

Supplementary Materials

1. Supplementary Methods

Single-Cell MDA. A schematic of the microdevice is in Figure S1. The device is composed of PDMS and consists of two layers of architecture. The top layer contains 10 μm -tall channels (black) used to move cells and reagents within the chip, as well as 25 μm -tall chambers (blue) that comprise the MDA microreactors. The bottom layer contains a 25 μm -tall control architecture for the pneumatic valves (red) as well as 15 μm -tall hydration lines (green), used to prevent evaporation in the microreactors. The chip is mounted to a thin glass coverslip. Poly(dimethylsiloxane) (PDMS) was purchased from R.S. Hughes (Sunnyvale, CA, USA).

The chip was placed on an inverted microscope (Nikon Eclipse TE2000-U, Melville, NY, USA) and imaged in real-time via an EM-CCD camera (Andor iXon+, Belfast, UK). Cells were visualized via laser-induced fluorescence emission using a laser beam, 25 mW at 638 nm (CrystaLaser, Reno, NV, USA), expanded to a square imaging field. The device was placed on a precisely movable stage (Lstep Märzhäuser, Wetzlar, Germany), which was controlled remotely by a computer program. scMDA of *Synechocystis* was conducted using the new lysis protocol described below.

400 μL of *Synechocystis* was extracted from a whole culture and subjected to pre-lysis. Following centrifugation and removal of the supernatant, the pellet was washed five times in 400 μL TES buffer to reduce exogenous sample DNA. Supernatants were saved for quantification of exogenous nucleic acid fragments. The pellet was resuspended in 400 μL PBS buffer and then diluted by a factor of 200 into Injection Buffer, phosphate-buffered saline (PBS) containing 0.1% Tween-20. Tween-20 was used to prevent adhesion of the cells to PDMS channel surfaces.

After placing a microfluidic chip on the inverted microscope and preparing it for use, the inlet of the main cell flow channel was injected with 10 μL of injection buffer and filled via negative pressure. Excess injection buffer was removed from the inlet and replaced with 10 μL of the cell suspension, diluted by a factor of 200 in Injection Buffer.

Single cells were moved through the main cell flow channel via negative pressure. Once a cell reached an intersection neighboring a microreactor entrance (Figure S1-1), it was isolated via actuation of pneumatic valves. The cross-flow of Lysis buffer, SoluLyse containing 200 U/ μL lysozyme, was used to capture the cell and fill the 3.0-nL lysis chamber (Figure S1-2). Two of the eight microreactors on each chip were designated as negative controls for detection of sample exogenous DNA. No cell, only the diluted suspension in injection buffer, was captured with lysis buffer in these negative controls. Addition of Qiagen Repli-G DLB, Stop, and Master Mix reagents were added as described in the main text. The chip was incubated for 16 h at 34 °C on a hot plate. TES Buffer, SoluLyse, TE Buffer, and water used in the Master Mix for first- and second-round amplification were filtered with 0.2- μm filters prior to use and exposed to UV for one hour.

After MDA incubation, the samples were extracted from the chip by injecting TE Buffer, pH 8.0, into the microreactors via the reagent-addition channels, thus pushing the reaction volume through the microreactor outlets (Figure S1-6) of the chip. A 20- μL gel-loading pipette tip was inserted into each outlet to receive the sample. The sample was extracted until 5 μL of TE Buffer had been passed through each microreactor, denoted by a mark on the pipette tip. The pipette tip was then pinched shut

with tweezers and moved into a 200- μ L Eppendorf Tube, into which the diluted sample was injected. The sample was stored at 4 °C with minimum light exposure.

2. Supplementary Figures

Figure S1. Schematic of one of eight replicate microreactors in the microfluidic scMDA chip. Red and yellow colors represent pneumatic valve control and hydration line architecture on the bottom layer, respectively. The two layers are separated by a PDMS membrane. A cell is captured at (1) and moved to (2) for lysis with lysis buffer. Addition of alkaline DLB increases volume to (3), completes lysis, and denatures DNA. Addition of Stop buffer increases volume to (4) and neutralizes pH. Addition of Master Mix increases volume to (5). Amplification is conducted at 33 °C for 16 h. Amplified DNA is extracted with TE Buffer through (6). Black and blue colors represent channel and chamber architecture on the top layer, respectively.

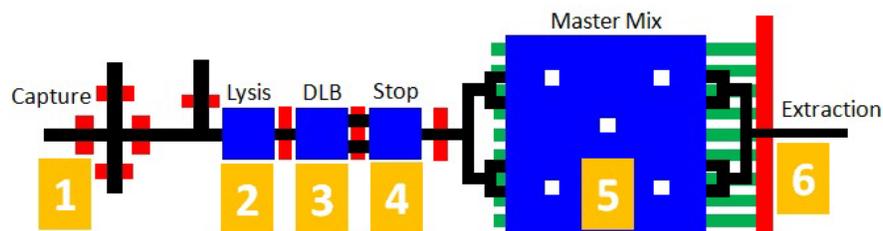


Figure S2. Amplification factors from microscale and macroscale MDA reactions. Amounts of produced DNA were quantified via PicoGreen assay. The amount of the template DNA for 60-nL reaction was calculated to be 50 attograms, derived from the estimated genome copy number of *Synechocystis* and the known size of the genome.

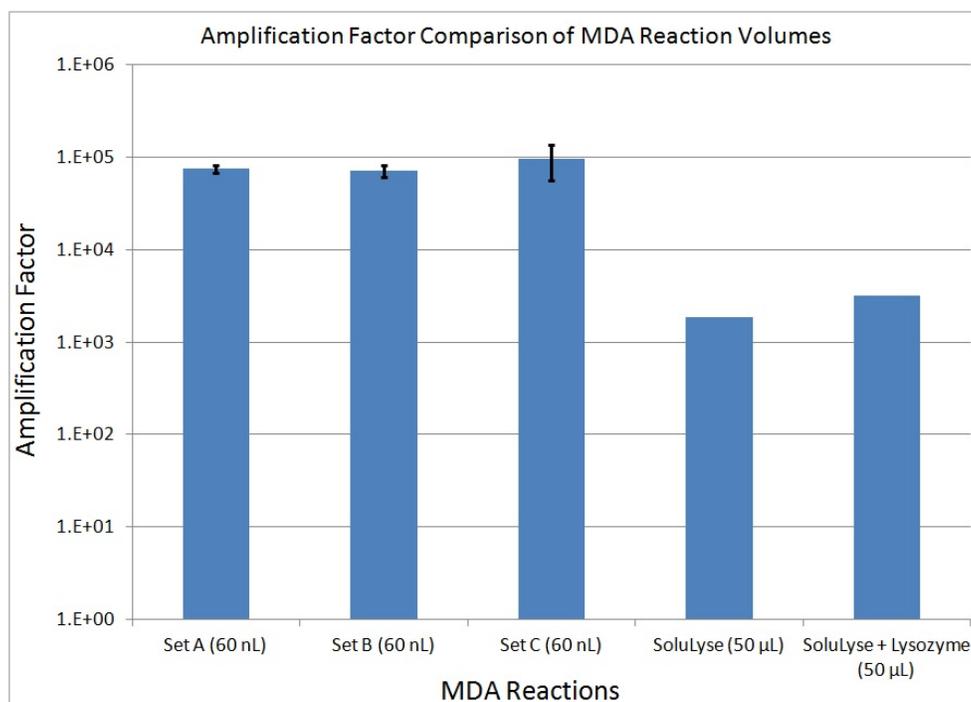


Table S1. Coverage primers for *Synechocystis* sp. PCC 6803.

Primer#	Locus ID	Gene Name	Sequencing & PCR Primer	T_m (°C)	Product Size	Start Position	End Position
1F	slr0611	sds solanesyl diphosphate synthase	AGGGCGGCGATCACCCAAA	60.8	1003	3573152	684
1R			GCCAGTTGCGCTTGGTTCGC	60.0			
2F	slr1291	NAD(P)H-quinone oxidoreductase subunit 4	TTGGCGTGTTTCGTGGCCCAG	60.2	1057	286543	287599
2R			ATGGCATTGCCGGGGAGCAC	60.0			
3F	sll1009	frpC iron-regulated protein	GTCATTGCCGTGACCGCCCA	60.0	1020	506729	507748
3R			GCGAGTGCTGGTGGTGGCAT	60.0			
4F	sll1920	cation-transporting ATPase E1–E2 ATPase	GTCCTGCCACCCACAACCG	59.9	1022	765029	766050
4R			GGGCACCAGTGCGGCGTATT	60.0			
5F	sll1453	nrtD nitrate transport protein NrtD	CGGTTGCGGGGACGGTCAAA	59.9	1001	1005440	1006440
5R			CGGGTACCCGTCCTGACCT	60.3			
6F	sll2010	UDP- <i>N</i> -acetylmuramoyl-L-alanyl-D-glutamate synthetase	GCACAGGCCGGGAAAGCAA	60.2	1102	1256978	1258079
6R			AGGAAGCTTGGCCCGAACGC	60.0			
7F	slr0260	cobA cob(I)yrinic acid a,c-diamide adenosyltransferase	GCCTGGGAACCGGCGGAAAA	59.9	1040	1507694	1508733
7R			GGCATCGGCAGTGAGCAGGG	60.1			
8F	sll1245	cytochrome; CytM	TCTGGGACCGCGTTGGGAT	59.9	1166	1750788	1751953
8R			CATCTGGTTGCGGAGGGCCG	60.1			
9F	slr0946	arsC arsenate reductase	CGTGCGGGGCCAGGTTAAGG	60.0	1100	2012572	2013671
9R			CCCACCACATCGGAACGGGC	60.0			
10F	slr1950	cation-transporting ATPase E1–E2 ATPase	CGGTTAGTGGGGCGGGGAGA	60.0	1050	2254850	2255899
10R			GGTGGCCTTGGCTTCCGGTC	60.0			
11F	sll0006	aspartate aminotransferase	CCCACGGGACAGGGAACCCA	60.1	1176	2494383	2495558
11R			CGGCAATGGGCCCTGGCTTT	60.2			
12F	slr0897	endo-1,4- β -glucanase	TGGCGGGGAGATTCCGGGTT	59.9	1124	2767405	2768528
12R			CGGAAACCGTCCCAGCCCAC	60.0			
13F	slr0118	thiamine biosynthesis protein ThiC	CTCCGTCCCGGCTGTACCCA	60.0	1032	2999892	3000923
13R			GGCGGCCCCATATCCATGC	60.0			

Table S1. Cont.

14F	slr0550	dapA dihydrodipicolinate synthase	TGCGGCCAAGTTGGGAGTGG	59.6	1065	3249682	3250746
14R			TTGGAGCCGGTGGGGAGAGG	59.9			
15F	slr0452	ilvD dihydroxy-acid dehydratase	CATGCTCCGGGCCGTTGGTT	60.0	1115	3498965	3500079
15R			CACTGCCTTCGGTGGCCAGG	60.0			

Table S2. BLAST result for scMDA amplicon sequences.

Set A. *Synechocystis* sp. 6803 coverage sequences.

Sample	Primer	Organism	Protein	Identity	Query Coverage
1	1F	<i>Synechocystis</i> sp. PCC 6803	thiol:disulfide interchange protein DsbD	91%	82%
1	1R	<i>Synechocystis</i> sp. PCC 6803	thiol:disulfide interchange protein DsbD	97%	41%
1	2F	<i>Synechocystis</i> sp. PCC 6803	NAD(P)H-quinone oxidoreductase subunit 4	99%	98%
1	2R	<i>Synechocystis</i> sp. PCC 6803	NAD(P)H-quinone oxidoreductase subunit 4	99%	98%
1	5F	<i>Synechocystis</i> sp. PCC 6803	nitrate transport protein NrtD	99%	98%
1	5R	<i>Synechocystis</i> sp. PCC 6803	nitrate transport protein NrtD	97%	63%
1	6F	<i>Synechocystis</i> sp. PCC 6803	UDP- <i>N</i> -acetylmuramoyl-L-alanyl-D-glutamate synthetase	98%	95%
1	6R	<i>Synechocystis</i> sp. PCC 6803	UDP- <i>N</i> -acetylmuramoyl-L-alanyl-D-glutamate synthetase	99%	99%
1	7F	<i>Synechocystis</i> sp. PCC 6803	hypothetical protein	98%	37%
1	7R	<i>Synechocystis</i> sp. PCC 6803	cob(I)yrinic acid a,c-diamide adenosyltransferase	92%	47%
1	13F	<i>Synechocystis</i> sp. PCC 6803	thiamine biosynthesis protein ThiC	98%	82%
1	13R	<i>Synechocystis</i> sp. PCC 6803	thiamine biosynthesis protein ThiC	99%	61%
2	1F	<i>Synechocystis</i> sp. PCC 6803	solanesyl diphosphate synthase	97%	84%
2	1R	<i>Synechocystis</i> sp. PCC 6803	solanesyl diphosphate synthase	98%	94%
2	7F	<i>Synechocystis</i> sp. PCC 6803	extracellular nuclease	99%	95%
2	7R	<i>Synechocystis</i> sp. PCC 6803	extracellular nuclease	99%	95%
4	5F	<i>Synechocystis</i> sp. PCC 6803	nitrate transport protein NrtD	98%	99%
4	5R	<i>Synechocystis</i> sp. PCC 6803	nitrate transport protein NrtD	99%	96%
4	8F	<i>Synechocystis</i> sp. PCC 6803	cytochrome; CytM	96%	67%
4	8R	<i>Synechocystis</i> sp. PCC 6803	50S ribosomal protein L9	93%	48%

Table S2. Set A. Cont.

6	1F	<i>Synechocystis</i> sp. PCC 6803	solanesyl diphosphate synthase	98%	93%
6	1R	<i>Synechocystis</i> sp. PCC 6803	solanesyl diphosphate synthase	99%	96%
6	3F	<i>Synechocystis</i> sp. PCC 6803	iron-regulated protein	99%	96%
6	3R	<i>Synechocystis</i> sp. PCC 6803	iron-regulated protein	99%	97%
6	4F	<i>Synechocystis</i> sp. PCC 6803	cation-transporting ATPase E1–E2 ATPase	99%	99%
6	4R	<i>Synechocystis</i> sp. PCC 6803	cation-transporting ATPase E1–E2 ATPase	99%	97%
6	5F	<i>Synechocystis</i> sp. PCC 6803	nitrate transport protein NrtD	99%	98%
6	5R	<i>Synechocystis</i> sp. PCC 6803	nitrate transport protein NrtD	99%	98%
6	6F	<i>Synechocystis</i> sp. PCC 6803	UDP- <i>N</i> -acetylmuramoyl-L-alanyl-D-glutamate synthetase	98%	97%
6	6R	<i>Synechocystis</i> sp. PCC 6803	UDP- <i>N</i> -acetylmuramoyl-L-alanyl-D-glutamate synthetase	99%	96%
6	7F	<i>Synechocystis</i> sp. PCC 6803	cob(I)yrinic acid a,c-diamide adenosyltransferase	99%	99%
6	7R	<i>Synechocystis</i> sp. PCC 6803	cob(I)yrinic acid a,c-diamide adenosyltransferase	97%	93%
6	8F	<i>Synechocystis</i> sp. PCC 6803	cytochrome; CytM	95%	66%
6	8R	<i>Synechocystis</i> sp. PCC 6803	50S ribosomal protein L9	87%	32%
6	10F	<i>Synechocystis</i> sp. PCC 6803	cation-transporting ATPase E1–E2 ATPase	97%	50%
6	10R	<i>Synechocystis</i> sp. PCC 6803	cation-transporting ATPase E1–E2 ATPase	93%	53%
6	11F	<i>Synechocystis</i> sp. PCC 6803	aspartate aminotransferase	99%	71%
6	11R	<i>Synechocystis</i> sp. PCC 6803	aspartate aminotransferase	98%	95%
6	13F	<i>Synechocystis</i> sp. PCC 6803	thiamine biosynthesis protein ThiC	99%	95%
6	13R	<i>Synechocystis</i> sp. PCC 6803	thiamine biosynthesis protein ThiC	99%	96%
8	1F	<i>Synechocystis</i> sp. PCC 6803	solanesyl diphosphate synthase	99%	65%
8	1R	<i>Synechocystis</i> sp. PCC 6803	solanesyl diphosphate synthase	97%	65%
8	2F	No similarity found			
8	2R	No similarity found			
8	3F	<i>Synechocystis</i> sp. PCC 6803	iron-regulated protein	96%	88%
8	3R	<i>Synechocystis</i> sp. PCC 6803	iron-regulated protein	96%	93%
8	4F	<i>Synechocystis</i> sp. PCC 6803	cation-transporting ATPase E1–E2 ATPase	99%	97%
8	4R	<i>Synechocystis</i> sp. PCC 6803	cation-transporting ATPase E1–E2 ATPase	99%	97%

Table S2. Set A. *Cont.*

8	5F	<i>Synechocystis</i> sp. PCC 6803	nitrate transport protein NrtD	99%	99%	
8	5R	<i>Synechocystis</i> sp. PCC 6803	nitrate transport protein NrtD	99%	98%	
8	6F	<i>Synechocystis</i> sp. PCC 6803	UDP- <i>N</i> -acetylmuramoyl-L-alanyl-D-glutamate synthetase	97%	97%	
8	6R	<i>Synechocystis</i> sp. PCC 6803	UDP- <i>N</i> -acetylmuramoyl-L-alanyl-D-glutamate synthetase	98%	97%	
8	7F	<i>Synechocystis</i> sp. PCC 6803	cob(I)yrinic acid a,c-diamide adenosyltransferase	98%	99%	
8	7R	<i>Synechocystis</i> sp. PCC 6803	cob(I)yrinic acid a,c-diamide adenosyltransferase	98%	98%	
8	8F	<i>Synechocystis</i> sp. PCC 6803	cytochrome; CytM	94%	93%	
8	8R	No similarity found				
8	12F	<i>Synechocystis</i> sp. PCC 6803	endo-1,4- β -glucanase	97%	97%	
8	12R	<i>Synechocystis</i> sp. PCC 6803	endo-1,4- β -glucanase	99%	95%	
8	13F	<i>Synechocystis</i> sp. PCC 6803	thiamine biosynthesis protein ThiC	98%	99%	
8	13R	<i>Synechocystis</i> sp. PCC 6803	thiamine biosynthesis protein ThiC	99%	99%	

Set B. *Synechocystis* sp. 6803 coverage sequences.

Sample	Primer	Organism	Protein	Identity	Query Coverage	
1	15F	No similarity found				
1	15R	No similarity found				
5	2F	No similarity found				
5	2R	<i>Synechocystis</i> sp. PCC 6803	NADH dehydrogenase subunit 4	98%	82%	
5	3F	<i>Synechocystis</i> sp. PCC 6803	iron-regulated protein	95%	73%	
5	3R	<i>Synechocystis</i> sp. PCC 6803	iron-regulated protein	94%	76%	
5	4F	<i>Synechocystis</i> sp. PCC 6803	cation-transporting ATPase E1-E2 ATPase	97%	96%	
5	4R	<i>Synechocystis</i> sp. PCC 6803	cation-transporting ATPase E1-E2 ATPase	98%	92%	
5	5F	<i>Synechocystis</i> sp. PCC 6803	plasmid pSYSX	84%	48%	
5	5R	No similarity found				
5	8F	<i>Synechocystis</i> sp. PCC 6803	cytochrome CytM	99%	84%	
5	8R	<i>Synechocystis</i> sp. PCC 6803	50S ribosomal protein L9	88%	15%	
5	11F	<i>Synechocystis</i> sp. PCC 6803	aspartate aminotransferase	96%	70%	
5	11R	<i>Synechocystis</i> sp. PCC 6803	aspartate aminotransferase	94%	85%	

Table S2. Set B. Cont.

5	13F	<i>Synechocystis</i> sp. PCC 6803	thiamine biosynthesis protein ThiC	93%	76%
5	13R	<i>Synechocystis</i> sp. PCC 6803	thiamine biosynthesis protein ThiC	89%	65%
6	1F	<i>Synechocystis</i> sp. PCC 6803	solanesyl diphosphate synthase	98%	60%
6	1R	<i>Synechocystis</i> sp. PCC 6803	solanesyl diphosphate synthase	95%	62%
6	8F	<i>Synechocystis</i> sp. PCC 6803	cytochrome; CytM	97%	94%
6	8R	<i>Synechocystis</i> sp. PCC 6803	cytochrome; CytM	91%	87%
6	10F	<i>Synechocystis</i> sp. PCC 6803	cation-transporting ATPase E1–E2 ATPase	95%	20%
6	10R	<i>Synechocystis</i> sp. PCC 6803	cation-transporting ATPase E1–E2 ATPase	87%	44%
6	11F	No similarity found			
6	11R	<i>Synechocystis</i> sp. PCC 6803	aspartate aminotransferase	87%	66%
6	12F	<i>Synechocystis</i> sp. PCC 6803	endo-1,4- β -glucanase	99%	82%
6	12R	<i>Synechocystis</i> sp. PCC 6803	endo-1,4- β -glucanase	98%	94%
6	13F	No similarity found			
6	13R	No similarity found			
7	1F	<i>Synechocystis</i> sp. PCC 6803	thiol:disulfide interchange protein DsbD	91%	11%
7	1R	<i>Synechocystis</i> sp. PCC 6803	thiol:disulfide interchange protein DsbD	91%	9%
7	2F	<i>Synechocystis</i> sp. PCC 6803	NAD(P)H-quinone oxidoreductase subunit 4	97%	31%
7	2R	No similarity found			
7	4F	<i>Synechocystis</i> sp. PCC 6803	cation-transporting ATPase E1–E2 ATPase	96%	51%
7	4R	No similarity found			
7	5F	<i>Synechocystis</i> sp. PCC 6803	nitrate transport protein NrtD	99%	68%
7	5R	<i>Synechocystis</i> sp. PCC 6803	nitrate transport protein NrtD	99%	98%
7	7F	<i>Synechocystis</i> sp. PCC 6803	cob(I)yrinic acid a,c-diamide adenosyltransferase	95%	90%
7	7R	<i>Synechocystis</i> sp. PCC 6803	cob(I)yrinic acid a,c-diamide adenosyltransferase	95%	60%
7	10F	<i>Synechocystis</i> sp. PCC 6803	cation-transporting ATPase E1–E2 ATPase	90%	87%
7	10R	<i>Synechocystis</i> sp. PCC 6803	cation-transporting ATPase E1–E2 ATPase	99%	98%
7	13F	<i>Synechocystis</i> sp. PCC 6803	thiamine biosynthesis protein ThiC	99%	95%
7	13R	<i>Synechocystis</i> sp. PCC 6803	thiamine biosynthesis protein ThiC	95%	89%

Table S2. Set B. *Cont.*

7	15F	Synechocystis sp. PCC 6803	dihydroxy-acid dehydratase	93%	46%
7	15R	Synechocystis sp. PCC 6803	dihydroxy-acid dehydratase	91%	40%
8	2F	Synechocystis sp. PCC 6803	NAD(P)H-quinone oxidoreductase subunit 4	99%	67%
8	2R	No similarity found			
8	4F	Synechocystis sp. PCC 6803	cation-transporting ATPase E1–E2 ATPase	99%	94%
8	4R	Synechocystis sp. PCC 6803	cation-transporting ATPase E1–E2 ATPase	99%	94%
8	5F	Synechocystis sp. PCC 6803	nitrate transport protein NrtD	96%	85%
8	5R	Synechocystis sp. PCC 6803	nitrate transport protein NrtD	91%	34%
8	12F	Synechocystis sp. PCC 6803	endo-1,4- β -glucanase	99%	94%
8	12R	Synechocystis sp. PCC 6803	endo-1,4- β -glucanase	98%	93%
8	14F	No similarity found			
8	14R	No similarity found			
8	15F	Synechocystis sp. PCC 6803	dihydroxy-acid dehydratase	94%	55%
8	15R	Synechocystis sp. PCC 6803	dihydroxy-acid dehydratase	88%	32%

Set C. *Synechocystis* sp. 6803 coverage sequences.

Sample	Primer	Organism	Protein	Identity	Query Coverage
1	5F	<i>Synechocystis</i> sp. PCC 6803	nitrate transport protein subunit NrtD	96%	90%
1	5R	<i>Synechocystis</i> sp. PCC 6803	nitrate transport protein subunit NrtD	95%	90%
2	5F	No similarity found			
2	5R	No similarity found			
2	6F	<i>Synechocystis</i> sp. PCC 6803	UDP- <i>N</i> -acetylmuramoyl-L-alanyl-D-glutamate synthetase	89%	52%
2	6R	No similarity found			
2	6F	<i>Synechocystis</i> sp. PCC 6803	UDP- <i>N</i> -acetylmuramoylalanine--D-glutamate ligase	92%	92%
2	6R	<i>Synechocystis</i> sp. PCC 6803	UDP- <i>N</i> -acetylmuramoylalanine--D-glutamate ligase	89%	79%
2	8F	<i>Synechocystis</i> sp. PCC 6803	cytochrome; CytM	95%	49%
2	8R	<i>Synechocystis</i> sp. PCC 6803	solanesyl diphosphate synthase	100%	77%
2	15F	<i>Synechocystis</i> sp. PCC 6803	dihydroxy-acid dehydratase	94%	74%
2	15R	<i>Synechocystis</i> sp. PCC 6803	dihydroxy-acid dehydratase	95%	83%

Table S2. Set C. Cont.

3	3F	<i>Synechocystis</i> sp. PCC 6803	iron-regulated protein	95%	74%
3	3R	<i>Synechocystis</i> sp. PCC 6803	iron-regulated protein	97%	54%
3	4F	<i>Synechocystis</i> sp. PCC 6803	cation-transporting ATPase E1–E2 ATPase	98%	92%
3	4R	<i>Synechocystis</i> sp. PCC 6803	cation-transporting ATPase E1–E2 ATPase	96%	93%
3	5F	<i>Synechocystis</i> sp. PCC 6803	nitrate transport protein NrtD	96%	77%
3	5R	<i>Synechocystis</i> sp. PCC 6803	nitrate transport protein NrtD	89%	36%
3	9F	No similarity			
3	9R	No similarity			
3	10F	No similarity found			
3	10R	No similarity found			
3	15F	<i>Synechocystis</i> sp. PCC 6803	dihydroxy-acid dehydratase	94%	50%
3	15R	<i>Synechocystis</i> sp. PCC 6803	hypothetical protein	90%	37%
4	1F	<i>Synechocystis</i> sp. PCC 6803	solaneyl diphosphate synthase	97%	57%
4	1R	<i>Synechocystis</i> sp. PCC 6803	solaneyl diphosphate synthase	95%	77%
4	2F	<i>Synechocystis</i> sp. PCC 6803	NAD(P)H-quinone oxidoreductase subunit 4	97%	86%
4	2R	<i>Synechocystis</i> sp. PCC 6803	NAD(P)H-quinone oxidoreductase subunit 4	96%	89%
4	3F	<i>Synechocystis</i> sp. PCC 6803	iron-regulated protein	87%	34%
4	3R	<i>Synechocystis</i> sp. PCC 6803	iron-regulated protein	88%	19%
4	5F	<i>Synechocystis</i> sp. PCC 6803	nitrate transport protein subunit NrtD	95%	92%
4	5R	<i>Synechocystis</i> sp. PCC 6803	nitrate transport protein subunit NrtD	97%	88%
4	6F	<i>Synechocystis</i> sp. PCC 6803	UDP- <i>N</i> -acetylmuramoylalanine--D-glutamate ligase	97%	95%
4	6R	<i>Synechocystis</i> sp. PCC 6803	UDP- <i>N</i> -acetylmuramoylalanine--D-glutamate ligase	97%	98%
4	7F	<i>Synechocystis</i> sp. PCC 6803	cob(I)yrinic acid a,c-diamide adenosyltransferase	99%	63%
4	7R	<i>Synechocystis</i> sp. PCC 6803	hypothetical protein	90%	45%
4	10F	<i>Synechocystis</i> sp. PCC 6803	cation-transporting ATPase E1–E2 ATPase	98%	98%
4	10R	<i>Synechocystis</i> sp. PCC 6803	cation-transporting ATPase E1–E2 ATPase	99%	99%
4	12F	<i>Synechocystis</i> sp. PCC 6803	endo-1,4- β -glucanase	98%	93%
4	12R	<i>Synechocystis</i> sp. PCC 6803	endo-1,4- β -glucanase	94%	52%

Table S2. Set C. Cont.

4	14F	<i>Synechocystis</i> sp. PCC 6803	dihydrodipicolinate synthase	93%	81%
4	14R	<i>Synechocystis</i> sp. PCC 6803	solaneyl diphosphate synthase	93%	16%
5	2F	<i>Synechocystis</i> sp. PCC 6803	NAD(P)H-quinone oxidoreductase subunit 4	86%	54%
5	2R	<i>Synechocystis</i> sp. PCC 6803	NAD(P)H-quinone oxidoreductase subunit 4	98%	65%
5	5F	<i>Synechocystis</i> sp. PCC 6803	plasmid pSYSX	83%	32%
5	5R	<i>Synechocystis</i> sp. PCC 6803	plasmid pSYSX	98%	60%
5	6F	<i>Synechocystis</i> sp. PCC 6803	UDP- <i>N</i> -acetylmuramoyl-L-alanyl-D-glutamate synthetase	99%	87%
5	6R	No similarity found			
5	6F	<i>Synechocystis</i> sp. PCC 6803	UDP- <i>N</i> -acetylmuramoylalanine--D-glutamate ligase	93%	43%
5	6R	<i>Synechocystis</i> sp. PCC 6803	UDP- <i>N</i> -acetylmuramoylalanine--D-glutamate ligase	89%	35%
5	9F	<i>Synechocystis</i> sp. PCC 6803	OmpR subfamily protein Ycf27/Rre26	95%	90%
5	9R	<i>Synechocystis</i> sp. PCC 6803	OmpR subfamily protein Ycf27/Rre26	96%	84%
5	10F	<i>Synechocystis</i> sp. PCC 6803	cation-transporting ATPase E1–E2 ATPase	99%	98%
5	10R	<i>Synechocystis</i> sp. PCC 6803	cation-transporting ATPase E1–E2 ATPase	99%	97%
5	13F	<i>Synechocystis</i> sp. PCC 6803	thiamine biosynthesis protein ThiC	85%	56%
5	13R	<i>Synechocystis</i> sp. PCC 6803	thiamine biosynthesis protein ThiC	96%	65%
5	14F	<i>Synechocystis</i> sp. PCC 6803	ABC transporter	95%	61%
5	14R	<i>Synechocystis</i> sp. PCC 6803	ABC transporter	99%	60%
5	15F	No similarity			
5	15R	No similarity			
6	1F	<i>Synechocystis</i> sp. PCC 6803	solaneyl diphosphate synthase	96%	79%
6	1R	<i>Synechocystis</i> sp. PCC 6803	solaneyl diphosphate synthase	97%	51%
6	2F	<i>Synechocystis</i> sp. PCC 6803	NADH dehydrogenase subunit 4	99%	88%
6	2R	<i>Synechocystis</i> sp. PCC 6803	NADH dehydrogenase subunit 4	95%	91%
6	3F	<i>Synechocystis</i> sp. PCC 6803	iron-regulated protein	96%	62%
6	3R	<i>Synechocystis</i> sp. PCC 6803	iron-regulated protein	98%	69%
6	4F	<i>Synechocystis</i> sp. PCC 6803	hypothetical protein	97%	79%
6	4R	<i>Synechocystis</i> sp. PCC 6803	cation-transporting ATPase E1–E2 ATPase	99%	79%

Table S2. Set C. Cont.

6	5F	<i>Synechocystis</i> sp. PCC 6803	nitrate transport protein NrtD	96%	27%
6	5R	<i>Synechocystis</i> sp. PCC 6803	nitrate transport protein NrtD	93%	23%
6	6F	<i>Synechocystis</i> sp. PCC 6803	UDP- <i>N</i> -acetylmuramoylalanine--D-glutamate ligase	96%	88%
6	6R	<i>Synechocystis</i> sp. PCC 6803	UDP- <i>N</i> -acetylmuramoylalanine--D-glutamate ligase	98%	96%
6	8F	<i>Synechocystis</i> sp. PCC 6803	DNA gyrase subunit A	93%	86%
6	8R	<i>Synechocystis</i> sp. PCC 6803	DNA gyrase subunit A	94%	81%
6	9F	<i>Synechocystis</i> sp. PCC 6803	arsenate reductase	96%	71%
6	9R	<i>Synechocystis</i> sp. PCC 6803	OmpR subfamily	88%	12%
6	10F	<i>Synechocystis</i> sp. PCC 6803	gamma-glutamyl phosphate reductase	99%	92%
6	10R	<i>Synechocystis</i> sp. PCC 6803	high-affinity branched-chain amino acid transport ATP-bin	99%	85%
6	12F	<i>Synechocystis</i> sp. PCC 6803	endo-1,4- β -glucanase	97%	88%
6	12R	<i>Synechocystis</i> sp. PCC 6803	endo-1,4- β -glucanase	97%	91%
6	13F	<i>Synechocystis</i> sp. PCC 6803	thiamine biosynthesis protein ThiC	90%	52%
6	13R	<i>Synechocystis</i> sp. PCC 6803	serum resistance locus; BrkB	97%	77%
6	14F	<i>Synechocystis</i> sp. PCC 6803	penicillin-binding protein 4	97%	75%
6	14R	<i>Synechocystis</i> sp. PCC 6803	dihydrodipicolinate synthase	93%	62%
7	1F	<i>Synechocystis</i> sp. PCC 6803	solaneyl diphosphate synthase	94%	65%
7	1R	<i>Synechocystis</i> sp. PCC 6803	solaneyl diphosphate synthase	93%	77%
7	4F	<i>Synechocystis</i> sp. PCC 6803	cation-transporting ATPase E1–E2 ATPase	99%	89%
7	4R	<i>Synechocystis</i> sp. PCC 6803	cation-transporting ATPase E1–E2 ATPase	98%	86%
7	6F	<i>Synechocystis</i> sp. PCC 6803	UDP- <i>N</i> -acetylmuramoylalanine--D-glutamate ligase	95%	94%
7	6R	<i>Synechocystis</i> sp. PCC 6803	UDP- <i>N</i> -acetylmuramoylalanine--D-glutamate ligase	95%	94%
7	8F	<i>Synechocystis</i> sp. PCC 6803	cytochrome CytM	95%	89%
7	8R	<i>Synechocystis</i> sp. PCC 6803	50S ribosomal protein L9	93%	84%
7	9F	No similarity			
7	9R	No similarity			
7	13F	<i>Synechocystis</i> sp. PCC 6803	thiamine biosynthesis protein ThiC	97%	81%
7	13R	<i>Synechocystis</i> sp. PCC 6803	thiamine biosynthesis protein ThiC	94%	83%

Table S2. Set C. *Cont.*

7	14F	<i>Synechocystis</i> sp. PCC 6803	hypothetical protein	93%	88%
7	14R	<i>Synechocystis</i> sp. PCC 6803	bifunctional nicotinamide mononucleotide adenylyltransfer	99%	13%
8	1F	<i>Synechocystis</i> sp. PCC 6803	solanesyl diphosphate synthase	99%	93%
8	1R	<i>Synechocystis</i> sp. PCC 6803	solanesyl diphosphate synthase	99%	84%
8	2F	<i>Synechocystis</i> sp. PCC 6803	NAD(P)H-quinone oxidoreductase subunit 4	95%	29%
8	2R	<i>Synechocystis</i> sp. PCC 6803	NAD(P)H-quinone oxidoreductase subunit 4	92%	65%
8	3F	<i>Synechocystis</i> sp. PCC 6803	iron-regulated protein	98%	73%
8	3R	<i>Synechocystis</i> sp. PCC 6803	iron-regulated protein	99%	85%
8	4F	<i>Synechocystis</i> sp. PCC 6803	cation-transporting ATPase E1–E2 ATPase	95%	50%
8	4R	<i>Synechocystis</i> sp. PCC 6803	cation-transporting ATPase E1–E2 ATPase	93%	54%
8	5F	<i>Synechocystis</i> sp. PCC 6803	nitrate transport protein NrtD	94%	88%
8	5R	<i>Synechocystis</i> sp. PCC 6803	nitrate transport protein NrtD	96%	77%
8	6F	No similarity found			
8	6R	No similarity found			
8	8F	<i>Synechocystis</i> sp. PCC 6803	cytochrome; CytM	98%	87%
8	8R	<i>Synechocystis</i> sp. PCC 6803	solanesyl diphosphate synthase	98%	86%
8	10F	<i>Synechocystis</i> sp. PCC 6803	cation-transporting ATPase E1–E2 ATPase	99%	99%
8	10R	<i>Synechocystis</i> sp. PCC 6803	cation-transporting ATPase E1–E2 ATPase	99%	99%
8	13F	<i>Synechocystis</i> sp. PCC 6803	thiamine biosynthesis protein ThiC	98%	67%
8	13R	<i>Synechocystis</i> sp. PCC 6803	thiamine biosynthesis protein ThiC	98%	78%
8	14F	<i>Synechocystis</i> sp. PCC 6803	dihydrodipicolinate synthase	96%	33%
8	14R	<i>Synechocystis</i> sp. PCC 6803	solanesyl diphosphate synthase	95%	15%

Table S3. Lysis protocols for *Synechocystis* sp. PCC 6803 and their effects assessed by visual inspection. Each column is a separate protocol numbered in order of attempt. Each “protocol step” cell is subdivided into reagents used, duration, temperature, and observations of the supernatant and cell pellet following centrifugation after each step.

Conditions	Protocol 0	Protocol 1	Protocol 2	Protocol 3	Protocol 4
Step 1	1% Sarkosyl in Buffer A	0.1% Sarkosyl in Buffer A	0.1% Sarkosyl in Buffer A	0.1% Sarkosyl in Buffer A	0.1% Sarkosyl in Buffer A
Time	2 h	Wash	Wash	Wash	Wash
Temperature	30 °C	Room Temp	Room Temp	Room Temp	Room Temp
Supernatant	Clear	Clear	Clear	Clear	Clear
Pellet	No effect	No effect	No effect	No effect	No effect
Step 2	200 U/μL Lysozyme in TES Buffer	10 μg/mL Proteinase K + 0.1% Sarkosyl in TES Buffer	10 μg/mL Proteinase K + 0.1% SDS in TES Buffer	10 μg/mL Proteinase K + 0.1% SDS in TES Buffer	10 μg/mL Proteinase K + 0.1% SDS in TES Buffer
Time	2 h	2 h	2 h	2 h	2 h
Temperature	37 °C	57 °C	57 °C	57 °C	57 °C
Supernatant	Clear	Yellow color	Dark rust color	Dark rust color	Dark rust color
Pellet	No effect	No effect	Slight deflation	Slight deflation	Slight deflation
Step 3	5 μg/mL Proteinase K in TES Buffer	200 U/μL Lysozyme in TES Buffer	200 U/μL Lysozyme in TES Buffer	200 U/μL Lysozyme in SoluLyse	200 U/μL Lysozyme in SoluLyse
Time	1 h	2 h	2 h	2 h	2 h
Temperature	57 °C	37 °C	37 °C	37 °C	37 °C
Supernatant	Clear	Clear	Clear	No effect	Gold color
Pellet	No effect	No effect	More deflation	Very degraded	Very degraded
Step 4	DLB	DLB	DLB		DLB
Time	1 h	1 h	1 h		1 h
Temperature	Room Temp	Room Temp	70 °C		37 °C–57 °C
Supernatant	Clear	Clear	Green		Gold color
Pellet	No effect	No effect	Smaller, brown		No cell pellet