Candidatus Chloracidobacterium thermophilum: An Aerobic Phototrophic Acidobacterium

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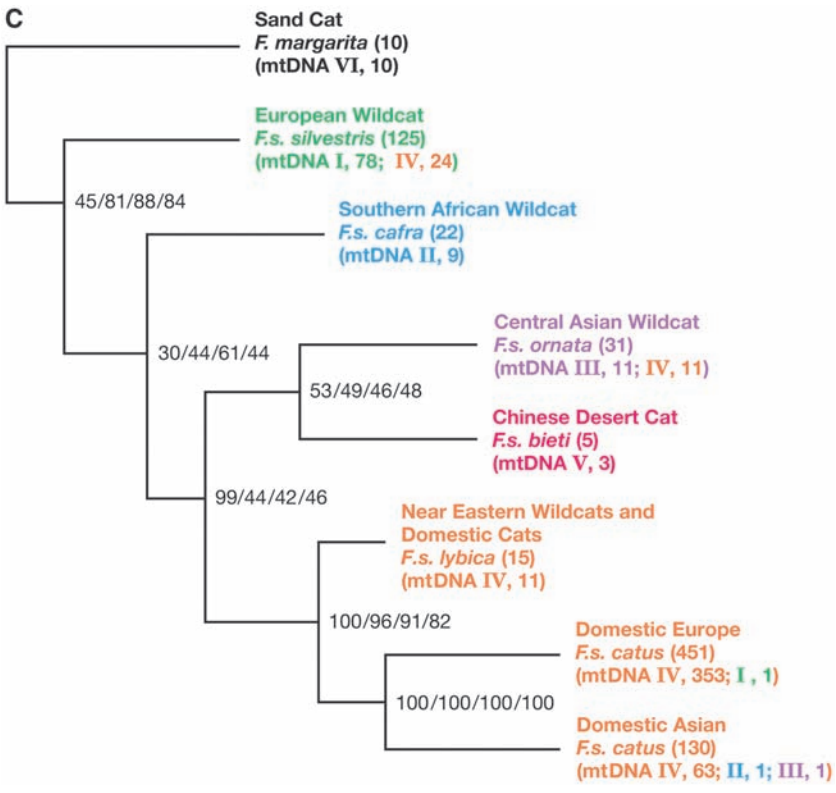

farmers of the Fertile Crescent domesticated grains and cereals as well as livestock (*1*, *3*, *4*, *30*–*32*). In parallel, the endemic wildcats of the region may have adapted by both regulating the rodents in the grain stores and abandoning their aggressive wild-born behaviors. The archaeological imprints left in the genomes of living cats here weigh into inferences about the timing, steps, and provenance of domestication—a dynamic exercise depicted in art, in history, and in human cultural development since recorded evidence began.

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Supporting Online Material

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Candidatus Chloracidobacterium thermophilum: An Aerobic Phototrophic Acidobacterium

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Only five bacterial phyla with members capable of chlorophyll (Chl)–based phototrophy are presently known. Metagenomic data from the phototrophic microbial mats of alkaline siliceous hot springs in Yellowstone National Park revealed the existence of a distinctive bacteriochlorophyll (BChl)–synthesizing, phototrophic bacterium. A highly enriched culture of this bacterium grew photoheterotrophically, synthesized BChls a and c under oxic conditions, and had chlorosomes and type 1 reaction centers. "*Candidatus* Chloracidobacterium thermophilum" is a BChl-producing member of the poorly characterized phylum *Acidobacteria*.

Sequencing environmental DNA is a powerful approach for predicting the physiological and metabolic potential of microbial ecosystems. Metagenomic analyses have provided insights into the properties of uncultured microorganisms that have escaped detection in field studies (*1*–*6*). We used metagenomic data from the microbial mat communities

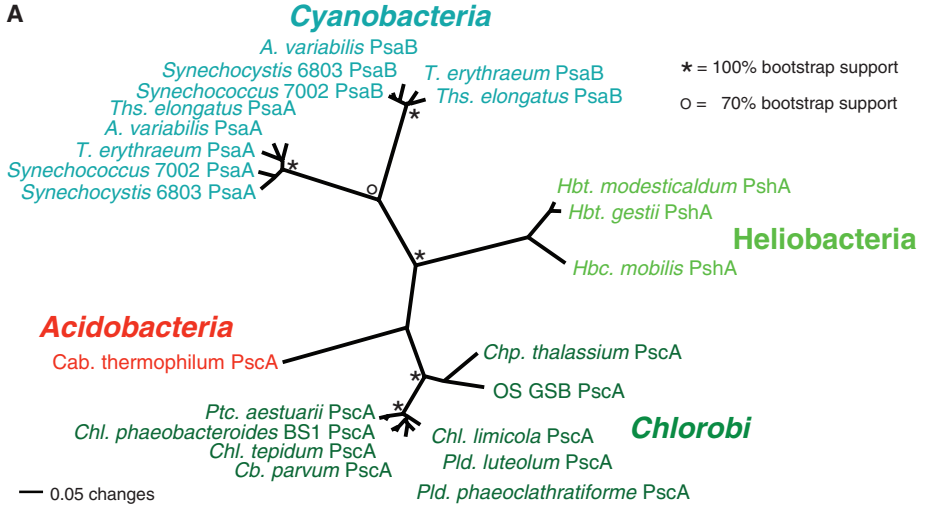
of Octopus and Mushroom Springs in Yellowstone National Park (Yellowstone NP) (*5*–*7*) to search for previously unrecognized BChl/Chl-synthesizing phototrophs (chlorophototrophs).

Only five bacterial phyla contain chlorophototrophs: *Cyanobacteria*, *Chlorobi*, *Proteobacteria*, *Chloroflexi*, and *Firmicutes* (*8*, *9*). In chlorophototrophs, light energy is transduced into chemical potential energy by reaction centers, photo-oxidoreductases that form two families of BChl/Chl-containing, pigment-protein complexes (*10*). Type 1 reaction centers include cyanobacterial Photosystem I and the homodimeric reaction centers of *Chlorobi* and heliobacteria (*Firmicutes*). Type 2 reaction centers include cyanobacterial Photosystem II and the reaction centers of *Proteobacteria* and *Chloroflexi*. Although their subunits are not discernibly similar in sequence, the two reaction-center types probably share a common evolutionary origin because their electron-transfer domains have similar structures and cofactor arrangements (*11*).

16*S* ribosomal RNA (rRNA) surveys of the Yellowstone NP phototrophic mat communities suggested the presence of green sulfur bacteria (*12*). Metagenomic data obtained from these mats (*5*–*7*, *9*) were queried with the tblastn algorithm and the amino acid sequence of PscA, the BChl a–binding apoprotein of a homodimeric, P840-binding, type 1 reaction center from *Chlorobium tepidum* (*9*, *13*). Two incomplete sequences that encode (B)Chl-binding apoproteins of type 1 reaction centers were recovered. Phylogenetic analyses suggested that one sequence (OS GSB PscA) belonged to a green sulfur bacterium that grouped with PscA from *Chloroherpeton thalassium* (Fig. 1A). The second sequence, labeled Cab. thermophilum PscA, was only very distantly related to other PscA sequences and other type 1 reaction-center proteins (Fig. 1A and figs. S1 to S3); this suggested the existence of a previously unrecognized chlorophototroph in the mat community. Plasmids encoding this gene were recovered and sequenced (*9*), and the data revealed a probable operon, 5′*pscAB-fmoA* (Fig. 1B). *pscB* encodes the apoprotein of an 8Fe-8S ferredoxin of a type 1 reaction center (*13*), and *fmoA* encodes the BChl a–binding, Fenna-Matthews-Olson protein (Fig. 1B and figs. S4 and S5) (*14*). The *pscA* gene predicted a protein of 865 amino acids that was larger than the apoproteins of other type 1 reaction centers. Most of the size difference was caused by an insertion of ~165 amino acids into a periplasmic loop between transmembrane α helices VII and VIII (Fig. 1C and fig. S1). Many of the genes flanking the *pscAB-fmoA* operon predicted proteins that were most similar to those of *Acidobacterium* sp. Ellin345 or *Solibacter usitatus* Ellin6076, two soil bacteria belonging to the poorly characterized phylum *Acidobacteria*, whose genomes were recently sequenced. Thus, we hypothesized that the unknown phototroph might belong to the phylum *Acidobacteria*.

Analyses of metagenomic sequence data and end-reads from a bacterial artificial chromosome (BAC) library predicted that the *pscAB-fmoA*, *recA*, and rRNA genes were encoded on a single BAC insert (*9*). We confirmed this prediction by sequencing the 271,846–base pair (bp) insert (fig. S6; GenBank accession number EF531339). The 16*S* rRNA sequence derived from this BAC clone was identical to a partial sequence assembled from the metagenome and was nearly identical (differences at 2 of 1348 shared positions) to that from an acidobacterium denoted GFP1 [see 16*S* rRNA tree in figure 1 of (*15*); or see (*16*)] (fig. S7). The 16*S* rRNA of GFP1 was recovered from Green Finger Pool in the Lower Geyser Basin of Yellowstone NP, a site ~5 km from Octopus Spring. These data unequivocally establish that the divergent *pscAB-fmoA* genes are derived from a GFP1-like organism belonging to the phylum *Acidobacteria*.

To gain insights into the physiology and metabolism of this GFP1-like organism, we computer-annotated and analyzed the binned sequence assemblies putatively derived from the GFP1-like acidobacterium (*9*). The binned sequences contained several genes for BChl (*bchG*, *bchK*, *bchR*, *bchU*, *bchY*, and *acsF*) and carotenoid (*crtB*, *crtP*, and *crtH*) biosynthesis (figs. S6 to S10). A *csmA* gene, the product of



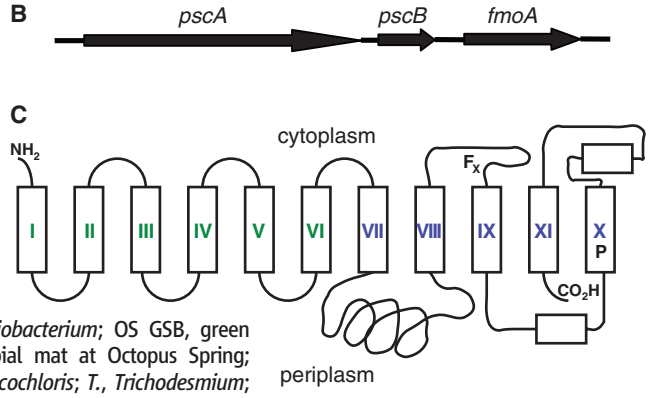


Fig. 1. (**A**) Unrooted neighbor-joining tree of protein sequences for type 1 reaction centers from *Cyanobacteria*, *Chlorobi*, heliobacteria, and a divergent PscA-like sequence (Cab. thermophilum) obtained from the mat metagenome of Octopus and Mushroom Springs, Yellowstone NP. *A.*, *Anabaena*; Cab., Chloracidobacterium; *Cb.*, *Chlorobaculum*; *Chl.*, *Chlorobium*; *Chp.*, *Chloroherpeton*; *Hbc.*, *Heliobacillus*; *Hbt.*, *Heliobacterium*; OS GSB, green sulfur bacterium from microbial mat at Octopus Spring; *Pld.*, *Pelodictyon*; *Ptc.*, *Prosthecochloris*; *T.*, *Trichodesmium*; *Ths.*, *Thermosynechococcus*. Nodes marked with a "*" have 100% bootstrap support; the node separating the PsaA and PsaB clades is marked with a "o" and has 70% bootstrap support. (**B**) Organization of the *pscA*, *pscB*, and *fmoA* genes in Cab. thermophilum. (**C**) Diagram showing the organization of the 11 predicted transmembrane α helices of Cab. thermophilum PscA. "F_X" denotes the positions of two cysteine residues that are predicted to be ligands to the intersubunit [4Fe-4S] cluster F_X, and "P" indicates the approximate position of the conserved histidine residue predicted to form a ligand to one of the two predicted BChl a molecules of the reaction-center special pair. Green Roman numerals I to VI indicate the antenna domain, and blue Roman numerals VII to XI indicate the electron-transfer domain.

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which forms the baseplate of chlorosomes, the light-harvesting antenna complexes in *Chlorobi* and *Chloroflexi* (*17*), was also found. The presence of genes encoding subunits of a nicotinamide adenine dinucleotide, reduced (NADH): quinone oxidoreductase, the quinol:cytochrome c oxidoreductase, and cytochrome oxidase implied that the acidobacterium might respire aerobically. The data collectively predicted that the mat acidobacterium is probably an aerobic photoheterotroph that synthesizes BChl a, methylated BChl c, chlorosomes, FmoA, and type 1 reaction centers. The organism seemed physiologically most similar to aerobic anoxygenic phototrophs or to facultatively photo(auto/hetero)trophic organisms like *Roseiflexus* and *Chloroflexus* spp. (*8*).

Allewalt *et al*. (*18*) described the establishment of uni-cyanobacterial enrichments for thermophilic *Synechococcus* spp. from Octopus Spring (Fig. 2A). The presence of a closely related acidobacterium in an oxic enrichment was indicated by specific polymerase chain reaction (PCR) amplification of genes for acidobacterial *pscA*, *fmoA*, *csmA*, *acsF*, *bchU*, *recA*, and 16*S* rRNA (*9*) (table S1). By serially culturing this enrichment culture in a modified cyanobacterial growth medium containing ammonium, a mixture of carbon sources, and the Photosystem II inhibitor atrazine (*9*), we eliminated *Synechococcus* sp. strain JA-2-3B'a (2-13). The resulting brownish-orange culture contained only the acidobacterium and *Anoxybacillus* sp. (Fig. 2A). The latter could be isolated on Luria-Bertani plates, did not synthesize BChl (Fig. 2A), and did not possess any genes for BChl biosynthesis or formation of a light-harvesting apparatus. The absorption spectrum of the enrichment culture shows a maximum at 743 to 745 nm that is characteristic of BChl c aggregates in chlorosomes (Fig. 2B). Using a method for the isolation of chlorosomes from green sulfur bacteria (*9*), we isolated chlorosomes that were morphologically similar to those of *C. tepidum* (*17*) (Fig. 3). Serial culturing of the *Anoxybacillus* sp.–acidobacterium enrichment in the dark resulted in the simultaneous loss of the 746-nm absorbance (Fig. 2B) and acidobacterial 16*S* rRNA (Fig. 2C). This experiment definitively establishes that the acidobacterium grows photoheterotrophically. The enrichment did not grow with bicarbonate as the sole carbon source.

High-performance liquid chromatography (HPLC) analyses of pigments extracted from cells from the *Anoxybacillus* sp.–acidobacterium enrichment verified the presence of both BChl c and BChl a (Fig. 4). The complex pattern of BChl c homologs, appearing in groupings of four (fig. S13), was consistent with methylation of both the C-8[2] and C-12[1] carbons, as occurs in *C. tepidum* and other *Chlorobi* strains (*19*). The elution profile also indicated that BChl c was esterified by several alcohol species. Only trace amounts of farnesylated BChl c were detected, and the major BChl c homologs were more hydrophobic than farnesylated BChl c, the esterifying alcohol most commonly found in green sulfur bacteria (Fig. 4). The major BChl c homologs were slightly more hydrophobic than the BChl c homologs produced by *Chloroflexus aurantiacus* Y-400-fl (Fig. 4). However, *Chloroflexus* spp. do not methylate BChl c at the C-8[2] or C-12[1] positions, and their BChl c is typically esterified with multiple alcohols including phytol, geranylgeraniol, and stearol (*8*, *19*).

16*S* rRNA analyses, including the present study, indicate that the acidobacterial chlorophototroph grows at temperatures from ~50° to 66°C at Mushroom Spring, Octopus Spring, and Green Finger Pool (*15*, *20*). 16*S* rRNA sequences closely related to that of this acidobacterium have also been recovered from Mammoth Hot Springs in Yellowstone NP and from hot springs in Tibet and Thailand (*21*, *22*). Therefore, acidobacterial chlorophototrophs may be members of microbial mat communities associated with thermal features worldwide. Because strains of *Acidobacteria* are also widely distributed in soils and other environments (*15*, *23*), it will be interesting to determine whether phototrophy is widespread in this poorly characterized phylum. Analyses of the genomes of two acidobacteria, *S. usitatus* Ellin6076 and *Acidobacterium* sp. Ellin345, demonstrate that these organisms do not have this capability (*24*).

In this study we applied metagenomics to discover a previously unknown chlorophototroph, and we used enrichment techniques and biochemical methods to verify that this organism is a bacillus (Fig. 2, D and E) that synthesizes BChls

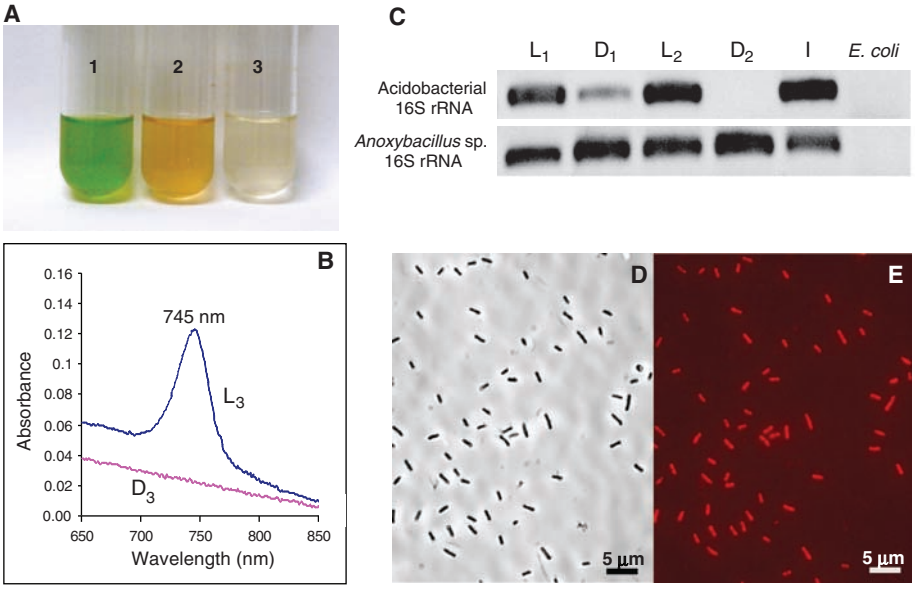

Fig. 2. (**A**) Cultures containing (1) *Synechococcus* sp. strain JA-2-3B'a (2-13), Cab. Thermophilum, and *Anoxybacillus* sp.; (2) Cab. thermophilum and *Anoxybacillus* sp.; and (3) *Anoxybacillus* sp. (**B**) Absorption spectra of an enrichment culture containing Cab. thermophilum and *Anoxybacillus* sp. after serial culturing three times in the light (L_3) or in the dark (D_3). The 745-nm absorption due to aggregated BChl c is only observed in the light-grown cells. Note the change from 746 to 745 nm to match the number in the figure. (**C**) PCR amplification with the use of primers (*9*) (table S1) specific for Cab. thermophilum (top) and *Anoxybacillus* sp. (bottom) and DNA templates isolated from an initial light-grown inoculum (I), and serial cultures 1 and 2 grown for two periods of 5 days exclusively in the light (L_1, L_2) or in the dark (D_1, D_2). *Escherichia coli* DNA was tested as a negative control with both primer sets. For additional details, see (*9*). (**D**) Light micrograph of a 5-day-old enrichment culture containing Cab. thermophilum and *Anoxybacillus* sp. grown in the light. (**E**) Fluorescence micrograph of the field of cells in (D). Cells were treated with 1-hexanol to disrupt the BChl c aggregates and to enhance BChl c fluorescence (*9*).

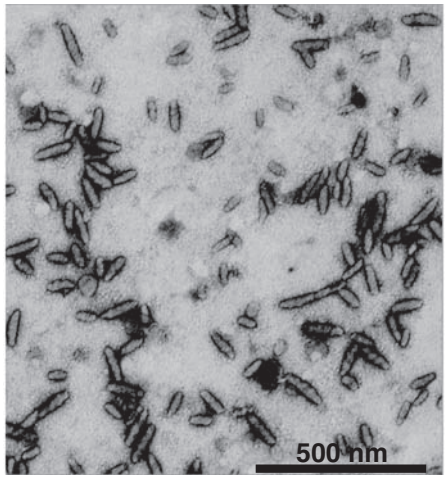

Fig. 3. Transmission electron micrograph of isolated chlorosomes from an enrichment culture containing Cab. thermophilum and *Anoxybacillus* sp. after negative staining with 1% (w/v) uranyl acetate.

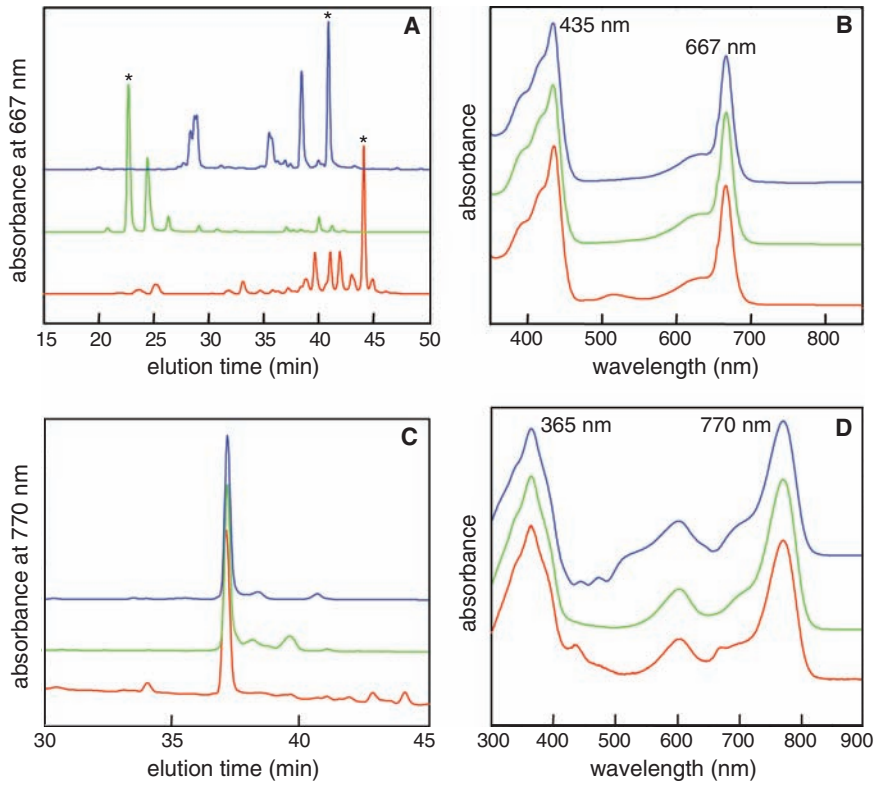

Fig. 4. HPLC elution profiles monitored at 667 nm for BChl c (**A**) and 770 nm for BChl a (**C**) for pigments extracted from a light-grown culture containing Cab. thermophilum and *Anoxybacillus* sp. (red line); *Chlorobium tepidum* (green line); and *Chloroflexus aurantiacus* strain Y-400-fl (blue line). The spectra of the BChl c peaks indicated by stars in (A) are shown in (**B**); the spectra of the BChl a peaks eluting at 37 min in (C) are shown in (**D**). All other peaks in (A) also had the absorption spectrum of BChl c.

a and c and produces chlorosomes under oxic conditions. Although chlorosomes are also found in some *Chloroflexi*, the new chlorophototroph is the only described organism outside the phylum *Chlorobi* that produces FmoA. Growth of this acidobacterium is strongly stimulated by light under photoheterotrophic conditions, but additional studies will be required to establish whether the organism is capable of autotrophic growth. Because no chlorophototroph with these properties has yet been described, we propose the name "*Candidatus* Chloracidobacterium thermophilum," gen. nov., sp. nov., for this BChl-synthesizing, phototrophic member of the phylum *Acidobacteria*.

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Supporting Online Material

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Noise in Gene Expression Determines Cell Fate in *Bacillus subtilis*

Hédia Maamar,† Arjun Raj,*† David Dubnau‡

Random cell-to-cell variations in gene expression within an isogenic population can lead to transitions between alternative states of gene expression. Little is known about how these variations (noise) in natural systems affect such transitions. In *Bacillus subtilis*, noise in ComK, the protein that regulates competence for DNA uptake, is thought to cause cells to transition to the competent state in which genes encoding DNA uptake proteins are expressed. We demonstrate that noise in *comK* expression selects cells for competence and that experimental reduction of this noise decreases the number of competent cells. We also show that transitions are limited temporally by a reduction in *comK* transcription. These results illustrate how such stochastic transitions are regulated in a natural system and suggest that noise characteristics are subject to evolutionary forces.

Variability in gene expression within a population of genetically identical cells enables those cells to maintain a diversity of phenotypes, potentially enhancing fitness (*1*, *2*). When the underlying gene network contains regulatory positive feedback loops, indi-