PROGRAM

1997 GORDON CONFERENCE ON MICROBIAL POPULATION BIOLOGY

Plymouth State College, Plymouth N.H.
July 27 - August 1, 1997

Chair: Julian Adams **Vice Chair: Susan Rosenberg**

The Organizers are very grateful to the following Organizations and Companies for their Financial Support of this Conference:

Gordon Research Conferences
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Sunday July 27, 1997

2:00 - 11:00 p.m. Registration

6:00 - 7:00 p.m. Dinner

SESSION I. EVOLUTION OF VIRUSES AND PHAGES

7:30 p.m. - 7:45 p.m. Announcements: Julian Adams and Conference Staff

7:45 p.m. - 8:15 p.m. Introduction - Chair: *Allan Campbell* - Department of Biological Sciences, Stanford University

8:15 p.m. - 8:45 p.m. *Roger Hendrix* - Dept. of Biological Sciences, University of Pittsburgh
Genetic mosaicism in natural isolates of temperate bacteriophages

8:50 p.m. - 9:20 p.m. *Sebastian Bonhoeffer* - Dept. Zoology, University of Oxford, U.K.
Dynamics of HIV Infection

9:25 p.m. - General Discussion
Leader: *Rosemary Redfield* - Dept. Zoology, University of British Columbia, Canada.

9:45*ish* p.m. Reception

Monday, July 28, 1997

7:30 - 8:30 a.m. Breakfast

SESSION II. ANTIBIOTIC RESISTANCE AND EVOLUTION

9:00 - 9:30 a.m. Introduction - Chair: *Stuart Levy* - Tufts University Medical School, Boston

9:30 - 10:00 a.m. *Julian Davies* - Dept. of Microbiology, University of British Columbia, Ca
Origins of Antibiotic Resistance

10:05 - 10:30 a.m. Break and Group Photograph (Weather Permitting)

10:30 - 11:00 a.m. *Fernando Baquero Morales* - Servicio de Microbiología, Hospital Ramón y Cajal, Madrid, Spain
Selective environments and the diversity of resistance mechanisms

11:05 - 11:35 a.m. *Timothy Palzkill* - Dept. of Microbiology, Baylor College of Medicine.
Role of protein plasticity in β-lactamase evolution

11:40 a.m. General Discussion
Leader: *B. Levin* - Dept. Biology, Emory University

12:30 Lunch

1:30 - 6:00 p.m. Free Time & Poster Viewing

6:00 - 7:00 p.m. Dinner

SESSION III. EVOLUTION IN LONG TERM LABORATORY CULTURES

7:30 - 8:00 p.m. Introduction - Chair: *Michel Blot* - Institut de Biologie, Université de Grenoble, France

8:00 - 8:30 p.m. *Richard Lenski* - Center for Microbial Ecology, Michigan State University
Dynamics of adaptation and divergence during 10,000 generations of evolution in E. coli

8:35 - 9:05 p.m. *Roberto Kolter* - Dept. Microbiology and Molecular Genetics, Harvard Medical School
GASPing for life in stationary phase

9:10 p.m. General Discussion: ***Susan Rosenberg*** - Dept. Biochemistry, University of Alberta, Edmonton

Tuesday, July 29, 1997

7:30 - 8:30 a.m. Breakfast

SESSION IV. EVOLUTION OF VIRULENCE/PATHOGENICITY

9:00 - 9:30 a.m. Introduction - Chair: ***Peter Reeves*** - Dept. Microbiology, University of Sydney, Australia

9:30 - 10:00 a.m. ***Matthew Waldor*** - Division of Geographic Medicine and *Infectious Diseases, New England Medical Center*
Horizontal transfer events in the evolution of pathogenic V. cholerae

10:05 - 10:30 a.m. Break (and group photo if necessary)

10:30 - 11:00 a.m. ***Thomas Cebula*** - Food and Drug Administration, Washington *D.C.*
Significance of mutator phenotype among E. coli and S. typhimurium pathogens

11:05 - 11:35 a.m. ***Daniel Dykhuizen*** - Dept. Ecology and Evolution, S.U.N.Y. Stonybrook
The lyme disease agent as a stealth pathogen

11:40 a.m. General Discussion
Leader: ***Richard Goldstein*** - Boston University Medical School

12:30 Lunch

1:00 - 6:00 p.m. Free Time & Poster Viewing

6:00 - 7:00 p.m. Dinner

SESSION V. GENOME STRUCTURE

7:30 - 8:00 p.m. Introduction Chair: ***John Roth*** - Dept. of Biology, University of Utah

8:05 - 8:35 p.m. ***Ruth Hall*** - C.S.I.R.O., North Ryde Australia
The role of gene cassettes and integrons in genome evolution

8:40 - 9:10 p.m. ***Abigail Salyers*** - Dept. of Microbiology, University of Illinois
Congugative transposons: a new family of integrative gene transfer elements

9:15 p.m. General Discussion
Leader: ***Howard Ochman*** - Dept. *Biology, University of Rochester, Rochester,* N.Y.

Wednesday, July 30, 1997

7:30 - 8:30 a.m. Breakfast

SESSION VI. APPLICATION OF THE INFORMATION FROM GENOME PROJECTS TO QUESTIONS IN MICROBIAL EVOLUTION.

9:00 - 9:30 a.m. Introduction - Chair: ***Paul Sharp*** - Dept. Genetics, University of Nottingham, U.K.

9:35 - 10:05 a.m. ***Steve Oliver*** - Manchester Biotechnology Center, Manchester U.K. M60 1QD UK
Gene and genome evolution in yeast

10:05 - 10:30 a.m. Break

10:30 - 11:00 a.m. ***Henry M. Krisch*** - CNRS, Toulouse, France
The Role of Genomic Polymorphism in the Evolution of the T-even Bacteriophages

11:05 - 11:35 a.m. ***Gary Olsen*** - Dept. Microbiology, University of Illinois, Urbana
Tracing the histories of genes in prokaryotes

11:40 a.m. General Discussion
Leader: ***George Weinstock*** - Dept. Biochemistry, University of Texas Medical School, Houston

12:30 Lunch

1:00 p.m. - 6:00 p.m. Free Time & Poster Viewing

6:00 p.m. - 7:00 p.m. Dinner

SESSION VII. MACROEVOLUTIONARY QUESTIONS AND MICROBES

7:30 - 8:00 p.m. Introduction - Chair: ***Daniel Hartl*** - Dept. Organismal and Evolutionary Biology, Harvard University

8:00 - 8:30 p.m. ***Margaret Saks*** - Division of Biology, California Institute of Technology, Pasadena
An experimental approach to the question of the evolution of the genetic code

8:35 - 9:05 p.m. ***Nancy Moran*** - Dept. Ecology and Evolutionary Biology, University of Arizona
Evolution of prokaryotic endosymbionts in insects

9:05 p.m. General Discussion
Leader: ***Peg Riley*** - Dept. Biology, Yale University

Thursday, July 31, 1997

7:30 - 8:30 a.m. Breakfast

SESSION VIII. HORIZONTAL TRANSFER

9:00 - 9:30 a.m. Introduction Chair: ***Elizabeth Raleigh*** - New England Bio Labs, Beverly MA

9:30 - 10:00 a.m. *Ichizo Kobayashi* - University of Tokyo, Department of Molecular Biology
Sex and selfish genes

10:05 - 10:30 Break

10:30 - 11:00 a.m. *Miroslav Radman* - Institut Jacques Monod, Paris France
Control of Interspecies recombination and the definition of species

11:05 - 11:35 a.m. *Michael Lorenz* - Universität Oldenberg, Germany
Natural transformation in the soil

11:40 a.m. General Discussion
Leader: *David Shub* - Dept. Biology, S.U.N.Y. Albany

12:30 Lunch

1:00 - 6:00 p.m. Free Time & Poster Viewing

6:00 - 7:30 p.m. Dinner

SESSION IX - PLENARY LECTURE

7:45 - 8:00 p.m. Elections for new chair and introduction - *Julian Adams*

8:00 - 8:45 P.M. PLENARY LECTURE
John Maynard Smith - School of Biological Sciences, University of Sussex, U.K.
Population structure and evolution in prokaryotes

8:45 - 9:00 p.m. Discussion/Response
Richard Moxon - Institute of Molecular Medicine, University of Oxford

9:00 p.m. Open Discussion
Leader: *Julian Adams*

[redacted]

Allen Campbell

I never engage in that kind of dating game myself.

7-27-97

Viral evolution

Historical

- Ultimate origins
  - Degenerate parasites (like organelles) - losing favor for viruses
  - Relics of precellular life - maybe only for RNA viruses
  - Cellular dropouts - (large DNA viruses)
- Change through time
  - Phylogenies
    - Genes vs. Genomes (Chimeras)
      - RNA replicases
      - Tracing lineages backward
    - Methods
      - Alignable sequences
      - Signatures
    - Speciation (Does concept apply?) How much recombination is there within populations

Ongoing population biology

- Origins (emerging viruses) → suggests most "new" viruses aren't really new, just changed a little.
- Maintenance (detective proving)
  - → suggests most are degenerate old viruses

Maintenance

- viruses have been around a long time so suggests that there is some sort of steady state.

- maintained over LONG periods of time (not necessarily constant but little major change)

Recombination

Influenza -

- segmented genome
- get reassorted of different chromosomes
- sporadic massive epidemics in humans
- very narrow lines of descent (very narrow bottlenecks)
- occasional replacement from Avian viruses

Suggests occasional replacements are an adaptation to muller's Ratchet

Lin Chao grew ϕ6 phage ... Compared some grown under small bottlenecks vs. others w/o bottlenecks.

4. Embedo

λ + its relo recombine frequently in nature

Comparison of two phages

1. Special explanation for sharpness of transitions.

2. Models of recombination unlikely to be the same as models for origin of virus

Signatures →

Homogenous w/in genomes } Despite variation
w/in phages } in GC.

Roger Hendrix - phage λ

Sequencing phage genomes

phage L5 - infects Mycobacterium smegmatis
- looks like λ-like phages, but no detectable sequence similarity

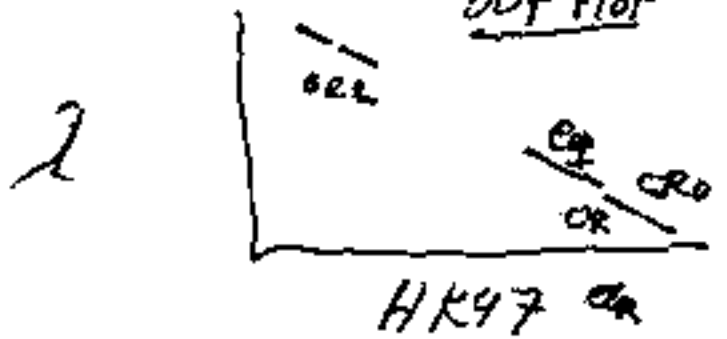
λ-like
HK97
P22
HK022
other
} stretches of high % similarity interspersed w/ low % similarity.

- boundaries are approximately at gene boundaries

- favors view that the recombination events are ~~not~~ random and that selection causes observed boundaries to be at gene boundaries

Examples of evidence

- Get some boundaries w/in genes -- but these are at module boundaries w/in genes



} Genes that f(e) together, segregate together (suggests selection did this)

- Also - head genes tend to stay together w/in a group and tail genes tend to stay together. Sometimes get recombination w/in FZ gene -- which they think FZ interacts w/ head + FZ w/ tail.

Despite tight packing of genes w/in λ-like phages head-tail genes ... there is a gap in ~~here~~ between two λ genes (L, K). However HK022 shows genes here contiguous + therefore suggests λ had frameshift and selection hasn't removed the gap yet.

MORons = new genes that are inserted into head-tail region. They have significant GC content difference from rest of genomes.

Tail of λ

V G T H M ← only translated w/ -1 frameshift from G

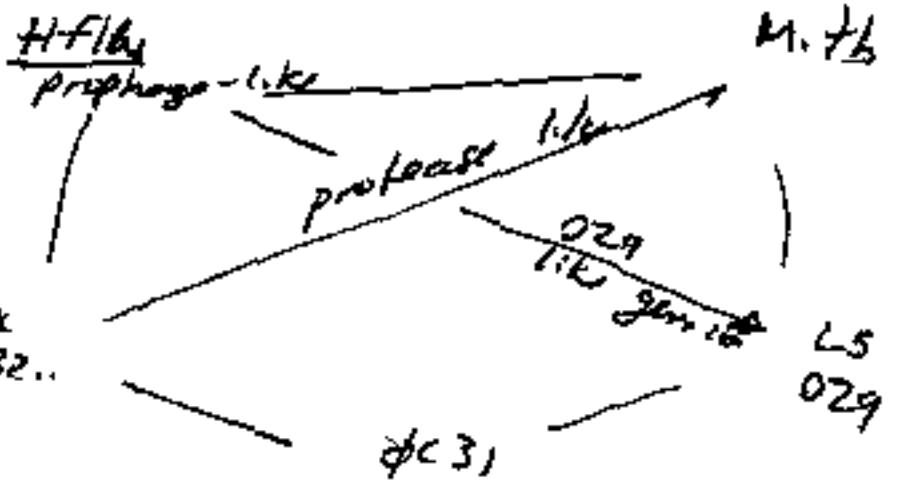
translated by itself

many other phages have two overlapping genes here even though no sequence similarity

Mycobacterium phages

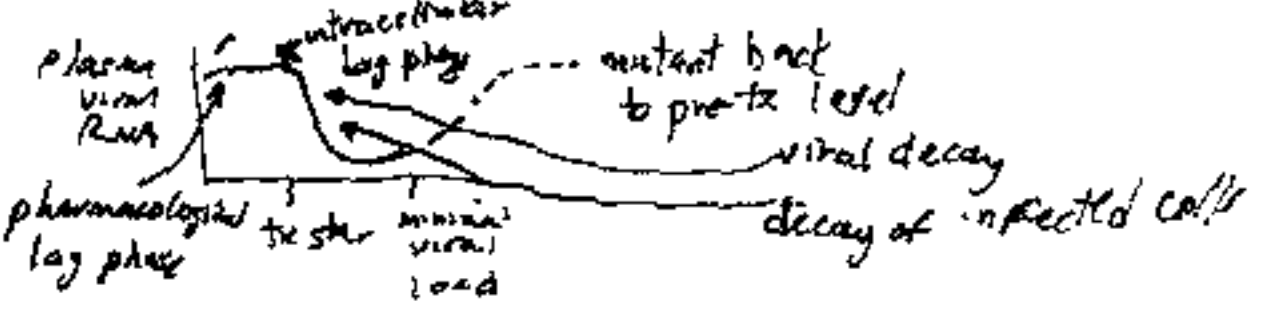
many seem to be mosaics

- this region similar to a region in the genome



- many connections found between variety of phage. Suggest lots of exchange over time.

HIV infection



RT inhibitors, PRT inhibitors

Hep B virus
RT inhibitors block two steps of viral cycle.

Reproductive Ratio (R_0)
- use this to define drug resistance
- if $R_{0\ w/drug} > 1$ then resistant

Discussion

What about

Species concept

- Long history of viruses
- How is genomics going to help?
  - e.g. phage T4 only ~1/3 show similarity to things in databases.

Recombination

- regd. for replication on many phages

Mutation v. high

What are the hosts?

- can ID a thing those grow on in labs but what about in field

The lightbulb wasn't invented by Geo. Thomas Edison but by another man of the same name.

Antibiotic Resistants

Two routes to resistance

① Mutation/altering of target

② Acquisition from another source

③ Acquisition from lineage

"The Earth is bathed in a dilute solution of tetracycline."
SFalkow

Where did they come from

① housekeeping genes
- β-lactamase (cell wall turnover)
- Aminoglycoside-acetyltransferase (peptidoglycan synthesis)

② antibiotic producing organisms

③ natural resistance in soil communities

Aminoglycoside Resistance

- can be caused by modification in 750 ways of aminoglycosides

Antibiotic producing strains

- many Ab^R appear to have originated in Ab producing organisms

Acquisition of new genes

① get ORF
② fusion w/ expression signal
③ low level expression.
⋮
④ association w/ replicon
⑤ inc. expression

Antibiotics III

How different does the concentration of Ab have to be in order to constitute diff selective environments.

Experiments

Mark-release recapture

Compartments in liquid media

β-lactamases

Random mutagenesis of all positions
&
Selection of Amp plate

what about cases where lab mutants don't correlate w/ evolution?

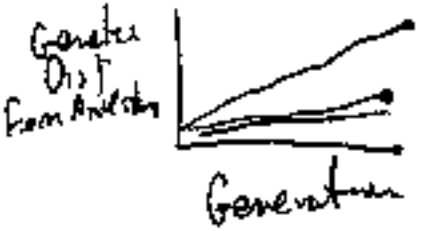
D

Blevin

Michel Blot

Suggests IS elements are designed to make mutations

To maintain IS's, must have potential for beneficial mutations.

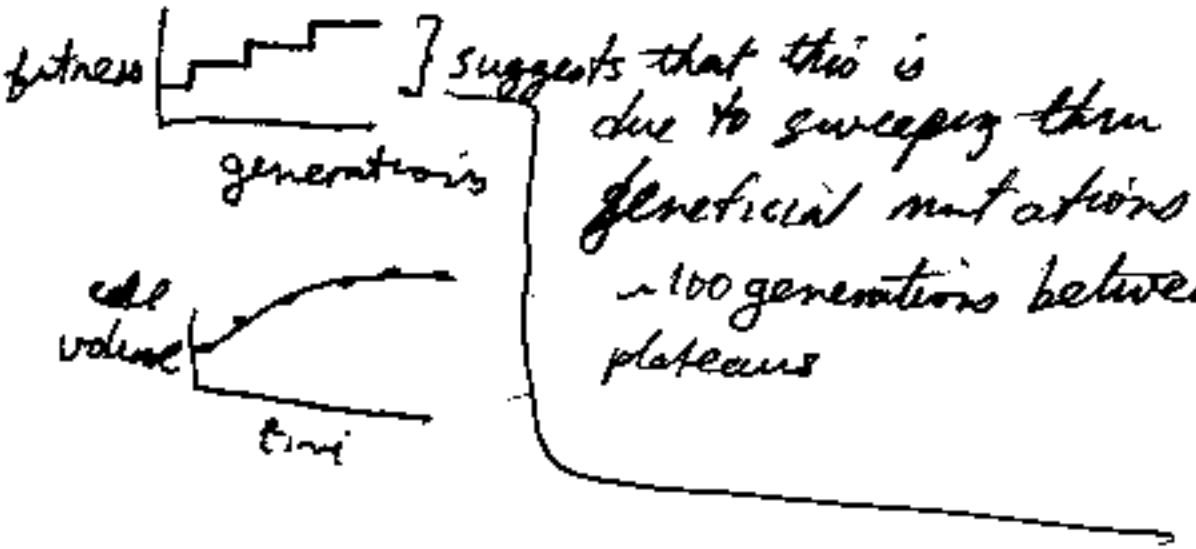


Lenski - Dynamics of Adaptation and Divergence During 10,000 Generations of Experimental Evolution

Escherichia Ahrlenmeris

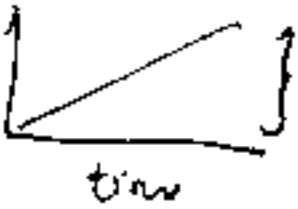
Tempo of evolution
- adaptation
- morphology
- molecular

F. fness = ratio of growth rates in head : head competition

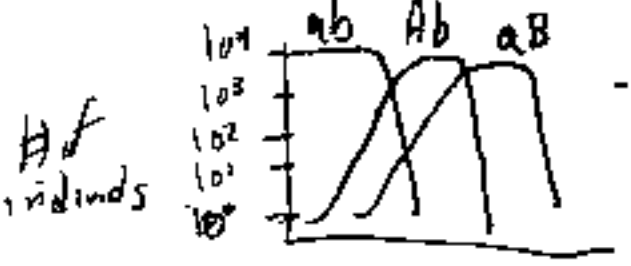


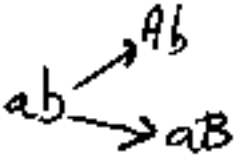
suggests that this is due to sweeping thru beneficial mutations
~100 generations between plateaus

Suggests IS elements are not causing large #'s of adaptive mutations b/c



expect linear w/ neutral changes





- if ab is replaced by a beneficial mutation, then the next beneficial mutation will be more likely to come from ab because it will still have large #'s.

$N = 3 \times 10^7$

$6 = 1 \times 10^4$ (generations)

$\mu = 4 \times 10^{-10}$

↓

600,000,000 mutations over 4 years

↓

but small % of double mutations

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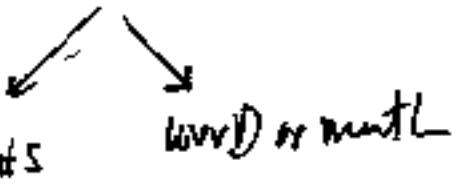
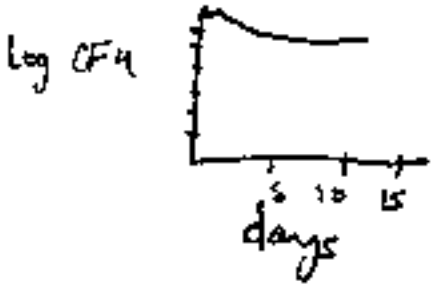
mutators

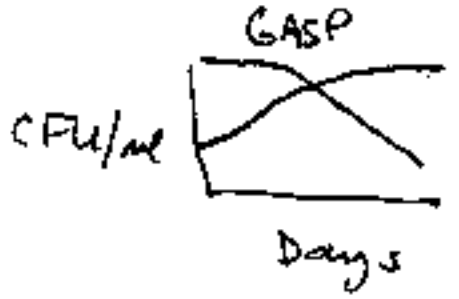
- 3 of lines have 2 orders of magnitude increase in μ



Roberto Kolter



take cells from late in SP, and ~~mix to~~ mix w/ early SP cells



Also
E. cloacae
S. aureus
E. faecalis
B. globigii
S. cerevisiae

RpoS change
- get many diff. types of changes
- many diff. ways of affecting rpoS levels

Take rpoS mutants ... do GASP again ... GASP2

GASP2 - LRP

Get physiological adaptation food.

Claire Cupples
- VSR up-regulated in Stat. phase

Ruben
- mutL limiting in SPM

Joel Torkleson EmboJ 16:3303

Lac+ revertants
look for other mutations in F
-16% of double-mutants are heritable mutators

	higher in lac+?
F	much higher
pBR	much higher
chromosome	much higher
upp	"
Mal-	"
Xyl-	"
Fruc-	not

Reuben Harris
- mutL overproduction diminishes leads to ↓ in SPM but not Log-phase-M.

- overexpression of vsr may KO mismatch repair. Protein not made much during growth phase. made a lot in SP. } Claire Cupples

- Barbara Wright

  - stringent response
  - Leucine starvation → Leu mRNA ↑
  - tx unc. mutation

- Barry Hall

  mini-Tn10 insertion
  - how affect adaptive mutation at ebgr locus
  - 5 genes ... ↓ unc. at ebgr in SP
  - 6 genes - ↓ decr. at ebgr in SP

F. Taddei

- how do mutators do in competition?
- mutators do well in novel competitions. But many have become very specialized, accumulating deleterious mutations.

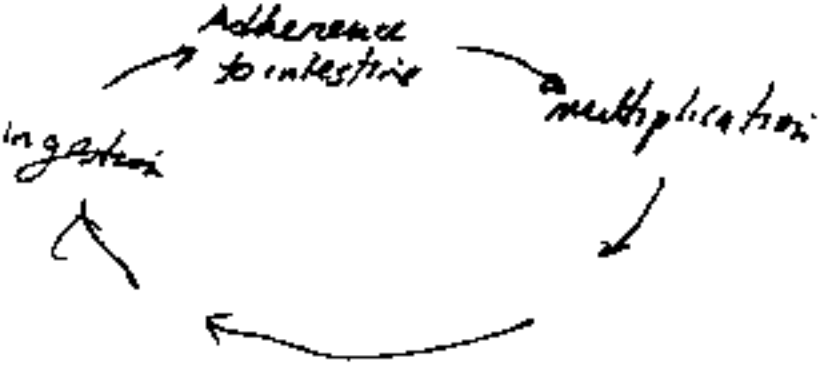
Peter Reeves

Environment for pathogens have changed a great deal recently.

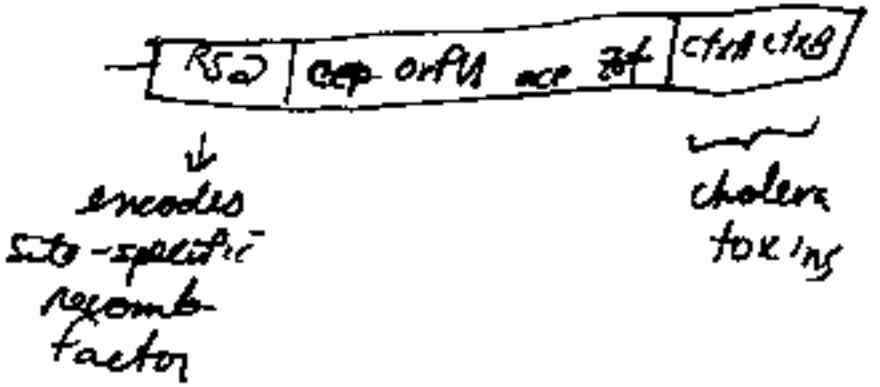
Clonality

- degree of clonality varies great deal
- e.g. Neisseria has lots of lateral transfer

Vi Cholerae "Promiscuity rules"



CTX Genetic element - found in all toxigenic strains



New strain of Cholera involved in pandemic. VC0139.

Single-double recomb. event explains origin of VC0139.

- Also carries genes for Sul^R Trim^R on a self-transmissible element.

Bacteroides TPON →

- can mobilize DNA in trans

So - can this VC0139 self-transmissible element move VCDNA? No - actually - the CTX element can move on its own.

Can get transduction in vivo (in mouse) (depends on expression of receptor)

Do other species have TCP homologs

Tom Cebula

pathogenicity - says must remember that pathogenicity by some organisms is very specific and some genes involved in pathogenecity have other roles

Hypermutability, Horizontal transfer + homeologous recombination: ingredients for rapid emergency of pathogens.

What is freq. of mutators w/in natural populations of bacteria.

Ecoli	total analyzed	# prod. mutators	
O157:H7	120	5	} 100-1000X incr in μ compared to non-mutator
Other types	20	3	
ECOR collection	72	1	
S. enterica			
S. enteritidis	15	1	
other serovars	106	14	
SARB strains	69	1	
SARC	16	2	

Frequency of mutators is much higher than you expect for a deleterious mutations

Complementation of mutators

- all mutators they isolated could be complemented by mismatch repair wt. alleles.

MMR mutants are promiscuous

MutsL inhibit strand exchange

Advantages of mutator phenotype

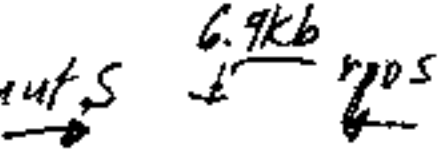
- genetic variation
- opportunity to quickly change
- incr. in genetic exchange

Always pull out MMR mutants

∴ Why always MMR mutants?

- why not other 50x↑ mutators
  - certain alleles may be more primed for mutator

- MOST of the mutators were mutS



in some mutator strains, the 6.9kb intergenic region is messed up
- 12 bp direct-repeat in Salmonella?
- all the E coli ones seemed to be deletions of part or all of mutS.

K12 vs O157 vs Shigella dysenteriae

5' K12, O157 v. similar

3' O157, Shigella v. similar

-this region highly variable in enterics

Yersinia enterocolitica → nuts ← rpoS Shigella sp.

-if you nutrient deprive strains rpoS ↓ leads to incr. in mutation

Suggests

- anti-nuts expressed (but not in K12)
- antisense might inhibit nuts and lead to a mutator

Dykhuizen - Lyme Disease

Lyme disease: suggests it been around a very long time

borelia hermsii - causing Relapsing fever
- replaces outer membrane proteins by recomb. mechanism

S. Levy

major antibiotic resistant bacteria

Hospital:

Community: Pneumococcus, MTB, N. gon, Strep, Ecoli

Vancomycin resistance

Van^A gene -- spread

- Enterococcus
- Corynebacterium
- L. lactis

Van^A gene found in lots of animals.

Animal use of antibiotics impact pool of resistant strains and plasmids.

Van^B gene -

New Van gene in Japan

Suggests using as little Ab as possible, to have as small an impact as poss. ble on non^R bacteria.

MAR locus

Ab^R
Microbial metabolism } may be responsible for multidrug resistance
NFo
SOX

Antibacterials } Also lead to Ab^R
Disinfectants

Posters

Reuben Harris

overexpression of MutL
- inhibits lac+ accumulation in SP
- fails to prevent decline of MutS and MutH proteins in SP

Claire Cupples + Gina MacIntyre

overexpression of Vsr leads to ↑ mutation

- Vsr protein v. low in growing cells
- Vsr protein ↑ in SP
- ∴ when replicating Vsr is low.

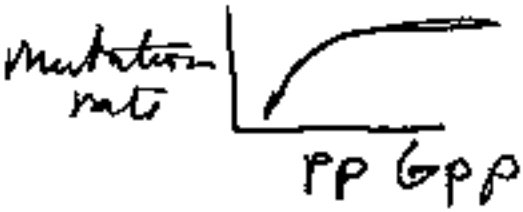
Blanchard + Lynch

V. Perot - Kinetics of Ab Action in slowly growing cultures

Peter Young (& Susan Lloyd) MCB1

RecA phylogeny in rhizobia

J Reeves + B. Wright



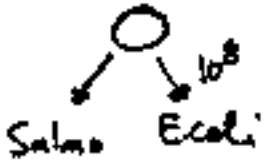
R Kolter SEFinkel

Ecoli remain viable for long pds of time
SP cultures are highly dynamic
cells acquire GASP phenotype during
prolonged SP
mutation freq. affects rates of
GASP appearance

Cooper + Lenski

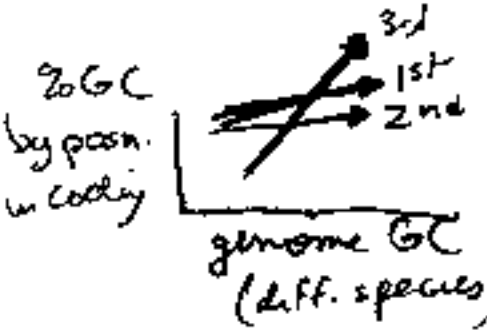
3 pops w/ incr. mutation rate

John Roth



How distinguish?

- lact (EC) vs. BL2(ST)
- many of these things appear to be foreign



- can predict age of such sequences by how long it would take to change GC to fit curve.

- ~15% of E coli genes look weird } claims most are older than 90 mya... but how old could it detect.
- mean age = 26 million yrs

Estimate

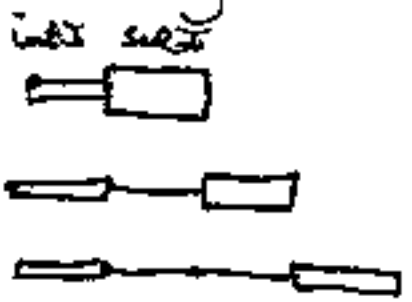
EC vs ST 75% = shared ancestral
25% = unique foreign + unique ancient

Who gets lost?

} essential
} important
} near neutral → small value always
→ important but rarely used

Genes responsible for species differences
unlikely to be essential for life.

Integrons - R. Hall CSIRO



- flanking sequences identical
- internal genes different
- 3 separate classes

Recombination Sites

- 57–141 bp
- RYYYAAC ... GTTRRRT
- ~20 bases at each end conform to a consensus
- imperfect inverted repeats

- Move by site-specific recombination
- Companion elements (integrons) code for int genes

3 families

class I :

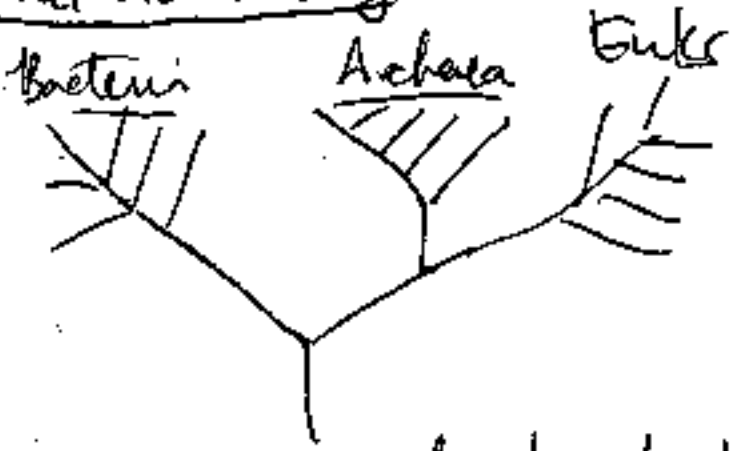
class II : Tn7

class III :

- can insert into 1° or 2° site
- most cassettes dont have promoters.
- integrons have promoters

Conjugative Transposons

Very broad host range



organism from v. distant taxa have the opportunity to interact + exchange.

The Colon

- complex environment
- is it a reservoirs for Ab^R genes

Ingested flora → Intestinal Microbiota → Bacteria pathogens

Kirsti is a bellydancer

Examples

Treponema denticola → ermF → Bacteroides

Enterococcus
Staph
Strep
Actin
B. F. do

- tetM
- all virtually identical

Campylo
Fuso
Gardnerella
Haemop.
Neisseria
Veillonella

Conjugative Exchange

Plasmids
Chromosomal elements

Bacteroides

integrated excision → transfer to recipient

- can also transfer NBUIs (non-autonomous elements)

Donor -- ~~can be~~ Bacteriodes -- recepient can be many

Integrate at end of tRNAs

Howard Ochman

- Evolutionary psychology
- Genome structure
  - Additions
  - Deletions
  - Inversions
  - Transpositions
- Size variation
  - Selection?
  - Rate of change?
  - Tolerable range of variation?
  - Role of horizontal transfer in phenotypic variation w/in + among species
    - Mechanisms?
    - Location influence?

- What role does genomics play
- How do genomes co-opt new genes

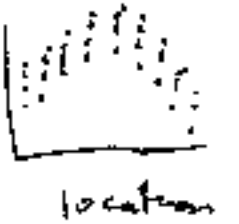
Microbial Evolution - Sharp

What can we get from genomes?

1. phylogeny

2. Genome content
   a. protein coding genes
   b. RNA-coding genes
   c. repetitive elements

3. Genome structure
   a. ancient duplication
   b. GC variation



Steve Oliver

Genes w/ reported known f(x): 2600

Genes w/ f(x) predicted by sequence: 990

Genes w/ unknown f(x): 2200

5790

Lots of redundancy

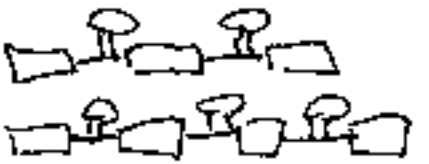
Can you expunge most of it?

- See KWolfe paper

Repeated elements

T4 population biology

T2
T4 } mostly highly similar, but many polymorphisms
T6



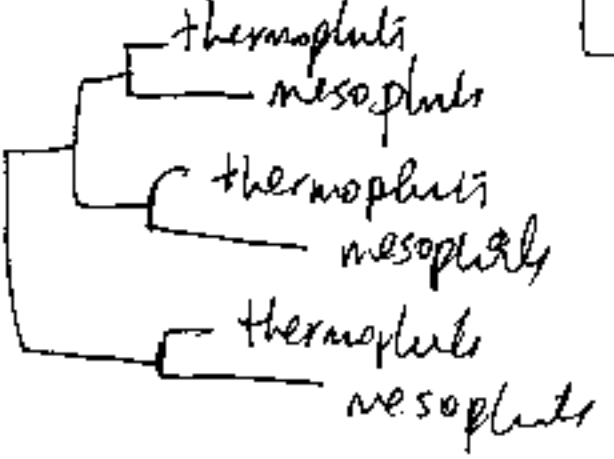
} much of the variation is in copies of repeats

- some "pseudo-T-Evens"
  that look like T4
  but not alike in most DNA/genes

Gary Olsen

① use + abuse of molecular phylogenies
② inventions of genes
③ site specific rate of change

Need a model for evolution



① rates should correlate w/ # inferred by parsimony

② rates should correlate betw. groups

③ rates from one group should help study other groups

Physicists start with questions and look for answers.

Biologists start w/ answers and look for questions.

D. Hartl

Macroevolution: what is it good for?

- Lederberg -- it shows the difference between your luck and Lederberg.
- Cavalli- story. HFR-C -- didn't know what ~~[illegible]~~, to Cavalli years but thinks it might be a type of clarification

What is it?

-
-
-
-

How does it apply to microbes?

- Suggests that microbes are not as prone to mass-extinctions as non-microbes

Plasmids -

what is natural distribution of F? → Now have IS in F in O

- ~15% of Ochman's Ecoli strains
- ~15% of Salmonella virulent strains
  - of these there are two groups:
    - some like Ecoli P
    - some very different } all have spv operon

Peggy Sats -

aa + tRNA $\xrightarrow[\text{aa synthetase}]{}$ tRNA-aa → translation

Evolution of code/tRNA isoacceptors

① Does evolution of tRNA mirror evolution of synthetases?

(can imagine switching might be relatively easy)

E.coli isoacceptors

② Replacement > complementation

③ Isoacceptors may not share common ancestors-

EVOLUTION OF AMINOACYLATION SPECIFITY

Mycoplasma
lacks GlnRS

Methanococcus
lacks GlnRS
AsnRS
CysRS - aided by SepRS

GluRS

↙ adds Glu to GluTRNA

↓ adds Glu to GlnTRNA → Glu & Gln ↓

Constraints

Another constraint I can put on this model, or this verbal thing.

N. Moran - Endosymbionts

Buchnera
- passed on from ♀ → offspring
- enclosed w/in vacuoles
- what gain for aphids?
  - provides essential nutrients
  - produces ftsp's
- phylogeny parallels host (w/in aphids)
- substitution rate looks ~2X > Ochman + Wilson
- Plasmids for (trp EC, leu ABCD) (used by host)
- ~28% GC
- 1 rRNA
- recF missing?
- Gene order similar to E coli?

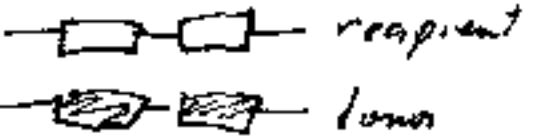
- multiple infections w/ diff. endosymbionts

Pop. Dynamics

Ne much lower than for free living

- long branches for endosymbiont
- d_S/d_N = lower than in other species — Stat. Phase
- suggests accumulation of slightly deleterious mutations
- rRNA structure analysis supports this

Restriction



integration
restriction
exonuclease
recombination

Restriction Systems

Type I - ~~not~~ widely distributed
Type II - very widely distributed
~~methylation sensitive~~ dependent
modification dependent

} don "missing" its restriction gene

Why sex?
Repair
Eliminating mutations
Parasite selection

Restriction-Modification as Selfish Genes

cell w/ restriction genes → hard to lose restriction system (cells will die).

- Suggests this is similar to meiotic drive
- If two systems have same recognition, then is no advantage to maintaining both systems. Suggests that this explains diversity of recognition system.

Bacterial Sex

Chi sequences in other species

- Suggests RecBCD system is involved in selfish gene system

- if DNA from outside, then RecBCD will degrade completely
- but if invading DNA has Chi, then it will be protected.

- DSBR protects agst genome parasites

Mini Review

Genetic barriers between species come down to recombination barriers

→ isolation

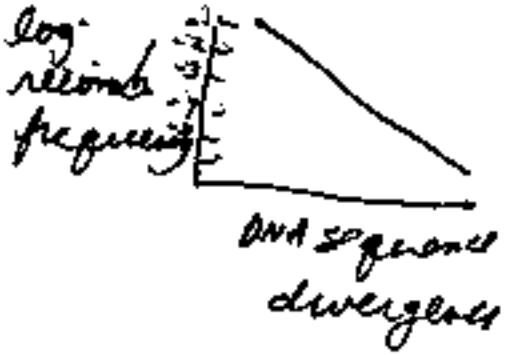
↓

O ⇔ O

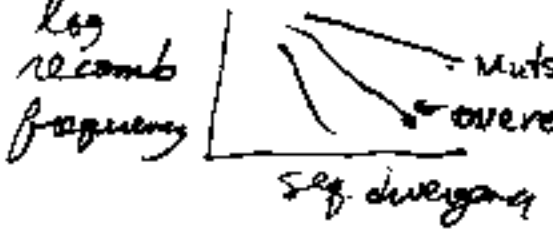
- MutS,L prevent exchanges
- SOS positively controls exchange

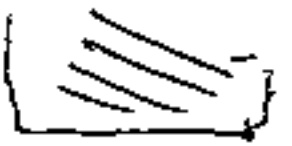
- MutSL controls accumulation of differences as well as whether exchange can occur

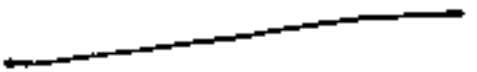
- RecA/SOS does same

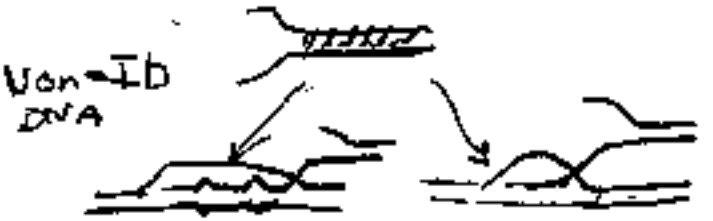


$R \sim N \approx L c^{-Hd}$




as you decr. RecA, get less recombination





If sequences are identical, will align

↓

MMR corrects and reduces recombination

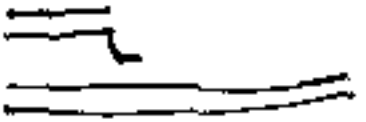
As RecA is searching for homology,
SOS is induced bec. of strand ends
↓
more RecA

Why this then?

- MutSL prevents recombination between repeats

- stress → incr. mutation → stress relieved
  via. SOS
  decr. mutSL
  ↓
  variation w/in population

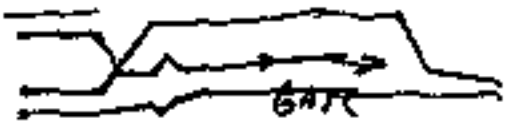
RecBCD
RecFOR
Exo VII (RecE)



RecA ↓↑ MutS, MutL can reverse, but only in RecBCD pathway

~~RecA~~

DNA synthesis ↓ PriA, RecF



Vsr on

MutH
MutH

cut unmethylated GATC's

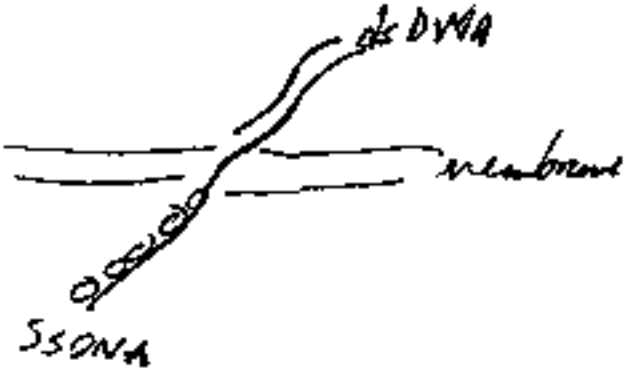
No RecA

Mike Lorenz

~~Sequence transfer~~

Transformation

- in B. subtilis
- ~120 genes involved



If mismatches prevent transfer then more highly conserved genes should be more prone to transfer.

Function for natural transformation

Natural transformation

Nutrients

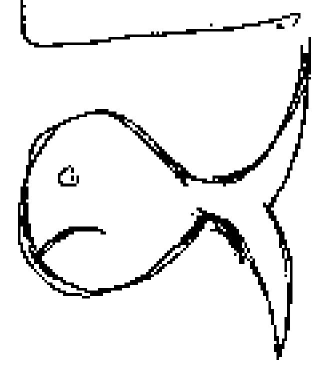
Repair of DNA

Gene regulation

John Maynard Smith - How much recombination is there?

Penicillin resistance
- penicillin binding sites
- recombination event required to acquire resistance

what are nucleotide substitution in newly acquired segment



How show recombination?
- alignments + statistics
- linkage disequilibrium (Feldman)

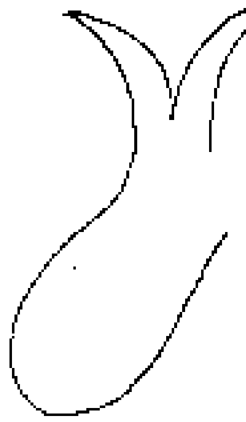
$$I_A = \frac{V_k}{E(V_k)} - 1$$

Nei. gon 0.04 +/- 0.09 (Indicated recomb ↑)
Salk 3.11 +/- 0.09 " " "
but probably due to separate subpopulations

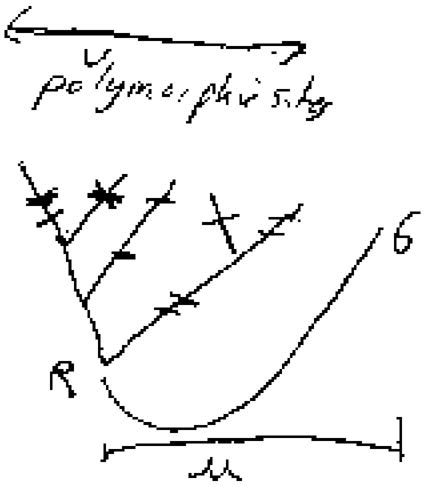
- parallel trees of same gene

rigF } similar phylogenies
recA }

adk - different than rigF, recA



But we ignore selection agst transfer of certain genes



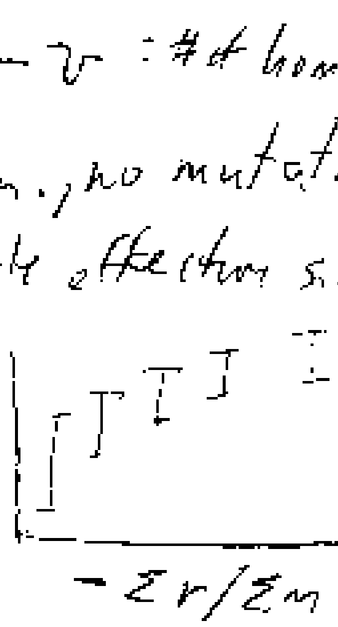
How calculate expectation for recombining strains?

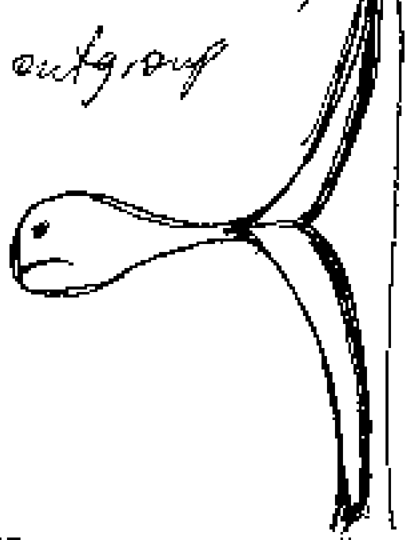
can you apply this to Hillis + Bull

- h = steps - v : # of homoplasies
- if no recom., no mutation, then h=0
- can calculate effective site # using outgroup

Homoplasy Ratio

$$= \frac{H_{obs} - H_{clonal}}{H_{sat} - H_{clonal}}$$





If no recombination then whole genome works as a unit and selection on one works on all.

But if there is recombination, then gene fitness can be different than genome.

why transform?