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What does the term microbiome mean? And where did it come from? A bit of a surprise ..

Jonathan Eisen

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"Microbiome" is such a hot term these days. And one key question many ask is "what does it mean?" A related question is - "where did the term come from?" I tried to tackle this many years ago on my blog with a post: The human microbiome - term being used in many ways - but at least it is getting some \npress. Basically my main point was that it seemed that the term "microbiome" then should be used to refer to the collection of genomes of microbes in a system and that "microbiota" should be used to refer to the collection of organisms. Some key quotes from that post:

Well, the human microbiome is all over the news recently thanks to a new paper on the diversity and biogeography of microbes in human saliva.

My only complaint is that I and Stoneking and many others have unfortunately made a mess of the terminology. The "microbiome" was originally used to refer to the collection of the genomes of the microbes in a particular ecosystem. And the terms "microbiota" was used to refer to the actual organisms. Since Stoneking et al did not survey the genomes, they surveyed rRNA (which really at best tells you about what types of organisms are present) then they should have used microbiota riight? (And if they had I would not have been searching for the genomics component of their work).

Not so fast, even the person who coined the term microbiome (Josh Lederberg) who originally seemed to use it to refer to all the genomes of the microbes also used the term ambiguously (e.g., in one paper he sad "the microbiome flora" meaning I guess the microbiota.

I note, everyone seems to cite A paper by Lederberg called "Infectious History" in Science (Science 14 April 2000:) as the place he used microbiome but I cannot find the term there. I did however find the term in a paper in 2001 by Lora Hooper and Jeff Gordon (Commensal Host-Bacterial Relationships in the Gut Science 11 May 2001: Vol. 292. no. 5519, pp. 1115 - 1118).

The Nobel laureate Joshua Lederberg has suggested using the term "microbiome" to describe the collective genome of our indigenous microbes (microflora), the idea being that a comprehensive genetic view of Homo sapiens as a life-form should include the genes in our microbiome (4).

And reference 4 is "Personal communication"

Anyway, others have taken the term microbiome and run with it because it does conjure up to many "microbial biome" which could be used to refer to all the microbes in a system. I prefer the original definitions with microbiota being the organisms and microbiome being the collective genomes of all the organisms.

I have been as guilty as others in mixing up the terms but in the future I plan to push for "microbiome" to be an omics word and not a biome word and for microbiota to be the biome word. That way if you skim a paper or title you might be able to better guess what it is about.

Alas, there are many ways in which this post was less than ideal, if not just wrong. First, and perhaps most interesting and important, the history of the term microbiome that I presented in the article is wrong. I found out about this error in an email I received from Alan Logan in October.

Hi Dr Eisen

I recall several years ago that you were querying on the origin of the term microbiome ... and, according to untold amounts of rinse-and-repeat scholarly articles and the fountainhead of misinformation known as wiki, it is stated to be "coined" by Joshua

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Science AMA Series: I'm Kim Barrett, Professor of Medicine University of California, San Di and Editor of The Journal of Physiology. This week, we pub an issue on the microbiota, so thought it would be a great opportunity to discuss how our microbes influence our wellbeir

Kim_Barrett et al., The Winnow

New papers, December 24, 20 Elisabeth Bik, The Winnower, 2 Lederberg. Coinage is, of course, distinct from helping to cajole a term into its current form...and there is little doubt that Dr Lederberg contributed to the latter.

In the English language the first use of the term, defined closely to its current use, appears to be by University of Warwick (UK) professor John M. Whipps and colleagues Karen Lewis and Roderic C. Cooke...(quoted as below and easily confirmed in less than a minute by searching "google books" website, restricting the search to pre-2001 when Lederberg was said to have coined the term).

With Respect

Alan

JM Whipps, Karen Lewis, RC Cooke: Mycoparasitism and plant disease control 161-87.

in NM Burge Editor, Fungi in Biological Control Systems. Manchester University Press, $\mathbf{1988}$

pg 176 – A convenient ecological framework in which to examine biocontrol systems is that of the microbiome. This may be defined as a characteristic microbial community occupying a reasonably well defined habitat which has distinct physio-chemical properties. The term thus not only refers to the microorganisms involved but also encompasses their theatre of activity.

So of course I looked at this in more detail. And I found the 1988 book on Google Books (direct link to the book section is here.)

A convenient ecological framework in which to examine biocontrol systems is that of the microbiome. This may be defined as a characteristic microbial community occupying a reasonably well defined habitat which as distinct physico-chemical properties. The term thus not only refers to the microorganisms involved but also encompasses their theatres of activity. In relation to fungal diseases of crops and their control, major microbiomes are the phylioplane, spermosphere, rhizosphere and rhizoplane, and numerous kinds of plant residues persisting no or in the soil. Mention should also be made of the wood of standing or felled trees as microbiomes where biocontrol of forest diseases using fungi has been achieved. However, in most cases competitive interactions other than mycoparasitism seem to be of greater importance.

So – that certainly changes things. They are referring to the "microbiome" as the "characteristic microbial community occupying a reasonably well defined habitat which has distinct physicochemical properties. The term thus not only refers to the microorganisms involved but also encompasses their theatres of activity."

I find this really interesting since, well, this is really how the term is being used in the community right now. Contrary to what I recommended in my post – the term **microbiome** is being used really with the emphasis on **BIOME** (as in community) and not **OME** (as in genomics). So even though it might have been cleaner to use microbiome to refer to the OMES and microbiota to refer to the organisms, that is just not what is happening.

So – what does this mean? I think it means that **the current usage of "microbiome" to refer to communities of organisms is not only common practice, it is consistent with the first definition of the term in the literature.**

Some notes of interest are below

As an aside, I have now searched Google Books in more detail and found one other even older example – from 1949 in French.

Revue odontologique - Volume 71 - Page 449

From Street Street

https://books.google.com/books?id... - Translate this page 1949 - Snippet view - More editions

On sait, d'autre part, le rôle que joue le PH dans l'évolution du **microbiome** intestinal. Il est plausible d'admettre qu'à la faveur des lésions intestinales et des modifications du PH intestinal, les migrations parasitaires ou microbiennes peuvent ...

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which Google translates into:

Toilet Ecology

Sean Gibbons, The Winnower,

Relating the metatranscriptome metagenome of the human gut Matthew R. Boylan et al., Proc Acad Sci U.S.A. 2014

Host-Associated Quantitative Abundance Profiling Reveals th Microbial Load Variation of Roc Microbiome

Xiaoxuan Guo et. al.éphane, Hacquard Xiangdong Fu, Yang Plant Communications, 2019

An interview with V. Craig Jord breast cancer, SERMs, tamoxit fsgadmin, Oncology Central, 20

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We know, on the other hand, the role of the PH in the evolution of gut microbiome. It is plausible to assume that the favor of the intestinal lesions and intestinal pH changes, parasitic or microbial migration can

No definition is presented as far as I can tell so I will stick with the 1988 one given above, but, well, Google Books is just really fun.

As another aside here are some links and quotes about the term that may be of relevance

'Ome Sweet 'Omics— A Genealogical Treasury of Words by Joshua Lederberg and Alexa T. Mccray in 2001

It includes Lederberg's own recent coinage of microbiome, to signify the ecological community of commensal, symbiotic, and pathogenic microorganisms that literally share our body space and have been all but ignored as determinants of health and disease.

Of men and microbes by Joshua Lederberg in New Perspectives Quarterly 2004

The great scientific news that greeted this century was the campaignto decode the human genome. We must now remind ourselves that much of thebiological composition of our bodies consists of genomes other than the human. Multitudes of bacteria and viruses occupy our skin, our mucous membranes and our intestinal tract. They are likely to play a much larger role in developing — and resisting — disease than we realize. Understanding this cohabitation of genomes within the human body — what I call the **microbiome** — is central to understand-ing the dynamics of health and disease

and

MICROBIOME | It would thus broaden our philosophical horizons if we think of a human — a body space in any human — as more than an organism. It is a superorganism with an extended genome that includes not only its own cells but also the fluctuating microbial genome set of bacteria and viruses that shares that bodyspace. Some of these one-time invaders have become permanently established in our cells, even crossed the boundary line and entered our own genome. I call that extended set of companions the **microbiome**, and pray for more research on how they impact our lives, besides the flare-ups, the blunders, we call disease. Understanding this means that we live in a cooperative arrangement — a truce —with those microbes that don't kill us.

and

We need to investigate how our **microbiome flora** — the ones that we live with all the time — don't cause disease and instead protect us against their competitors.

Joshua Lederberg Keynote Address "Beyond The Genome" FROM 2001

The current text is based on remarks given as a luncheon address at the Brooklyn Law School Symposium, DNA- Lessons from the Past-Problemsfor the Future, on March 9, 2001. A calculated diversion from the main theme, the address bore the dual title: "Beyond The Genome" and "Whose Germs Are They Anyhow?"

We are still not quite finished with our contemplation of the sources of individual identity. I refer now to our microbiome. These are the microbes that share our body space and that inhabit our skin, our mucous membranes, and our gut.

UPDATE 1 - April 9, 2015

Great find by Ed Yong

- ... On microbiome definitions, philosopher John Huss also makes the dual-meaning argument in this lovely paper http://t.co/ZQCsdfFnom
- Ed Yong (@edyong209) April 9, 2015

This refers to an open access paper from November 2014 by John Huss "Methodology and Ontology in Microbiome Research". Here is a relevant section, though the whole paper should be read

In the scientific literature on the human microbiome, folk- etymologizing on the part of scientists has led to a curious tension. On one hand, the term "microbiome" simply refers to the collective genome of the microbiota of an organism, and is modeled after other "omes" in molecular biology: genome, transcriptome, proteome, and the like (Lederberg 2001). This usage is relatively uncontroversial, the main points of disagreement concerning such issues as whether transient microbes or only autochthonous microbes should be included, and whether viruses should be included (or perhaps studied separately as the "virome"). On the other hand, some scientists, including several quite prominent in the field (Nicholson et al. 2005; Shade and Handelsman 2012; Weinstock 2012), have interpreted the term ecologically as a biome of microbes. Interestingly, the ecological usage seems to represent a bit of folk-etymologizing on the part of scientists, as the term microbiome (as in "microbial biome") was scarcely used prior to the genomic era (an exception being Mohr 1952). Of course one may regard this dual usage as reflecting a dual confusion-Lederberg dubbing a new "ome" using an existing term, and others simply inferring an ecological usage in the "post-genomics" era—but overall it may be more productive to view the contrast in usage as reflecting two research strategies or points of emphasis. One strategy is fundamentally molecular, and uses the techniques of systems biology to integrate information about molecular mechanisms and pathways. The other strategy is fundamentally ecological, and uses the techniques of genomics to identify the ecological actors in the microbial community. In the biomedical literature, the ecological connotations of the term "microbiome" have been enlisted in promoting a view of the Human Microbiome Project as fostering a holistic approach to human health, even when the underlying science is genomic, and in some cases simply genetic, identifying potential functional capacities by comparison to gene databases. The polysemy of the term "microbiome" provides ecological cover for what is essentially a molecular research program.

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