GENETICS AND MOLECULAR BIOLOGY FOR ENVIRONMENTAL ANALYSIS

MOLECULAR ECOLOGY

LESSON 18: MICROBIAL GENOMICS

Prof. Alberto Pallavicini

pallavic@units.it

A new evaluation of our life-support system

- After more than 150 years of research in microbiology, new technologies and new insights into the microbial world have sparked a revolution in the field.
- This is a much needed development, not only to renew interest in prokaryote research, but also to meet many emerging challenges in medicine, agriculture and industrial processes.

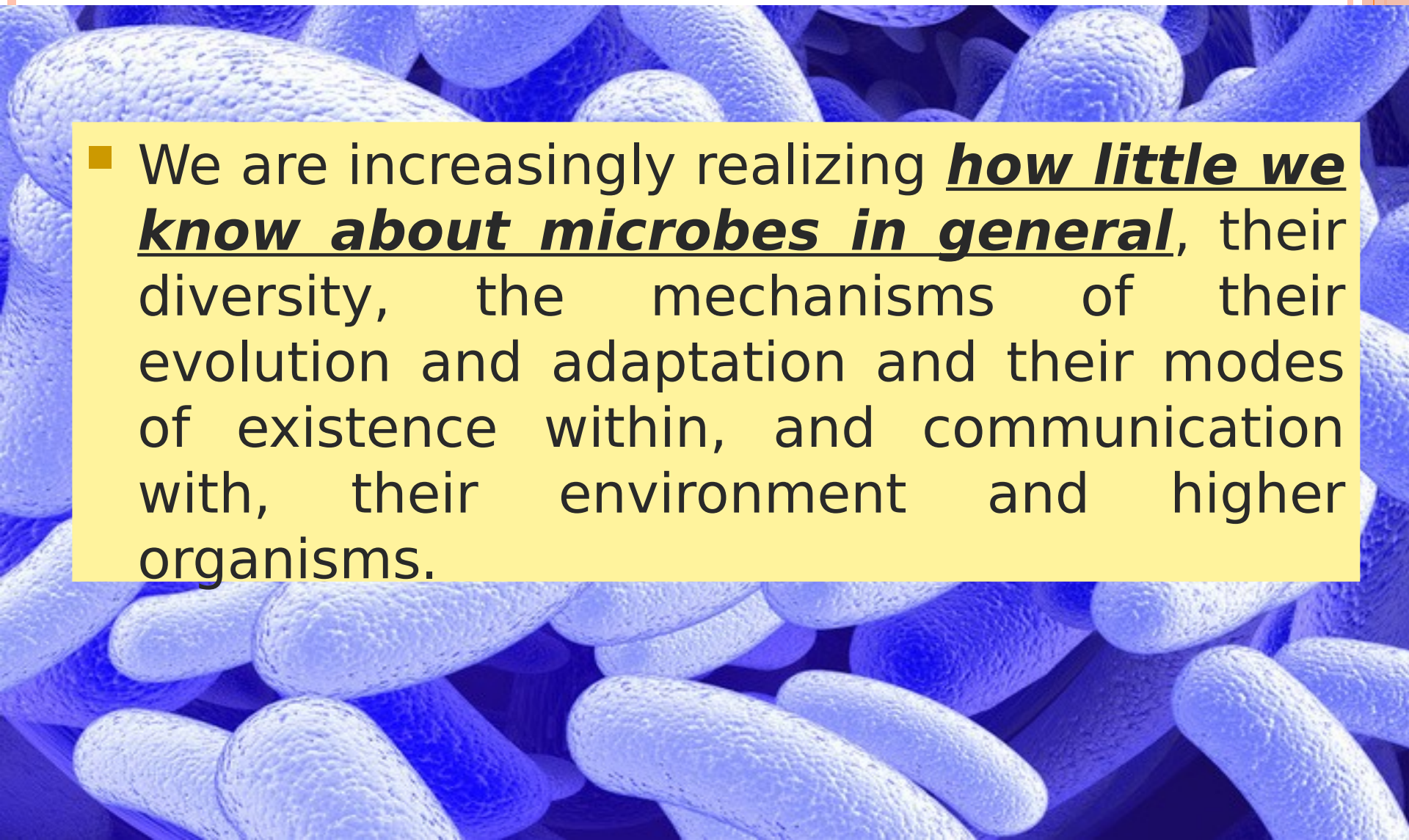
A new evaluation of our life-support system

Although many microbiologists, such as Emil von Behring, Robert Koch, Jacques Monod, François Jacob, André Lwoff, Alexander Fleming, Selman A. Waksman and Joshua Lederberg, grace the list of Nobel laureates, **attention moved away from microbiology as biologists focused their interest on eukaryotic cells and higher organisms in the 1970s and 1980s.**

A new evaluation of our life-support system

- Furthermore, from the beginning, research on prokaryotes has suffered from an **anthropocentric view**, regarding as interesting only those organisms that cause disease or that can be exploited for industrial or agricultural use.
- But the advent of new technologies, some of which have been driven by a need to understand eukaryotes, may change this.

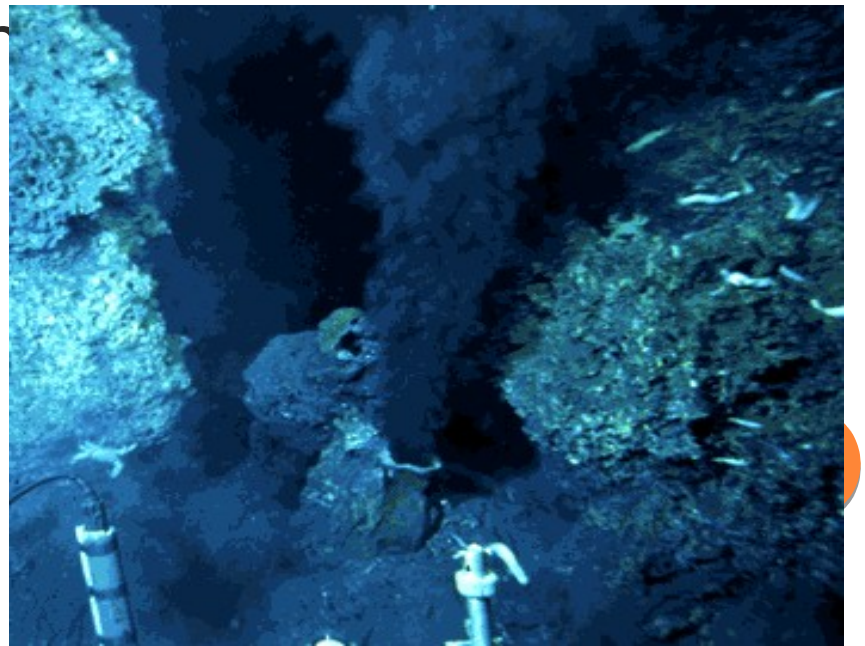
A new evaluation of our life-support system



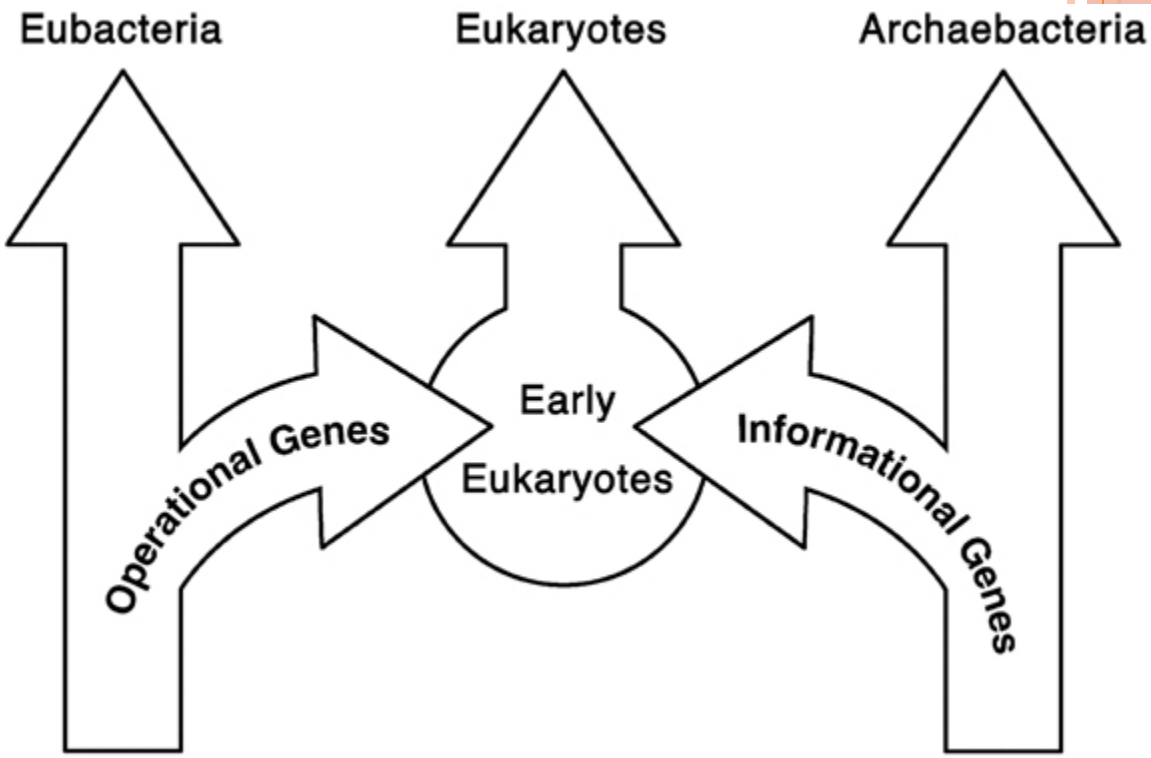
- We are increasingly realizing ***how little we know about microbes in general***, their diversity, the mechanisms of their evolution and adaptation and their modes of existence within, and communication with, their environment and higher organisms.

A new evaluation of our life-support system

- As bacteria have succeeded in occupying virtually all ecological niches on this planet, ranging from **arctic regions to oceanic hot springs**, they hold an immense wealth of genetic information that we have barely started to explore and that may provide many useful application



Microbes are the **founder members** of this planet and understanding bacterial function is a first priority in biology because of the critical role of microbes in the maintenance of all other forms of life.



A new evaluation of our life-support system

Bacterial benefactors—and other prokaryotic pursuits

- If the process of evolution is to be unraveled properly to elucidate **the evolution of biosynthetic pathways and their regulation**, **complete bacterial genome sequences** are obligatory to furnish the predictive information essential for functional genomic studies of more complex genomes, since gene identification and organization in higher organisms will be derived principally from comparative studies with simpler genomes.

A new evaluation of our life-support system

Bacterial benefactors—and other prokaryotic pursuits

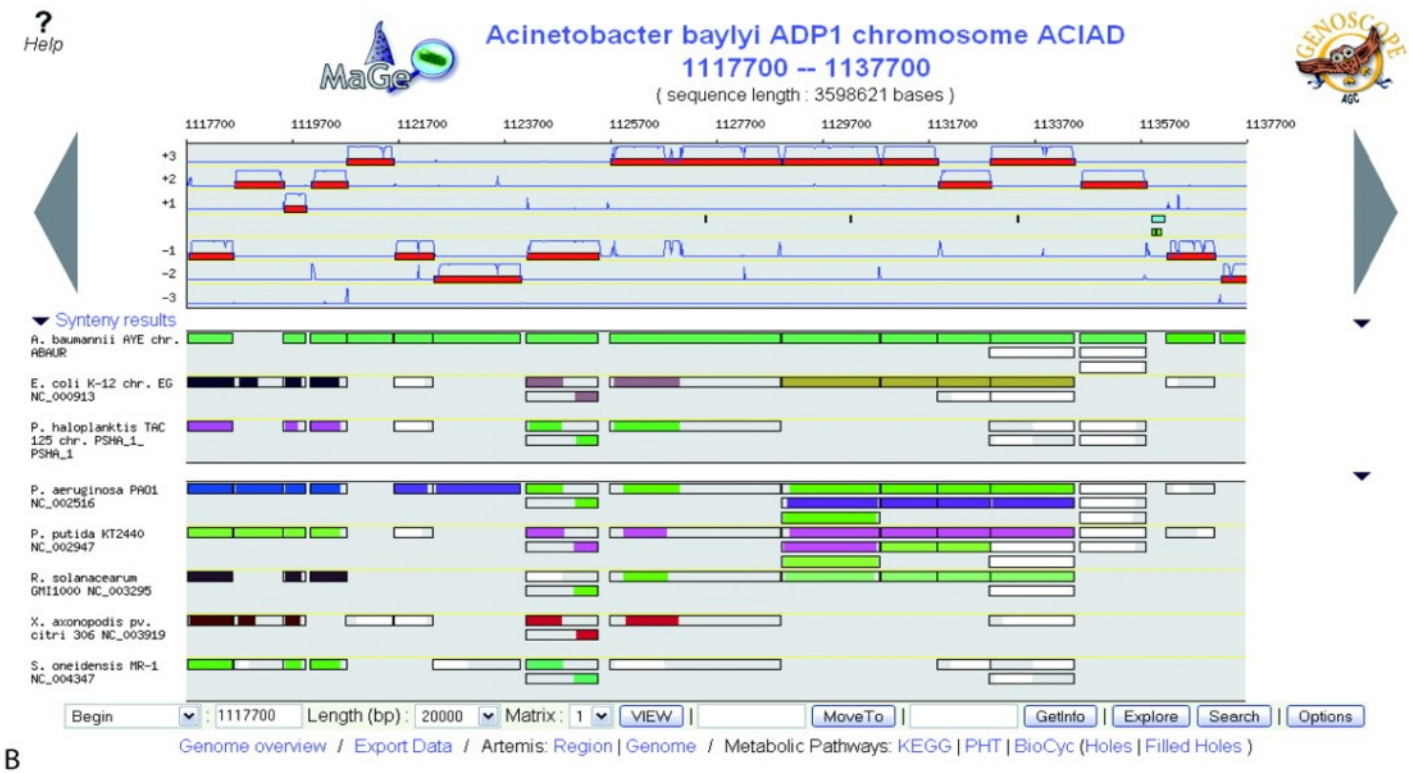
- The new technologies that allow us to sequence and annotate whole genomes more rapidly and to analyse the expression of thousands of genes in a single experiment are likely to speed up this change, **particularly as microbes are well suited for high-throughput analysis**.

A new evaluation of our life-support system

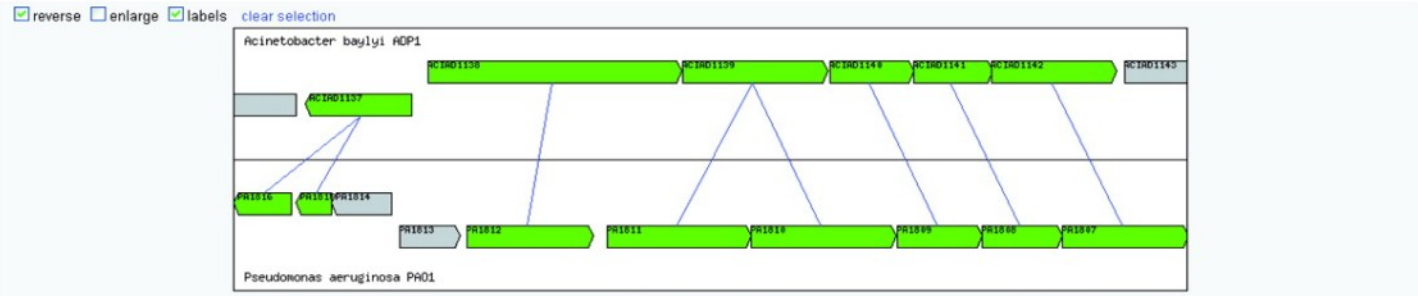
Bacterial benefactors—and other prokaryotic pursuits

- **Any microbial genome can now be sequenced within a few hours** and new bioinformatics tools will enable scientists not only to assemble and annotate them automatically, but also to infer metabolic pathways and other cellular processes from the sequence data *in silico*.

A



B



Acinetobacter baylyi ADP1

Label	Gene	Type	Product
ACIAD1136		CDS	conserved hypothetical protein
ACIAD1137	rnhA-dnaQ	CDS	bifunctional protein [Includes: ribonuclease HI; DNA polymerase III ,epsilon subunit, 3-5 exonucleolytic proofreading function]
ACIAD1138		CDS	bifunctional protein [Includes: lytic murein transglycosylase C, membrane-bound (MltD); putative cell wall hydrolase]
ACIAD1139		CDS	putative oligopeptide transport protein (ABC superfamily, peri_bind)
ACIAD1140		CDS	putative oligopeptide transport protein (ABC superfamily, membrane)
ACIAD1141		CDS	putative oligopeptide transport protein (ABC superfamily, membrane)
ACIAD1142		CDS	putative oligopeptide transport protein (ABC superfamily, atp_bind)
ACIAD1143		CDS	putative FMN oxidoreductase

Correspondences

Ident	MatchL	minLrap	LengthQ	LengthB	OrderQ	OrderB
51.72	524	0.975791	537	537	1	1
62.02	337	1.00298	336	340	1	1
61.94	360	1.01408	355	361	1	1
44.5	555	0.900974	616	616	1	1
37.1	601	0.985246	616	610	3	1
41.44	362	0.676636	1077	535	1	1
50.35	141	0.946309	456	149	2	1
43.75	240	0.97166	456	247	1	1

Pseudomonas aeruginosa PAO1

Label	Gene	Type	Product
PA1807			probable ATP-binding component of ABC transporter
PA1808			probable permease of ABC transporter
PA1809			probable permease of ABC transporter
PA1810			probable binding protein component of ABC transporter
PA1811			probable solute-binding protein
PA1812	mltD		membrane-bound lytic murein transglycosylase D precursor
PA1813			probable hydroxyacylglutathione hydrolase
PA1814			hypothetical protein
PA1815	rnhA		ribonuclease H
PA1816	dnaQ		DNA polymerase III, epsilon chain

RAST http://rast.nmpdr.org/
Manatee (IGV)
JGI
MAGE
Basys https://www.basys.ca/

BAKKE P, CARNEY N, DELOACHE W, GEARING M, INGVORSEN K, ET AL. (2009) EVALUATION OF THREE AUTOMATED GENOME ANNOTATIONS FOR HALORHABDUS UTAHENSIS. PLOS ONE 4(7): E6291.

A new evaluation of our life-support system

- However, the experimental approaches (**functional genomics**) for testing the *veracity of these predictions are likely to be rate-limiting for the foreseeable future*.

- This renewed research will have great usefulness if it means that we understand the microbial world on which all other species on this planet depend for survival.

A new evaluation of our life-support system

- **There is already a vast richness to explore in the known genomes.** Due to the high-density coding of microbial genomes, 10^9 base pairs of prokaryotic DNA—the equivalent of a eukaryotic genome—represents a million genes or proteins, compared with only about 25,000 for the human genome.

A new evaluation of our life-support system

- Furthermore, the total number of *protein families steadily increases with each new genome sequenced*, and bacterial genomes clearly contribute more to protein diversity than do eukaryotic genomes.

- Kunin *et al.* estimate that the genomes of *Borrelia burgdorferi* and *Xylella fastidiosa* will provide **380 new protein families** per million base pairs versus only 1.3 families per million for the whole human genome.

A new evaluation of our life-support system

- But all of these sequenced prokaryotic genomes are **only the tip of the iceberg of total microbial diversity.**
- Of the estimated 10^9 microbial species on Earth, only a minute number is accessible for analysis, as we are not able to cultivate most bacteria in the laboratory

A new evaluation of our life-support system

Table 1. Number of prokaryotes in aquatic habitats

Habitat	Volume,* cm^3	Cells/ml, $\times 10^5$	Total no. of cells, $\times 10^{26}$
Marine			
Continental shelf	2.03×10^{20}	5	1.0
Open ocean			
Water, upper 200 m	7.2×10^{22}	5	360
Water, below 200 m	1.3×10^{24}	0.5	650
Sediment, 0-10 cm	3.6×10^{19}	4600	170
Fresh			
Lakes	1.25×10^{20}	10	1.3
Rivers	1.2×10^{18}	10	0.012
Saline lakes	1.04×10^{20}	10	1.0
Total			1180

* Marine, freshwater, and saline lake volumes were calculated from refs. 7 and 8.

A new evaluation of our life-support system

Table 2. Number of prokaryotes in soil

Ecosystem type*	Area, $\times 10^{12}$ m^2	No. of cells,† $\times 10^{27}$
Tropical rain forest	17.0	1.0
Tropical seasonal forest	7.5	0.5
Temperate evergreen forest	5.0	0.3
Temperate deciduous forest	7.0	0.4
Boreal forest	12.0	0.6
Woodland and shrubland	8.0	28.1
Savanna	15.0	52.7
Temperate grassland	9.0	31.6
Desert scrub	18.0	63.2
Cultivated land	14.0	49.1
Tundra and alpine	8.0	20.8
Swamps and marsh	2.0	7.3
Total	123.0	255.6

* From ref. 73.

† For forest soils, the number of prokaryotes in the top 1 m was 4×10^7 cells per gram of soil, and in 1-8 m, it was 10^6 cells per gram of soil (16). For other soils, the number of prokaryotes in the top 1 m was 2×10^9 cells per gram of soil, and in 1-8 m, it was 10^8 cells per gram of soil (18). The boreal forest and tundra and alpine soils were only 1 m deep. A cubic meter of soil was taken as 1.3×10^6 g.

A new evaluation of our life-support system

Table 4. Total number of prokaryotes in some representative animals

Animal	Organ	Cells/ml or cells/g	Organ contents*	No. of animals†	No. of cells, $\times 10^{23}$	Refs.
Human	Colon	3.2×10^{11}	220 g	5.6×10^{9}	3.9	45, 46
Cattle	Rumen	2.1×10^{10}	106 liter	1.3×10^{9}	29.0	47, 48
Sheep and goats	Rumen	4.4×10^{10}	12 liter	1.7×10^{9}	9.0	47, 48
Pigs	Colon	5.4×10^{10}‡	9 liter	8.8×10^{8}	4.3	49, 50
	Cecum	2.8×10^{10}‡	1 liter	8.8×10^{8}	0.3	49, 50
Domestic birds§	Cecum	9.5×10^{10}	2 g	1.3×10^{10}	0.024	51, 52
Termites	Hindgut	2.7×10^{6}¶		2.4×10^{17}	6.5	53

* Organ contents in volume or grams of wet weight. For comparison, the volume of the human colon is 0.5 liter. For domestic birds, weight wet was calculated from a volume of 2 ml assuming that 1 ml - 1 g wet weight.

† Values from the *FAO Production Yearbook* (54), except for the termites value which was from ref. 55.

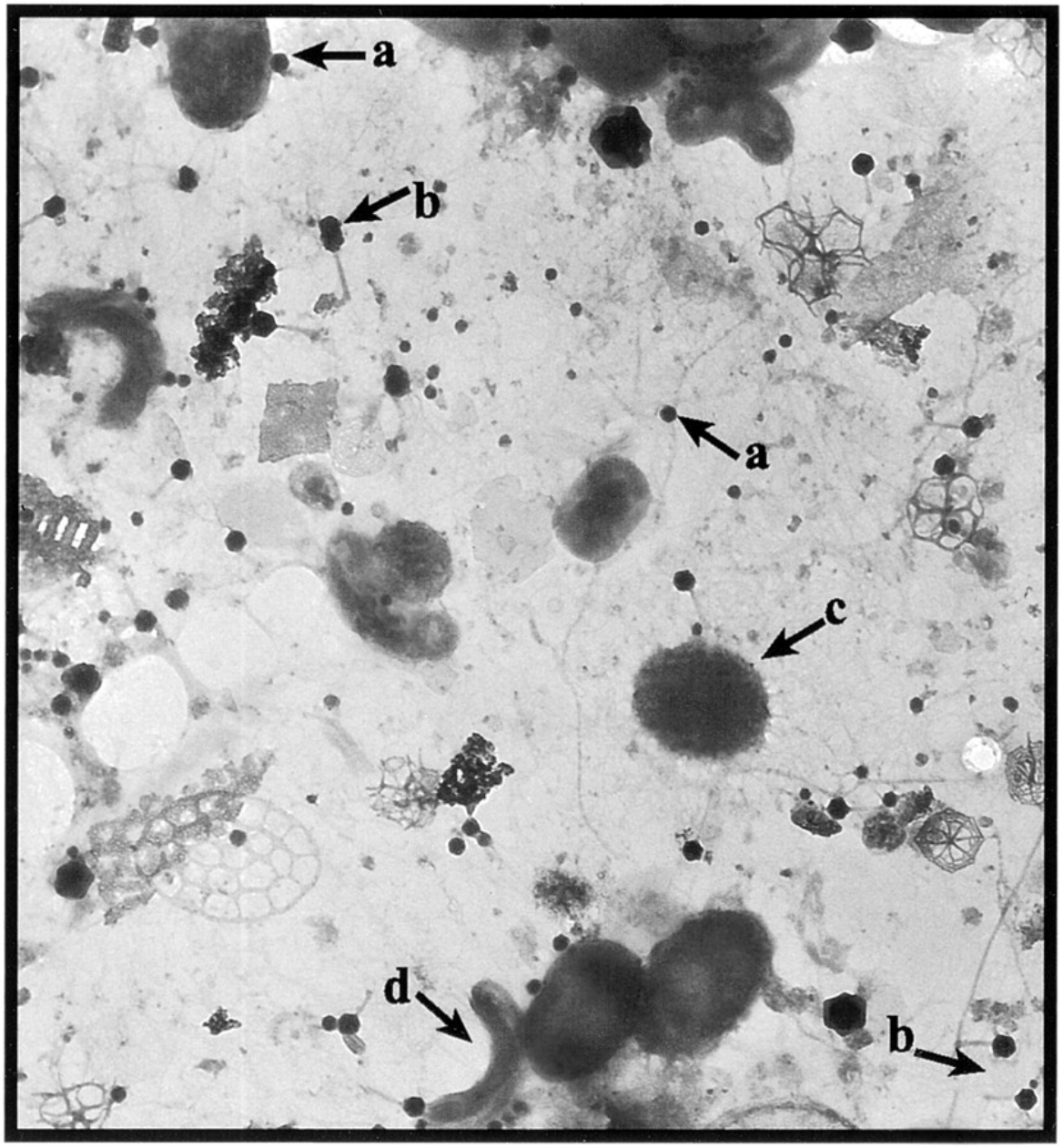
‡ The direct count was assumed to be 2.7 × viable count (56).

§ Includes chickens, ducks, and turkeys.

¶ Per termite.

A new evaluation of our life-support system

- **Bacteriophages also add to this diversity due to their enormous abundance** (estimated to be 10^{31} particles on the globe for tailed bacteriophages alone)
- recycling rate (every second, approximately 10^{25} phages initiate a lytic cycle)
- and gene product diversity



Transmission electron micrograph of an unfiltered Chesapeake Bay water sample (magnification, ca. ×36,000). a, short-tailed or nontailed virus-like particle; b, tailed virus-like particle; c, bacterium, coccal morphotype; d, bacterium, vibrio morphotype.

A new evaluation of our life-support system

- To circumvent the cultivation bottleneck, microbiologists have started extracting genes from what they call the '**metagenome**', that is, from DNA taken directly from environmental samples.
- This approach should uncover new genes, proteins, enzymes, metabolic compounds and pathways that could be exploited for industrial processes.

A new evaluation of our life-support system

- Such an expanded representative catalogue of microorganisms holds great promise. **It may allow us to understand and predict the impact of industrial, agricultural and other activities on prokaryotic diversity.**
- We will also better understand the mechanisms of the evolution of pathogens and of potentially useful bacteria, such as xenobiotic degraders.

A new evaluation of our life-support system

- A metagenomic approach also represents an important first step towards understanding what some have called the second human genome—the 10^{13} bacteria that populate our bodies, some of which are essential to our survival.
- However, before we are able to grasp fully the complex interactions between bacteria and ourselves, and their contribution to our well-being, **new analytical techniques are needed.**

A new evaluation of our life-support system

Trends Microbiol. 2001 May;9(5):206-8.

Related Articles, Links

ELSEVIER
FULL-TEXT ARTICLE

The meaning and impact of the human genome sequence for microbiology.

Relman DA, Falkow S.

Dept of Microbiology & Immunology, Stanford University School of Medicine, Stanford, CA 94305-5124, USA. relman@cmgm.stanford.edu

The characterization of life is immeasurably enhanced by determination of complete genome sequences. For organisms that engage in intimate interactions with others, the genome sequence from one participant, and associated tools, provide unique insight into its partner. We discuss how the human genome sequence will further our understanding of microbial pathogens and commensals, and vice versa. We also propose criteria for implicating a host gene in microbial pathogenesis, and urge consideration of a'second human genome project'.

A new evaluation of our life-support system

- Bacteria live in habitats where environmental and physiological homeostasis is the **exception**. Consequently, adaptive ability is a key feature of bacterial life, which necessitates ***metabolic plasticity***.

- Bacteria need to detect environmental cues in 'real time' and to integrate the resultant signals to trigger appropriate metabolic responses.

A new evaluation of our life-support system

- Evolution has created ***extremely efficient bacterial sensing and signal transduction systems*** for the monitoring of diverse environmental factors, such as temperature, pH, osmolarity and the availability of nutrients

A new evaluation of our life-support system

- One particularly important sensing system **is the ability to measure the density of the surrounding bacterial population— both** siblings and competitors—in any niche.
- Now known as **'quorum sensing'** (QS), it is the production of one or several molecular signals as intercellular messengers

A new evaluation of our life-support system

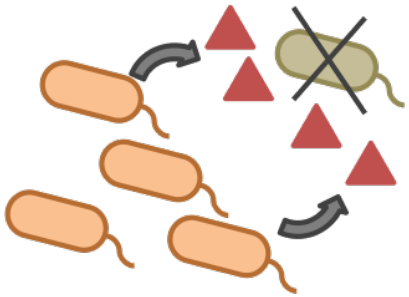
- The concentration of these signals indicates population density, and, by sensing these signals, a bacterium may effectively titrate the number of 'self' and 'non-self' cells.

- The potential advantages of QS for microorganisms are still speculative and depend on the physiological traits that are under QS control in any particular bacterium.

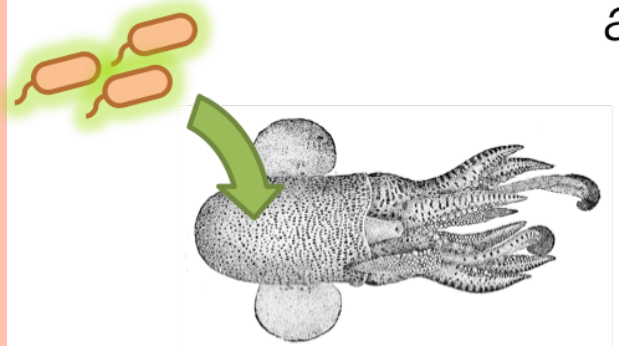
A NEW EVALUATION OF OUR LIFE-SUPPORT SYSTEM

BACTERIAL BENEFACTORS—AND OTHER PROKARYOTIC PURSUITS

- Bacteria that use quorum sensing produce and secrete certain signaling compounds (called *autoinducers* or *pheromones*), one example of which are *N*-acyl homoserine lactones (AHL).
- These bacteria also have a receptor that can specifically detect the AHL (inducer). **When the inducer binds the receptor, it activates transcription of certain genes, including those for inducer synthesis.** There is a low likelihood of a bacterium detecting its own secreted AHL.

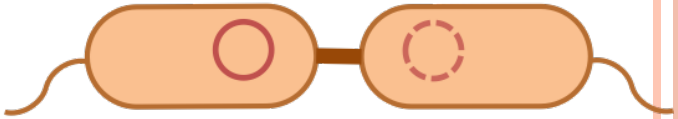


antibiotic production

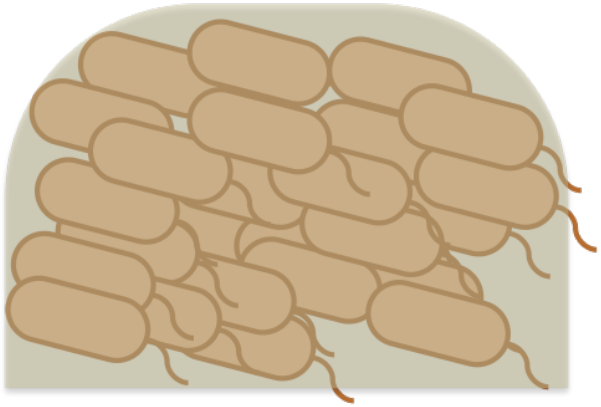


bioluminescence

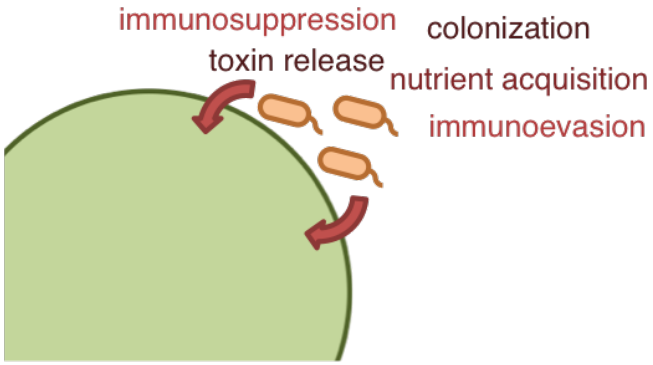
collective behaviors



conjugation



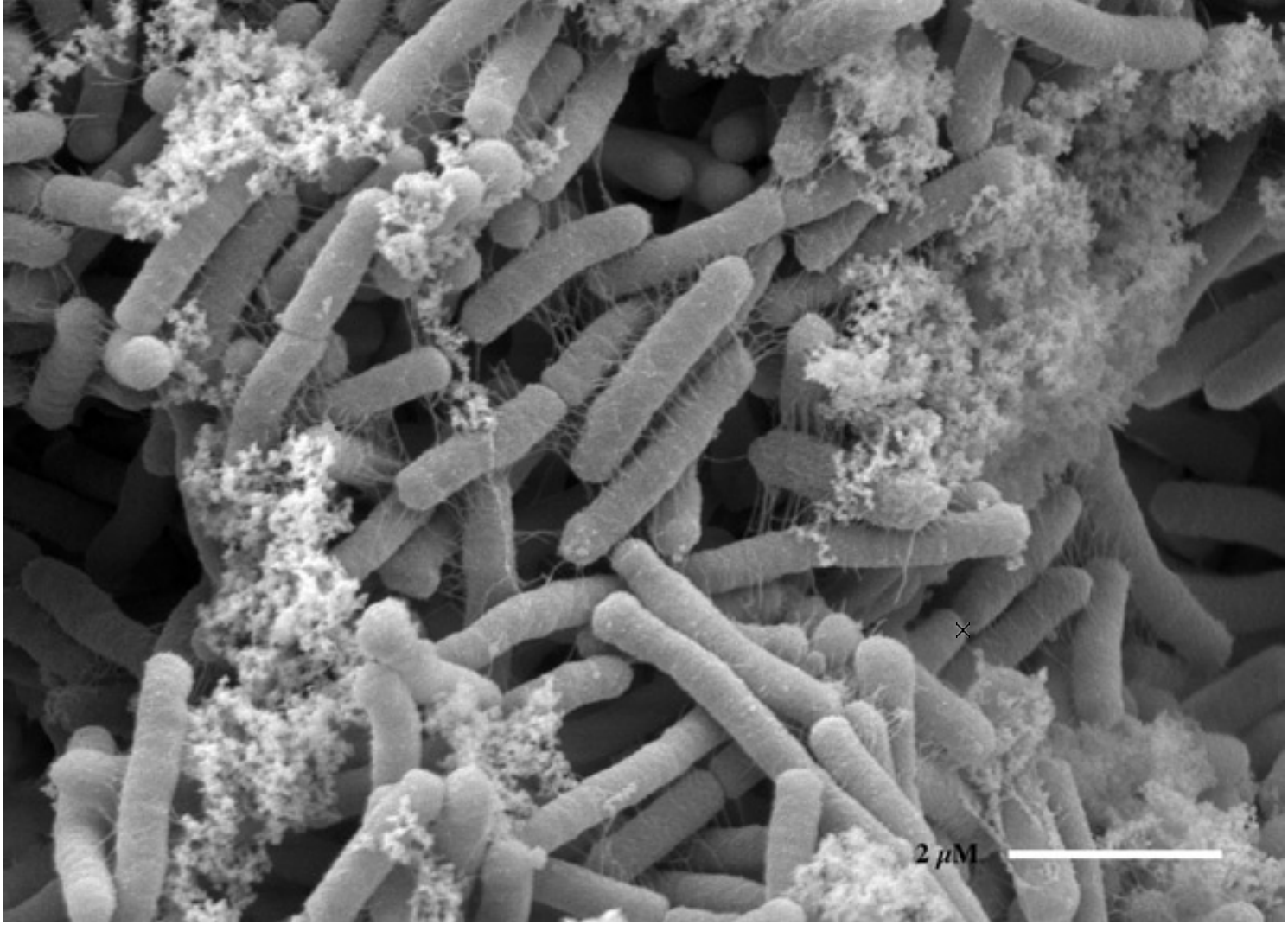
biofilm formation



virulence factors

A new evaluation of our life-support system

- During the past decade, much attention has concentrated on surface-attached microbial populations, so-called **biofilms**.
- These biofilms, which may account for most prokaryotic biomass, are multicellular and heterospecific matrix-enclosed bacterial communities found in almost all ecosystems that have clearly distinct morphological and physiological properties compared with free-floating, planktonic bacteria.



Laser-scanning micrograph of an *Escherichia coli* biofilm. The extracellular-matrix material remaining after fixation can be seen between tightly interconnected bacteria. Magnification, X10,000.

A new evaluation of our life-support system

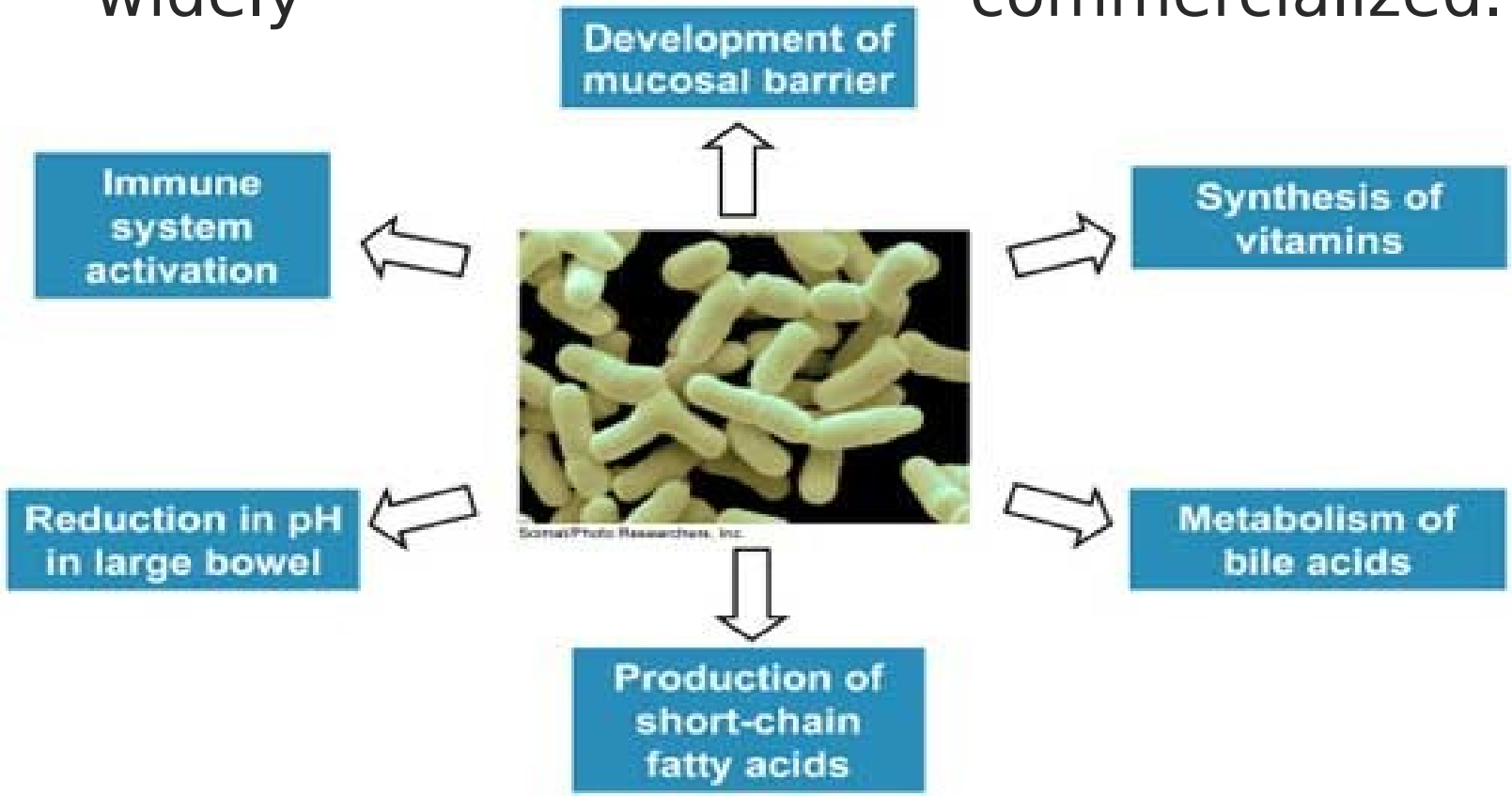
Bacterial benefactors—and other prokaryotic pursuits

- There are other important fundamental microbiological questions, such as **the nature of commensalism**. The genomes of commensals and pathogens can be compared, and DNA arrays can be used to investigate how bacteria interact within complex flora and eukaryotic hosts

A new evaluation of our life-support system

- Another neglected issue is the molecular basis of **probiotic effects**. It has long been known that mucosal flora have the capacity to limit the growth of, or kill, certain transient microbial pathogens by 'bacterial interference'.
- The alarming rise of **antimicrobial resistance** has spurred a renewed interest in the therapeutic use of this competition between enteric bacteria, a promising approach to protecting and controlling human bacterial flora.

- However, the methods used to identify, select and evaluate bacterial colonization factors are limited and little is known about the molecular basis of this phenomenon, even if the defined '**beneficial flora**' strains are now being widely commercialized.



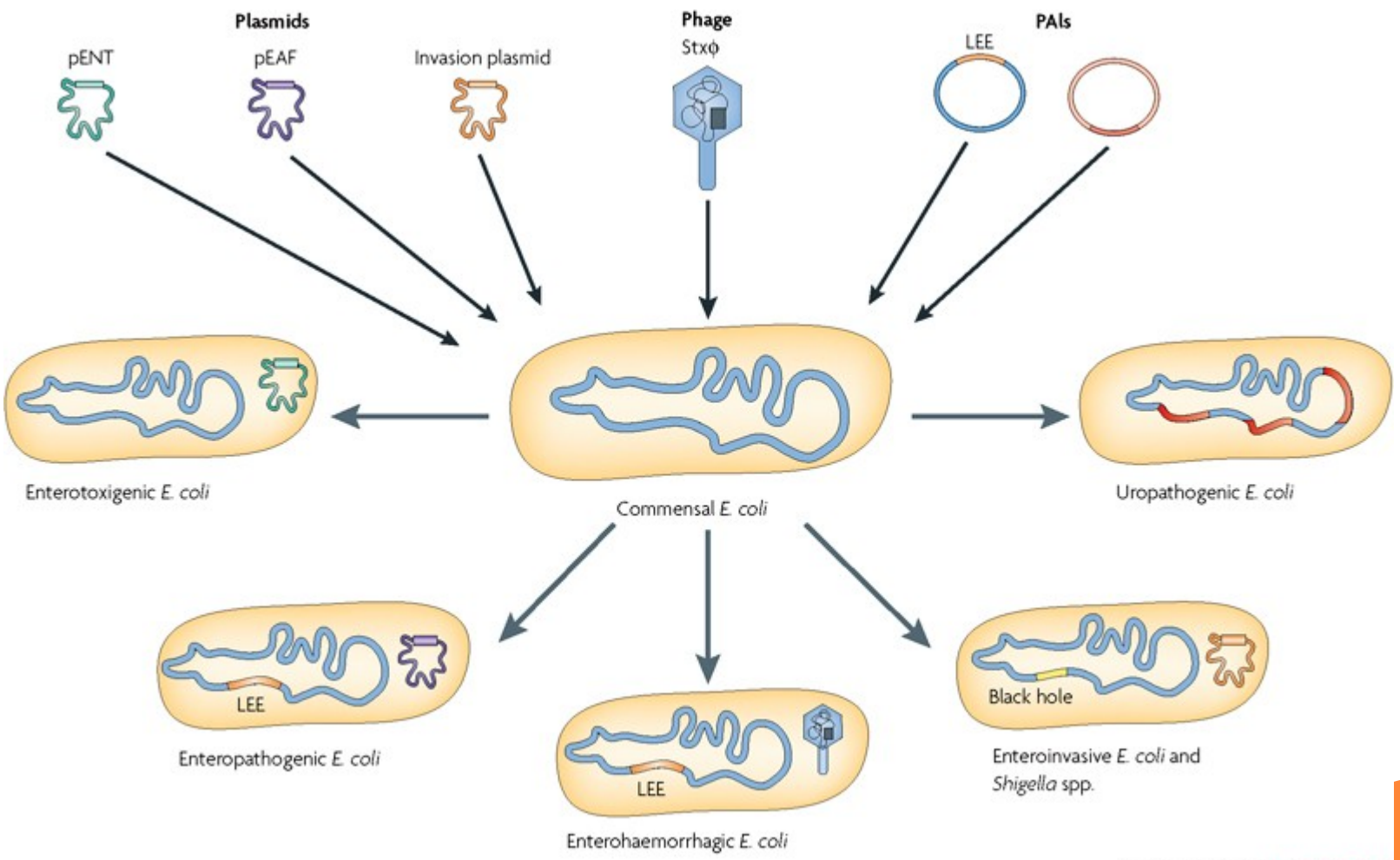
A new evaluation of our life-support system

- Any discussion about the future of microbiology cannot ignore gene transfer between bacterial species. Understanding this phenomenon will probably be one of the greatest challenges of this century.
- The 50-year long 'experiment' of the massive use of antibiotics gave us the first hints about exchange between bacteria of **mobile genetic elements (MGEs)** that allow rapid adaptation to cope with deadly compounds in the environment.

A new evaluation of our life-support system

- Many of these elements, which carry various combinations of genes that enable bacteria to degrade or detoxify a wide range of compounds, have been identified and characterized.

- More recently, **the complete sequencing of several strains of the same bacterial species revealed a new vision of lateral gene transfer in prokaryotes.**


Plasmids
pENT
pEAF
Invasion plasmid
Phage
Stxϕ
PAIs
LEE
Enterotoxigenic E. coli
Commensal E. coli
Uropathogenic E. coli
LEE
Enteropathogenic E. coli
LEE
Enterohaemorrhagic E. coli
Black hole
Enteroinvasive E. coli and
Shigella spp.
Nature Reviews | Microbiology

Nature. 2001 Oct 25;413(6858):848-52.

nature

Complete genome sequence of a multiple drug resistant Salmonella enterica serovar Typhi CT18.

Parkhill J, Dougan G, James KD, Thomson NR, Pickard D, Wain J, Churcher C, Mungall KL, Bentley SD, Holden MT, Sebaihia M, Baker S, Basham D, Brooks K, Chillingworth T, Connerton P, Cronin A, Davis P, Davies RM, Dowd L, White N, Farrar J, Feltwell T, Hamlin N, Haque A, Hien TT, Holroyd S, Jagels K, Krogh A, Larsen TS, Leather S, Moule S, O'Gaora P, Parry C, Quail M, Rutherford K, Simmonds M, Skelton J, Stevens K, Whitehead S, Barrell BG.

The Sanger Centre, Wellcome Trust Genome Campus, Hinxton, Cambridge, CB10 1SA, UK. parkhill@sanger.ac.uk

Salmonella enterica serovar Typhi (S. typhi) is the aetiological agent of typhoid fever, a serious invasive bacterial disease of humans with an annual global burden of approximately 16 million cases, leading to 600,000 fatalities. Many S. enterica serovars actively invade the mucosal surface of the intestine but are normally contained in healthy individuals by the local immune defence mechanisms. However, S. typhi has evolved the ability to spread to the deeper tissues of humans, including liver, spleen and bone marrow. Here we have sequenced the 4,809,037-base pair (bp) genome of a S. typhi (CT18) that is resistant to multiple drugs, revealing the presence of hundreds of insertions and deletions compared with the Escherichia coli genome, ranging in size from single genes to large islands. Notably, the genome sequence identifies over two hundred pseudogenes, several corresponding to genes that are known to contribute to virulence in Salmonella typhimurium. This genetic degradation may contribute to the human-restricted host range for S. typhi. CT18 harbours a 218,150-bp multiple-drug-resistance incH1 plasmid (pHCM1), and a 106,516-bp cryptic plasmid (pHCM2), which shows recent common ancestry with a virulence plasmid of Yersinia pestis.

- *Escherichia coli* and *Salmonella* share around 70% of their genes.

• Nature. 2001 Jan 25;409(6819):463, 465-6.

nature

Genome sequence of enterohaemorrhagic Escherichia coli O157:H7.

Perna NT, Plunkett G 3rd, Burland V, Mau B, Glasner JD, Rose DJ, Mayhew GF, Evans PS, Gregor J, Kirkpatrick HA, Posfai G, Hackett J, Klink S, Boutin A, Shao Y, Miller L, Grotbeck EJ, Davis NW, Lim A, Dimalanta ET, Potamousis KD, Apodaca J, Anantharaman TS, Lin J, Yen G, Schwartz DC, Welch RA, Blattner FR.

Genome Center of Wisconsin, and Department of Animal Health and Biomedical Sciences, University of Wisconsin, Madison 53706, USA. perna@ahabs.wisc.edu

The bacterium Escherichia coli O157:H7 is a worldwide threat to public health and has been implicated in many outbreaks of haemorrhagic colitis, some of which included fatalities caused by haemolytic uraemic syndrome. Close to 75,000 cases of O157:H7 infection are now estimated to occur annually in the United States. The severity of disease, the lack of effective treatment and the potential for large-scale outbreaks from contaminated food supplies have propelled intensive research on the pathogenesis and detection of E. coli O157:H7 (ref. 4). Here we have sequenced the genome of E. coli O157:H7 to identify candidate genes responsible for pathogenesis, to develop better methods of strain detection and to advance our understanding of the evolution of E. coli, through comparison with the genome of the non-pathogenic laboratory strain E. coli K-12 (ref. 5). We find that lateral gene transfer is far more extensive than previously anticipated. In fact, 1,387 new genes encoded in strain-specific clusters of diverse sizes were found in O157:H7. These include candidate virulence factors, alternative metabolic capacities, several prophages and other new functions--all of which could be targets for surveillance.

- A similar level of divergence is seen between the genomes of two *E. coli* strains (the laboratory strain K12 and the pathogen O157-H7), which differ by as much as 20−30% of their genomes. Strikingly, much of the difference is accounted for by prophages

Science. 2001 Oct 26;294(5543):849-52.

Science AAAS

Comparative genomics of Listeria species.

Glaser P, Frangeul L, Buchrieser C, Rusniok C, Amend A, Baquero F, Berche P, Bloecker H, Brandt P, Chakraborty T, Charbit A, Chetouani F, Couve E, de Daruvar A, Dehoux P, Domann E, Dominguez-Bernal G, Duchaud E, Durant L, Dussurget O, Entian KD, Fsihi H, Garcia-del Portillo F, Garrido P, Gautier L, Goebel W, Gomez-Lopez N, Hain T, Hauf J, Jackson D, Jones LM, Kaerst U, Kreft J, Kuhn M, Kunst F, Kurapkat G, Madueno E, Maitournam A, Vicente JM, Ng E, Nedjari H, Nordsiek G, Novella S, de Pablos B, Perez-Diaz JC, Purcell R, Remmel B, Rose M, Schlueter T, Simoes N, Tierrez A, Vazquez-Boland JA, Voss H, Wehland J, Cossart P.

Genomique des Microorganismes Pathogenes, Unite des Interactions Bacteries-Cellules, Service d'Informatique Scientifique, Institut Pasteur, 25-28 rue du Dr. Roux, 75724 Paris, France.

Listeria monocytogenes is a food-borne pathogen with a high mortality rate that has also emerged as a paradigm for intracellular parasitism. We present and compare the genome sequences of L. monocytogenes (2,944,528 base pairs) and a nonpathogenic species, L. innocua (3,011,209 base pairs). We found a large number of predicted genes encoding surface and secreted proteins, transporters, and transcriptional regulators, consistent with the ability of both species to adapt to diverse environments. The presence of 270 L. monocytogenes and 149 L. innocua strain-specific genes (clustered in 100 and 63 islets, respectively) suggests that virulence in Listeria results from multiple gene acquisition and deletion events.

- All of the major gaps in the alignment between the genomes of *Listeria monocytogenes* and *Listeria innocua* correspond to the prophages that are integrated into the latter.

The genome sequence of Bacillus anthracis Ames and comparison to closely related bacteria.

Read TD, Peterson SN, Tourasse N, Baillie LW, Paulsen IT, Nelson KE, Tettelin H, Fouts DE, Eisen JA, Gill SR, Holtzapple EK, Okstad OA, Helgason E, Rilstone J, Wu M, Kolonay JF, Beanan MJ, Dodson RJ, Brinkac LM, Gwinn M, DeBoy RT, Madpu R, Daugherty SC, Durkin AS, Haft DH, Nelson WC, Peterson JD, Pop M, Khouri HM, Radune D, Benton JL, Mahamoud Y, Jiang L, Hance IR, Weidman JF, Berry KJ, Plaut RD, Wolf AM, Watkins KL, Nierman WC, Hazen A, Cline R, Redmond C, Thwaite JE, White O, Salzberg SL, Thomason B, Friedlander AM, Koehler TM, Hanna PC, Kolsto AB, Fraser CM.

The Institute for Genomic Research, 9712 Medical Center Drive, Rockville, Maryland 20850, USA. anthrax@tigr.org).

Bacillus anthracis is an endospore-forming bacterium that causes inhalational anthrax. Key virulence genes are found on plasmids (extra-chromosomal, circular, double-stranded DNA molecules) pXO1 (ref. 2) and pXO2 (ref. 3). To identify additional genes that might contribute to virulence, we analysed the complete sequence of the chromosome of B. anthracis Ames (about 5.23 megabases). We found several chromosomally encoded proteins that may contribute to pathogenicity--including haemolysins, phospholipases and iron acquisition functions--and identified numerous surface proteins that might be important targets for vaccines and drugs. Almost all these putative chromosomal virulence and surface proteins have homologues in Bacillus cereus, highlighting the similarity of B. anthracis to near-neighbours that are not associated with anthrax. By performing a comparative genome hybridization of 19 B. cereus and Bacillus thuringiensis strains against a B. anthracis DNA microarray, we confirmed the general similarity of chromosomal genes among this group of close relatives. However, we found that the gene sequences of pXO1 and pXO2 were more variable between strains, suggesting plasmid mobility in the group. The complete sequence of B. anthracis is a step towards a better understanding of anthrax pathogenesis.

- The main differences between the pathogenic *Bacillus anthracis* and the closely related *Bacillus thuringiensis*, which is the source of Bt toxins, do not reside in their chromosomes but in the nature of the plasmids that they host.

A new evaluation of our life-support system

- The increasing volume of genomics research, coupled with information from **metagenomics**, may uncover new proteins, enzymes, pathways and metabolic products that could become useful tools for microbiology research and, if we are fortunate, novel chemotherapeutic agents.

A new evaluation of our life-support system

- Advances in **genomics, transcriptomics and proteomics** will also help to elucidate the nature and functions of gene products that have unknown functions at present. From a utilitarian perspective, the biotechnological spin-off could be even more exciting.
- It will allow us to address many current problems in agriculture, nutrition and medicine, which are all domains relying on complex microbial flora that have been, so far, used largely empirically.

A new evaluation of our life-support system

- These new approaches will clearly reshape many aspects of human activities, when we finally have the tools to explore the fantastic reservoir of biochemical know-how in the microbial world.
- Bacteria were on this planet long before we arrived and, no doubt, **will be here long after we have disappeared.**

A new evaluation of our life-support system

Table 1 Why study microbial diversity?

1. Explore the environmental limits of life.
2. Establish the organismal requirements for biosphere sustainability.
3. Provide new resources for biotechnology, pharmaceuticals, energy production, waste treatment.
4. Monitor and predict environmental change, understand global chemical cycling.
5. Broaden conservation biology and bioremediation.
6. Test community ecology principles.
7. Obtain records of early eras—evolutionary relationships and mechanisms (e.g., horizontal gene transfer) and their role in the evolution and maintenance of the biosphere.
8. Study gene transfer in nature: environmental safety, fate of released DNA, survival of introduced microbes. Examine the extent of natural gene exchange.
9. Define and prevent harmful microbial activities such as corrosion, biofouling, fertilizer degradation.
10. Expand knowledge of the gene pool.
11. Identify the nature of pathogenicity and other host-parasite relationships.
12. Understand the sociobiology of microbial communities and their maintenance.