such technologies and their human and financial cost? Does science ultimately benefit from the highest possible technological advance, and when does it become detrimental to its advancement?

Figure 1 - Boulter et al




360º -> 1 cycle
Cyclic Translation (pulling arm)
Fixed (guiding bore)
1:1
Drive
Substrate Stretching /
Cell Signaling & Biomechanics
0.2-1 Hz
12% stretch


10º -> 0.256 µL (1mL syringe)
reproducible: 20µL
26 revolutions <- 40mm
Compressing Translation (pulling arm)
Fixed (stopper)
1:3
Drive
8-rack
2-rack
Syringe Action /
Microfluidics & imaging


10º -> 2º -> 0.4º -> 3.556 µm
Guided micrometric translation (platform)
1:5
1:5
Drive
Fixed (rails)
LEMOLISH
Sample Translation,
Sample Rotation /
3D lightsheet
& mesoscopic
imaging
10º -> 0.357 º
Rotation (platform)
Fixed (guiding bore)
1:1
1:28
Drive
Free in-plane movement

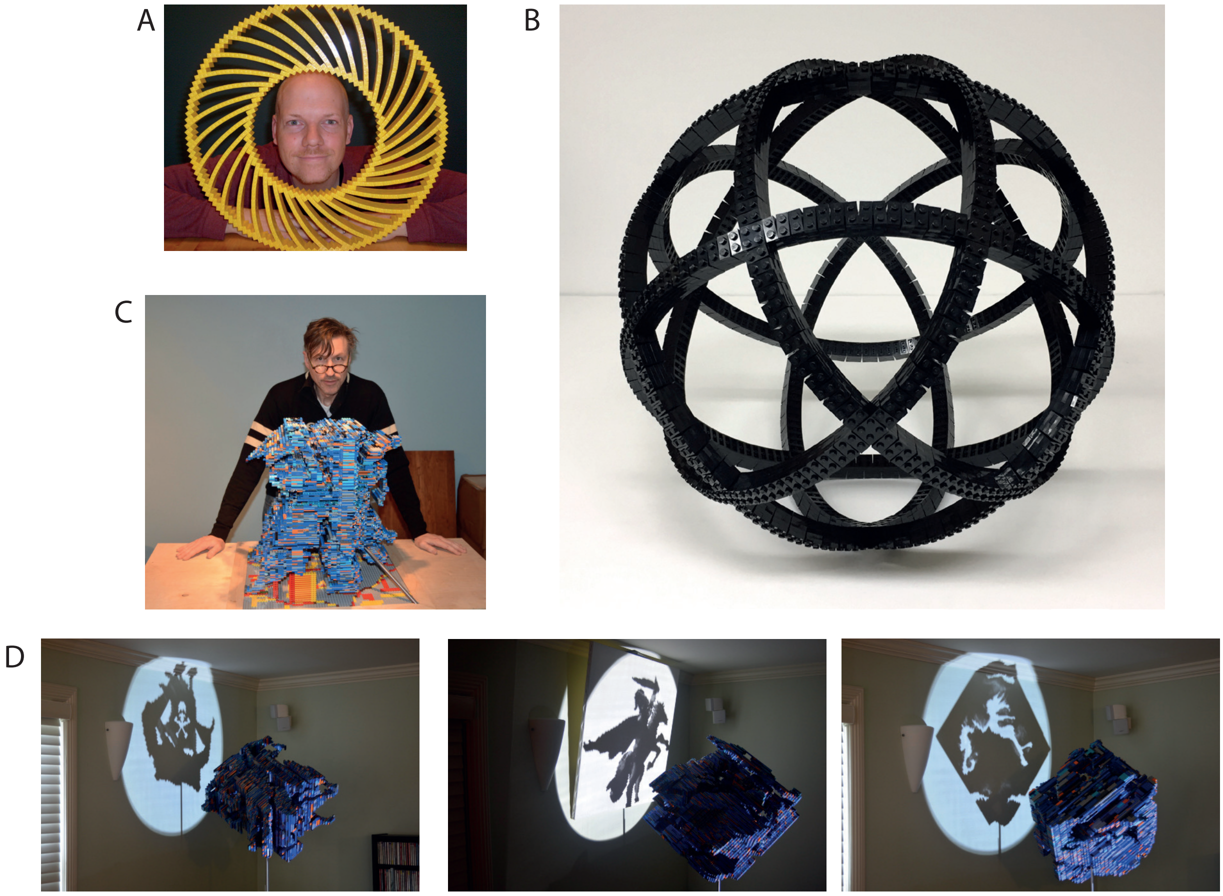
Creation	Inventor/artist	Reference
Miscellaneous Creations		
Various creations ranging from tensegrity sculpture to Hoberman sphere	JKBrickworks (Jason and Kristal Allemann)	https://jkbrickworks.com
Braigo (Braille printer)	Braigo Labs - Shubham Banerjee	https://www.braigolabs.com/products/
Cubestormer 3 (Rubik's cube solver)	David Gilday and Mike Dobson	https://youtu.be/cO5DLbpp3-M
Super Awesome Micro Project aka air powered LEGO® car	Steve Sammartino and Raul Oaida	https://youtu.be/_ObE4_nMCjE
Real LEGO® Bugatti Chiron	The LEGO Group	https://www.lego.com/en-us/campaigns/technic/bugatti-chiron/build-for-real
Bridge Girder erection machine SLJ900	Wolf Zipp	https://www.youtube.com/channel/UC2vjCc0CiaxF8bHHaOPQUXw
Various creations including clocks, braiding machines, etc…	Nico71	http://www.nico71.fr
Prosthetic Arm	David Aguilar	https://www.mrhandsolo.com

Table 1 – List of LEGO® creations from the general public

System/Tool	**Description**	**Creator/Reference**
	Education/STEM	
Conceptual AFM	AFM designed to scan LEGO® plates	(Hsieh et al., 2014)
Colorimeter	Two LEDs colorimeter	(Asheim et al., 2014)
Brickopore	Brick-based DNA sequencing	www.brickopore.co.uk
Influenza model		(Marintcheva, 2016)
LEGOLish	Light sheet microscope built from LEGO® parts	www.legolish.org
Liquid-handling robots	Liquid dispensing robot	(Gerber et al., 2017)
	Instrumentation	
General lab equipment	General lab equipment	Martin F Haase
LEGO Fraction Collector	Mindstorms-based fraction collector	(Caputo et al., 2020)
Spectrophotometer		(Pereira & Hosker, 2019)
MicroscoPy	Research Brightfield Microscope made of LEGO, 3D printing, arduino and raspberryPI	https://github.com/IBM/MicroscoPy
	Microfluidics	
µorgano	LEGO®-like system for multi-organ chips	(Loskill et al., 2015)
Supramolecular LEGO Assembly	LEGO®-like assembly of hydrogels	(Ma et al., 2014)
3D printed microfluidics	LEGO®-like microfluidics system	(Morgan et al., 2016)
	Biological Research	
Plant Growth System	Transparent tanks for monitoring plant growth	(Lind et al., 2014)
IMp	3D insect manipulator for observation	(Dupont et al., 2015)
LEMOLISH	LEGO®-based Motorized Lightsheet Microscope for 3D mesoscopic imaging of transparent organs	www.legolish.org/lemolish (ms. in prep)
Pumpy	Multimodal microscopy system	(Almada et al., 2019)
Stretchy	Cyclic Uniaxial cell stretcher	(Boulter et al., 2019)
Brick Strex	Motorized Cell Stretcher	(Mäntylä & Ihalainen, 2021)

Table 2 – List of LEGO® creations in Biotechnology and biological research.

Figure 2 - Boulter et al



Creation/Artwork Title	**Inventor/artist**	**Reference**
	Art	
Sculptures/Shadow Art	John V. Muntean	https://www.jvmuntean.com
Geometric Art	Jeff Sanders	http://www.brickbending.com
Sculptures/paintings	Nathan Sawaya	https://www.brickartist.com
Mosaics	Eric Harshbarger	http://www.ericharshbarger.org
Street art	Jan Vormann	https://www.janvormann.com
Lenticular mosaic	Arthur Gugick	

Table Box 2 – List of LEGO® artwork creators

System/Tool	Description	Creator/Reference
Behavioral sciences/Neurological Sciences		
CoRLEGO	Choice reaching task modeling using LEGO®robot	(Strauss et al., 2015)
LEGO® Therapy	Engage autistic spectrum disorder kids into social interactions	(DB, 2004; DB & M, 2006; LeGoff et al., n.d.)
LEGO Robots	Remote labs for experimenting with a team of robots	(Casini et al., 2014)
Physics		
CERN model	New parts prototyping	https://home.cern/news/news/experiments/using-lego-study-building-blocks-universe
Thermal Insulator	Characterization of LEGO® bricks as thermal insulators	(Chawner et al., 2019)
Tensile testers	Two models of tensile testers	(Moser et al., 2016; Talib et al., 2019)
Wave manipulator	Experimental platform for the investigation of phononic phenomena	(Celli & Gonella, 2015)
Chemistry		
Nerve gas detector		(Sun et al., 2018)

Table Box 3 – List of LEGO® creations in Science