nature biotechnology

PERSPECTIVE

Refinement and standardization of synthetic biological parts and devices

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The ability to quickly and reliably engineer many-component systems from libraries of standard interchangeable parts is one hallmark of modern technologies. Whether the apparent complexity of living systems will permit biological engineers to develop similar capabilities is a pressing research question. We propose to adapt existing frameworks for describing engineered devices to biological objects in order to (i) direct the refinement and use of biological 'parts' and 'devices', (ii) support research on enabling reliable composition of standard biological parts and (iii) facilitate the development of abstraction hierarchies that simplify biological engineering. We use the resulting framework to describe one engineered biological device, a genetically encoded cell-cell communication receiver named BBa_F2620. The description of the receiver is summarized via a 'datasheet' similar to those widely used in engineering. The process of refinement and characterization leading to the BBa_F2620 datasheet may serve as a starting template for producing many standardized genetically encoded objects.

Although many biotechnology applications have been developed[1], the scope and scale of imaginable applications exceed current abilities to implement them[2,3]. In part this is because the design and construction of engineered biological systems remains an *ad hoc* process for which costs, times to completion and probabilities of success are difficult to estimate accurately[4]. Ideally, biological engineers might develop a design and construction framework that makes routine the incorporation of basic biological functions into many-component integrated genetic systems that behave as expected. Mature engineering disciplines have developed similar frameworks by using the concept of abstraction to define sets of standardized, functional objects that can be used in combination, together with composition rules[5] that specify how such objects should be assembled.

Composition rules and abstraction are just beginning to be applied to the engineering of biology. For example, BioBrick standard biological parts (http://partsregistry.org/) are an early collection of genetically encoded functions that conform to simple rules supporting physical composition[6] and guidelines for functional composition[7] (**Box 1** and **Figs. 1** and **2**). As a second example, in support of functional composition, researchers recently developed a set of prokaryotic promoters that have reduced contextual dependencies in reported promoter activities[8]. We next need to produce quantitative descriptions[9] that facilitate the reuse of first-generation parts and devices and enable the development of specifications prescribing the design of next generation parts and devices that are engineered to better support composition and abstraction.

Lessons from engineering experiences

Quantitative descriptions of devices in the form of standardized, comprehensive datasheets are widely used in the electrical[10], mechanical, structural and other engineering disciplines (for examples see http://www.mcmaster.com/). A datasheet is intended to allow an engineer to quickly determine whether the behavior of a device will meet the requirements of a system in which the device might be used. Such a determination is based on a set of standard characteristics of device behavior, which are the product of engineering theory and experience[10–13]. The characteristics typically reported on datasheets are common across a wide range of device types, such as sensors, logic elements and actuators: first, a definition of the function and interfaces of the device (inputs and outputs); second, the operating context of the device; third, measured characteristics describing the quantitative behavior of the device.

A crucial measured characteristic is the transfer function, which details the static relationship between device input(s) and output(s) and allows prediction of the equilibrium behavior of composed devices. The dynamic behavior of the device is often reported so that the response time of the device can be compared to the expected timing of the overall system. It is important to report compatibility of device function with other devices or different operating conditions whenever the context in which the device operates is expected to vary. The reliability, or expected time to failure of a device, is also relevant whenever correct device performance over longer timescales is required. Finally, a description of the power and material resources consumed by a device informs the choice of a suitable power supply and resource pools for the system.

We propose to adopt a similar framework for describing engineered biological devices. Despite the differences in materials and mechanisms, biological devices may often be defined with functions that are identical to the functions of electrical, mechanical and other types of existing engineered devices. Biological equivalents of sensors[14–16], logic gates[17–19] and actuators[20] have all been demonstrated. Consequently, many of the characteristics found on existing device datasheets might also be useful for biological device datasheets. For example, the transfer function and dynamic behavior characteristics are directly applicable to any biological device with well-defined inputs and outputs. Compatibility of a biological device with genetic backgrounds, growth conditions or

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Published online 8 July 2008; doi:10.1038/nbt1413

other devices would also be useful information to biological engineers. Describing the reliability of a biological device is likely to be important but may require the invention of novel metrics due to the self-replicating and evolving nature of biological systems. For example, device failure across many generations might be measured by the number of culture doublings before a nonfunctional mutant becomes fixed in the population. Resource consumption, in the form of a demand for nucleotides, aminoacylated transfer RNAs, polymerases, ribosomes, and so on, is rarely reported for biological devices, yet such data would help biological engineers decide whether a cellular chassis is suitable to support a particular device or combination of devices.

Developing a prototypical device

We applied the generic framework outlined above to develop a genetically encoded receiver, BBa_F2620 (ref. 21). The receiver builds on work by biologists[22–24] and early device engineers[14,15,25–29] (**Box 2**);

Box 1 What is a standard biological part?

Each newly sequenced genome provides biotechnology researchers with additional natural genetic 'parts' to consider. These natural 'parts lists' include protein coding sequences, regulatory elements for gene expression and signaling and other functional genetic elements. However, such natural parts do not always behave as a would-be biological engineer might naively expect. For example, they cannot be reliably reused in combination with one another.

Most mature engineering fields depend on catalogs[10] of synthetic parts. These engineered, synthetic parts are often easily distinguished from natural objects because they conform to standards for manufacturing and use. The production of synthetic parts almost invariably requires that raw materials taken from nature be refined and modified in order to produce constrained sets of synthetic objects that meet prescribed requirements—for example, silicon is purified and processed to form wafers that are used to produce microprocessors, whereas iron is refined, processed and machined to produce standardized steel nuts and bolts. If such examples are relevant to the engineering of biology, then an important next step is to attempt to refine and standardize natural biological parts.

What then is a standard biological part? We define a standard biological part to be a genetically encoded object that performs a biological function and that has been engineered to meet specified design or performance requirements. The requirements of greatest interest to us are those that enable reliable physical and functional composition (below). Practically, the engineering of biology now depends mostly on the design, construction and use of engineered DNA. Thus, the standardization of biological parts whose activities are directly encoded via DNA (e.g., a promoter) or via molecules whose primary structure is directly derived from DNA, such as RNA (e.g., a ribozyme) or proteins (e.g., a kinase), is of immediate importance. Other classes of biomolecules (e.g., oligosaccharides, metabolites, small molecules), although also important, are not yet as readily or widely engineered as DNA, RNA or protein, and thus are not yet considered within the engineering framework described here.

Physical composition is the process by which two or more parts or devices are materially connected (devices are combinations of one or more parts that together encode a well-defined, higher-order function). Standards supporting reliable physical composition underlie all other compositional standards. One early example of a

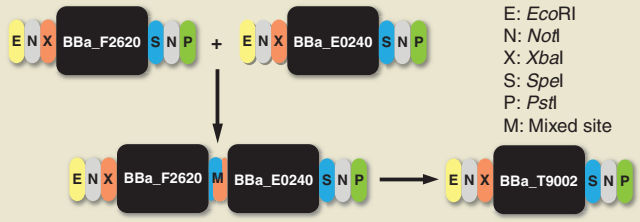


Figure 1 BioBrick assembly standard is a process that enables physical composition of BioBrick standard biological parts.

standard supporting physical composition of engineered biological parts and devices is the BioBrick assembly standard[6], which allows standard objects to be assembled in an idempotent manner (**Fig. 1**). The BioBrick assembly standard requires the use of defined prefix and suffix sequences that contain specific restriction endonuclease sites (*Eco*RI, *Xba*I, *Spe*I, *Pst*I and *Not*I). Consequently, to be compatible with the BioBrick assembly standard, a synthetic part must be engineered to remove any BioBrick restriction endonuclease sites found in the nucleotide sequence encoding the natural part.

Functional composition is the process and means of connecting the functional inputs and outputs of individual objects together such that the behavior of the composite object is as expected and not an emergent property of the connected parts or any expected interaction(s) with the environment. To support reliable functional composition, standardized objects must be designed to possess certain properties, only some of which are currently understood. For example, a standard signal carrier for device inputs and outputs supports the connection of engineered devices. One standard signal-carrier for transcription-based devices is the flow of RNA polymerases along DNA, measured in polymerases per second transcribing past a defined point on DNA (PoPS). The receiver BBa_F2620 is an engineered device that has been designed to produce a PoPS output signal and can therefore be connected to any other device that accepts a PoPS input signal (**Fig. 2**). The receiver itself was constructed from BioBrick standard parts via the BioBrick assembly standard.

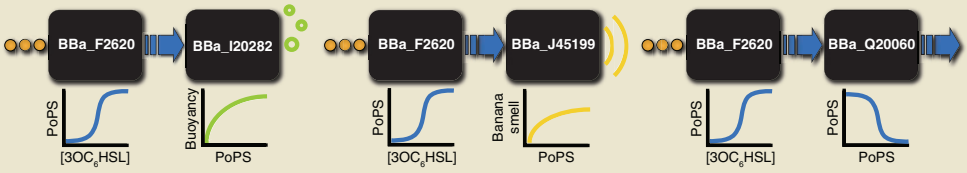


Figure 2 The use of PoPS, a standard signal carrier, enables functional composition of the receiver (BBa_F2620) with devices that accept a PoPS input.

ad hoc engineered constructs, similar in function to BBa_F2620, have been used to control programmed pattern formation, cell culture density and gene expression[30,31]. BBa_F2620 is a composite device constructed by standard assembly[6] from five BioBrick standard biological parts: a promoter (BBa_R0040), a ribosome binding site (BBa_B0034), the LuxR coding sequence (BBa_C0062), a transcription terminator (BBa_B0015) and the right lux promoter (BBa_R0062) (**Supplementary Table 1** online). Detailed descriptions for each part are freely available online through the Registry of Standard Biological Parts (http://partsregistry.org/). We defined the input to the receiver to be the extracellular level of a chemical (3-oxohexanoyl-*L*-homoserine lactone, $3OC_6HSL$) and the output to be a common gene expression signal, the flow of RNA polymerases along DNA (polymerases per second, or PoPS[7]). Hence, BBa_F2620 is a $3OC_6HSL$-to-PoPS receiver. We choose to use a PoPS output for the receiver because PoPS possesses many characteristics likely to be necessary in a common signal carrier. First, it is a generic signal that can be used as the input to many other devices. Second, PoPS is a spatially directed signal that can only pass through the DNA molecule connecting the output of an upstream device to the input of a downstream device.

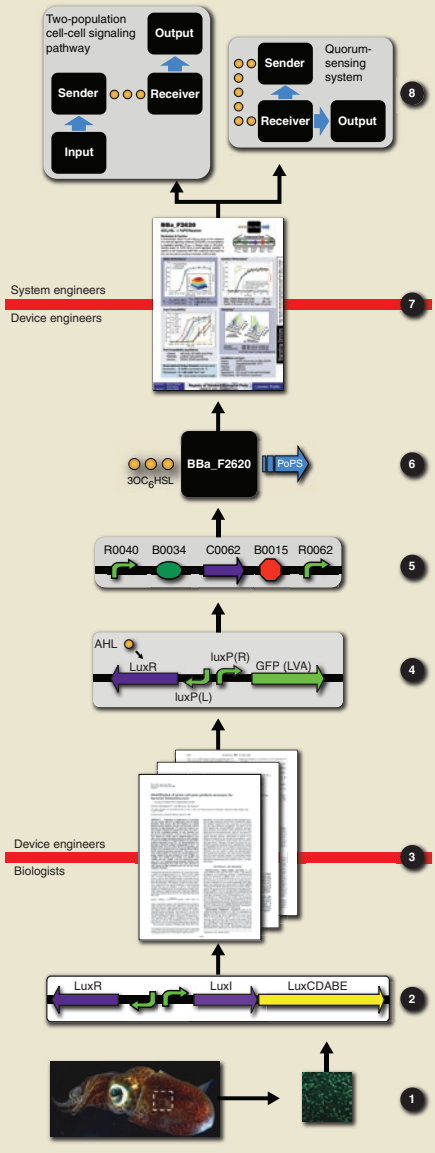
Characterizing the behavior of BBa_F2620

We used widely accessible technology to measure five characteristics that describe the behavior of the receiver under a particular set of operating conditions (described in **Supplementary Notes** and **Supplementary Fig. 1** online). In all experiments, we measured the behavior of the receiver indirectly by measuring green fluorescent protein (GFP) expression from a downstream reporter device (BBa_E0240). The combination of the receiver device and the reporter device is a composite 'system' (BBa_T9002). We used independent experiments to parameterize a model of the behavior of the reporter device. This quantitative model allowed us to calculate the specific molecular output of the receiver from our observations of the dynamic behavior of the system (BBa_T9002). The detailed quantitative description of the receiver and its behavior are summarized on a device datasheet (**Fig. 3** and **Box 3**).

We determined the transfer function of the receiver across a range of $3OC_6HSL$ input concentrations (see **Supplementary Notes** and **Supplementary Fig. 2** online). A Hill equation model with three parameters described the data well (**Supplementary Notes**). The maximum, saturated output of the reporter was 490

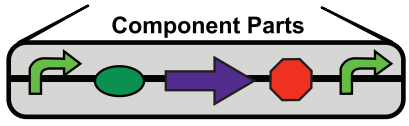
Box 2 From biological discovery to an engineered device

Very few synthetic biological parts are created from scratch (exceptions include RNA or peptide aptamers produced via multiple rounds of screening and selection, or a novel protein fold designed via modeling and simulation). Instead, most synthetic biological parts and devices are produced via a process that starts with the discovery and description of a natural biological function (Steps 1 and 2). Given the need for a particular biological function, engineers scour the scientific literature (Step 3) in hopes of finding suitable natural starting materials (if the necessary natural parts are unavailable or have not been discovered, engineers will often conduct or commission research to produce the needed parts). Once proof-of-principle engineered parts and devices have been demonstrated (Step 4), engineers can perform additional work (Steps 5 and 6) to improve the usability of the synthetic device by refining and standardizing the device in support of more reliable physical and functional composition (**Box 1**), as well as publishing a quantitative description of device behavior as a datasheet (Step 7; **Fig. 3**). Engineers working on higher-level systems, comprising many devices, can then readily make use of well-described synthetic biological devices (Step 8).



BBa_F2620

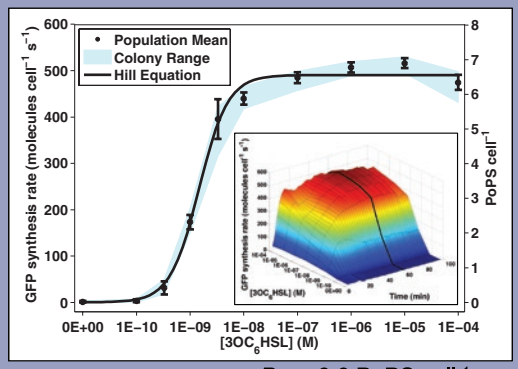
$3OC_6HSL \rightarrow$ PoPS Receiver



Mechanism & Function

A transcription factor (LuxR) that is active in the presence of a cell-cell signaling molecule ($3OC_6HSL$) is controlled by a regulated operator ($P_{LtetO-1}$). Device input is $3OC_6HSL$. Device output is PoPS from a LuxR-regulated operator. If used in a cell containing TetR then a second input such as aTc can be used to produce a Boolean AND function.

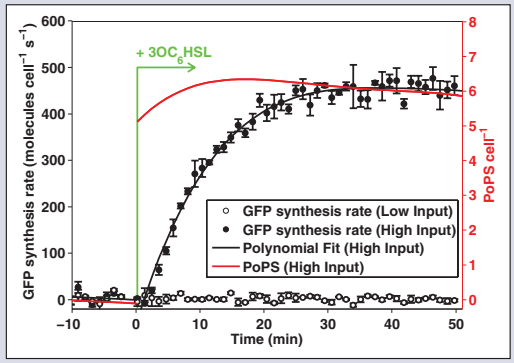
Static Performance*



$$P_{out} = \frac{P_{max}[3OC_6HSL]^n}{K^n + [3OC_6HSL]^n}$$

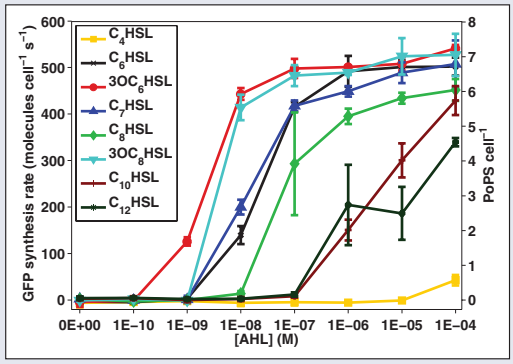
P_{max}: **6.6** PoPS cell^{-1}
K: **1.5E-09** M $3OC_6HSL$
n: **1.6**

Dynamic Performance*



BBa_F2620 Response Time: ***<1** min*
BBa_T9002 Response Time: ***6±1** min*
Inputs: 0 M (Low), 1E-07 M (High) $3OC_6HSL$

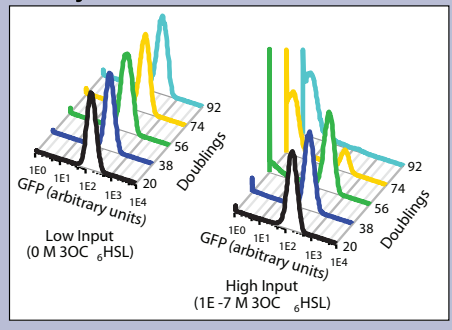
Input Compatibility*



Part Compatibility (qualitative)

Chassis: *MC4100, MG1655,* and *DH5α*
Plasmids: *pSB3K3* and *pSB1A2*
Devices: *E0240, E0430* and *E0434*

Reliability**



Genetic: **>92/>56** culture doublings
Performance: **>92/>56** culture doublings
(low/high input during propagation)

Transcriptional Output Demand (low/high input)
Nucleotides: **0 / 6.6xNt**ucleotides cell^{-1} s^{-1}
Polymerases: **0 / 1.5E-1xNt** RNAP cell^{-1}
(**Nt** = downstream transcript length)

Conditions (abridged)
Output: PoPS measured via *BBa_E0240*
Culture: Supplemented M9, 37°C
Plasmid: pSB3K3
Chassis: MG1655
**Equipment:* PE Victor3 multi-well fluorimeter
***Equipment:* BD FACScan cytometer

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Updated: March 2008

Registry of Standard Biological Parts
making life better, one part at a time

http://partsregistry.org/Part:BBa_F2620

Signaling Devices

Figure 3 A prototypical 'datasheet' that summarizes current knowledge of the behavior of the receiver BBa_F2620. The datasheet, which includes a general description and a summary of relevant performance characteristics, is designed to support rapid reuse of the device. The description of the receiver is also available in electronic format[21]. A glossary for the datasheet is provided in **Box 3**.

± 10 GFP molecules/cell/s (uncertainties represent the 95% confidence interval for the parameter). From the measured GFP synthesis rate, we estimated a maximum output from the receiver of 6.6 ± 0.3 PoPS/cell. The minimum observed output was determined to lie between 0 and 3 GFP molecules/cell/s corresponding to a device output of ~0 PoPS/cell. Given such a low minimum observed output, we did not include a basal PoPS output in the model describing the output of the receiver. The receiver switch point, the input required for half-maximal output, is 1.5E-9 ± 3E-10 M $3OC_6HSL$. The Hill coefficient describing the steepness of the transition from low to high output is 1.6 ± 0.4. The population distribution was monovariate at all input levels (data not shown). Given that the output of the receiver varies over two logs of input concentration, the receiver might be used either as an analog device with a graded output or as a digital device (with the high and low output levels still to be defined).

We determined the dynamic response of the receiver by quantifying the time-dependent increase in fluorescent protein synthesis rates after a step increase in input level from 0 to 1E-7 M $3OC_6HSL$ (as described in **Supplementary Notes**). Assuming a first-order linear response with time delay, we calculated a response time constant of 6 ± 1 min and a delay of 1.5 ± 0.5 min. Independent experiments demonstrated that the observed dynamic response is largely due to the maturation rate of GFP (**Supplementary Notes** and **Supplementary Fig. 3** online). The model of the reporter device was used to calculate the time-dependent response

Box 3 Details of a datasheet

The following is a glossary of terminology and concepts in the datasheet of BBa_F2620 (**Fig. 3**).

BBa_F2620. The unique part number assigned to the device. The prefix, BBa, denotes a BioBrick part from the alpha release of BioBrick standard biological parts collection (http://partsregistry.org/). F denotes a cell-cell signaling device and the remaining numbers identify the specific device.

Static performance. This section contains data describing the steady-state relationship between the input and output of the device. The transfer function shows the input/output relationship 60 min after addition of input signal at which time the reporter device (BBa_E0240) is assumed to be at steady state. Hence, there is a linear relationship between the measured GFP synthesis rate and the PoPS output of the receiver. The inset shows the time and dose-dependent response of the receiver; the 60 min time point is indicated by a solid black line.

Population mean. The mean output level for either six or nine independent cultures at a given input level. Error bars represent the 95% confidence interval of the mean of the independent cultures.

Colony range. A range bounded by the lowest and highest outputs among the independent cultures at a given input level.

Hill equation. An equation relating the PoPS output per cell of the receiver (P_{out}) to the input concentration of $3OC_6HSL$. P_{max} represents the maximum output of the receiver, K is the device switch point and n is the Hill coefficient.

Dynamic response. This section describes the response of the receiver to a step increase in input level at 0 min. The mean GFP synthesis rates measured for three cultures of the composite part (BBa_T9002) are shown as filled (high input) or empty (low input) circles. Error bars represent s.d. across the independent cultures. The solid black lines are a linear fit to the data (**Supplementary Notes**). The time-dependent PoPS output from the receiver (shown as a solid red line) was calculated using a model of the dynamic behavior of the reporter device (**Supplementary Notes**).

Response time. The time for the output of the receiver to reach 67% of its final value was estimated from the calculated PoPS output of the receiver. The response time of the composite part (BBa_T9002) was calculated by fitting an exponential function to the GFP synthesis rate data after the addition of 1E-7 M $3OC_6HSL$ (**Supplementary Notes**).

Input compatibility. The dose response of the receiver to a variety of signaling compounds similar to $3OC_6HSL$ is presented. The data points represent the mean of three independent cultures, and the error bars represent the s.d. of the data for the three independent cultures.

Part compatibility. A list of other biological objects with which the receiver is known to be qualitatively functional.

Chassis. An organism, or genetic background, that can be used to support and power a particular engineered biological device. Details of specific genetic backgrounds can be found online (http://partsregistry.org/).

Reliability. The ability of the device to continue to function over many generations is reported. Here, fluorescence-activated cell sorting (FACS) data show the response of the device to a high input signal as a function of culture doublings. Two cases are shown, one in which the culture is propagated under low input conditions and one in which the culture is propagated under high input conditions.

Genetic reliability. The number of culture doublings before a mutant device represents at least 50% of the population. The reported figures are derived from the FACS data and confirmed by DNA sequencing analysis.

Performance reliability. The number of culture doublings before 50% of the population is unable to correctly respond to an input. The reported figures are derived from the FACS data.

Transcriptional output demand. The receiver requires resources from the cellular chassis in order to function. The demand for resources related to transcription is presented as a function of the length of the transcript produced by the output of the receiver.

Conditions. The growth conditions and measurement methods used to characterize the receiver are summarized on the datasheet (see **Supplementary Notes** for details).

License. The ownership, sharing and innovation terms by which the authors provide access to, and use of, the receiver together with the associated characterization data.

of the receiver given the observed response of the reporter. Using this method, we calculated a response time for the receiver of <1 min.

We measured receiver input specificity, which is the ability of the receiver to distinguish between its cognate input signal and similar chemical signals that might also be used in composite systems containing the receiver. Input specificity also describes the compatibility of the receiver within a particular set of related devices. We measured the response of the receiver to input signals carried by different acyl-homoserine lactones, both lacking the 3-oxo moiety and varying in side-chain length (**Supplementary Notes** and **Supplementary Table 2** online). The receiver responds to $3OC_6HSL$ and acyl-homoserine lactones with side chains of similar length. Any device that produces one of this subset of like acyl-homoserine lactones may be used to send a signal to the receiver. The compounds with the shortest and longest side chains produce very weak device responses, suggesting that the receiver could be used independently in parallel with other devices that respond to these compounds. The datasheet also lists the compatibility of the receiver with a range of genetic backgrounds, output devices and plasmids.

We measured the evolutionary reliability of the receiver coupled to the reporter device by following receiver performance as a function of culture doubling at low input levels (**Supplementary Notes**). Because evolutionary reliability is known to be dependent on levels of recombinant protein expression[32], we measured the reliability of the receiver at low input levels so that GFP expression from the reporter device would be negligible. Receiver performance remained constant over 92 culture doublings. For comparison, we also measured the reliability of the composite system (BBa_T9002) at high input levels. Consistently, at high input levels, more than half the cells in the population were nonperforming within 74 culture doublings. Sequence analysis of nonperforming mutants indicated that system failure results from a deletion between DNA sequences that are repeated in both the receiver and the reporter devices. Additional experiments confirmed that we were unable to isolate a population of cells that did not already carry the deletion (**Supplementary Notes** and **Supplementary Figs. 4** and **5** online). The failure observed here is an emergent behavior specific to the combination of the receiver and reporter devices. Emergent behavior might be avoided by the development of appropriate design rules. For example, when system operation across many culture doublings is required, repeat sequences sufficient in length and proximity to promote deletion events should be avoided.

We computed the output demand of the receiver using the observed rates of downstream protein synthesis (**Supplementary Notes**). The transcriptional output demand depends both on the output of the receiver and on the length of the transcript encoded by the downstream device (**Supplementary Notes**). At low inputs, the output of the receiver is ~0 and so places a negligible demand on the host cell. At high inputs, the output of the receiver requires $6.6 \times$ Nt nucleotides/cell/s and $0.15 \times$ Nt polymerases/cell, where Nt is the number of nucleotides in the transcript being produced from the output of the receiver. We did not measure the cellular resources required to produce the LuxR protein (BBa_C0062), an essential component of the receiver whose expression places an additional basal demand on the cell.

One function, many devices?

The natural biological system on which the design of the receiver is based has been used to produce other, functionally similar devices[14,15,25–29]. We compared the behavior of our receiver to these earlier systems (none of which were constructed from BioBrick standard biological parts) to begin to evaluate whether or not the performance of the receiver might depend on external factors such as host cell genetic background, culture conditions or laboratory environment (**Supplementary Table 3** online). None of the prior studies reported all the characteristics by which the receiver has been described here. What comparisons could be made suggested that the receiver switch point and response time are insensitive to host cell genotype or growth conditions but that the input compatibility is sensitive to host cell genotype or other variables. Notably, two studies reported device switch points that are 100-fold or more different from all other studies[14,25]. This variation is likely explained by differences in sourcing genetic materials (**Supplementary Table 3**); the amino acid sequences of the LuxR proteins used in these two studies differ by 25% from those used in the other studies.

Summary and conclusions

Here, we developed a generic framework for defining and describing standard biological devices to support the reuse and refinement of many devices. To test the utility of our framework, we used relatively well-understood biological mechanisms to design a device that converts the extracellular level of $3OC_6HSL$ to PoPS, a common intracellular signal carrier that can be accepted as input by many standard biological devices. We constructed the receiver from five standard biological parts. We used a reporter device also encoded by standard biological parts to measure the quantitative and dynamic behavior of the receiver. Three aspects of our work enable easy reuse of the receiver: (i) our use of standards that support the reliable physical composition of genetic parts, (ii) a device design that produces an output signal that is a common signal carrier and (iii) our extensive and quantitative device description. As evidence, while this manuscript was in preparation, we made freely available the DNA encoding BBa_F2620 and its accompanying datasheet via the Registry of Standard Biological Parts (http://partsregistry.org/). Already, 18 higher-order systems incorporating the receiver have been successfully assembled and contributed back to the Registry by teams in the International Genetically Engineered Machines Competition (http://igem.org/).

The component parts of the receiver can be adapted to serve functions other than the one chosen here. For example, the behavior of the receiver could be modified in a predictable manner by choosing, as input, one of the acyl-homoserine lactones similar to $3OC_6HSL$ to which we have demonstrated that the receiver responds. As a second example, in a host cell that constitutively expresses Tet repressor, the receiver can perform a logical AND operation, producing a high output only in the presence of $3OC_6HSL$ and anhydrotetracycline (aTc). As a final example, removing the promoter regulating the transcription of the LuxR coding region would produce a device that has both a PoPS input and a $3OC_6HSL$ input. The resulting three-terminal device could be used to perform an AND operation, or as a $3OC_6HSL$-dependent PoPS amplifier/attenuator. These examples highlight the value in considering the internal components, inputs and outputs of the receiver in detail to design novel devices. However, such value is gained at the expense of the convenience afforded by choosing a well-described 'black-box' device, such as the BBa_F2620 receiver.

Looking forward, much additional work is needed to make routine the engineering of many-component biological systems that behave as expected[33]. For example, the framework for describing device behavior introduced here, or an improved framework, should be applied to describe many devices and device combinations. When characterizing combinations of devices, special attention should be paid to combinations that fail to produce the behavior predicted given descriptions of the individual devices. Careful characterization and analysis of such emergent behaviors is needed to support the development of design rules that prevent interactions between devices other than through the defined device inputs and outputs (such as the spontaneous selection for

a deletion within the composite system, BBa_T9002). As a second example, standard input and output signal levels might be defined so that any two devices, when connected, would be well matched. Understanding whether desired device behaviors (such as standard signal levels) can be best engineered via directed evolution, rational engineering or a combined approach[29,34–36] will help researchers to produce well-behaved devices more quickly.

Finally, because the receiver can be used in many systems and because we hope to promote the collaborative development and unfettered use of open libraries of standard biological parts and devices, all of the information describing the receiver is freely available through the Registry of Standard Biological Parts, as mentioned above. We encourage researchers to contribute improvements to the design and description based on experiences with the operation of the receiver (or other parts and devices) directly to the registry. Ultimately, device descriptions such as that presented here should be available online in a machine-readable format that will enable the computer-aided design of many-component engineered biological systems.

Note: Supplementary information is available on the Nature Biotechnology website.

ACKNOWLEDGMENTS

We thank T. Knight; R. Rettberg; members of the Endy, Knight and Sauer labs and staff of the Registry of Standard Biological Parts for discussions, advice and materials throughout the work. We thank R. Brent, U. RajBhandary, C. Smolke, B. Studier and anonymous reviewers for comments on earlier versions of this manuscript. This research was supported by grants to D.E. from the US National Science Foundation, Defense Advanced Research Projects Agency and National Institutes of Health. B.C. was supported by a National University of Ireland training fellowship. Additional support was provided by the Massachusetts Institute of Technology.

AUTHOR CONTRIBUTIONS

B.C. and D.E. initiated the work. B.C., D.E. and A.L. designed the experiments. B.C. and A.L. performed the experiments. B.C., A.L. and D.E. analyzed the data and wrote the paper.

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