Subject: Re: Presubmission enquiry
Date: Thursday, 6 June 2024 at 15:29:50 Central European Summer Time
From: Joshua Lawrence
To: Christopher J. Howe, Alberto Scarampi del Cairo di Prunetto

On the negative selection point, I've also found this new paper released on Biorxiv looking at similar things to us, although again with ABR casettes engineered into the chromosomes rather than looking at changes in native genes. They find that you have positive selection pressure applied from spatially or temporally fluctuating antibiotic concentration, with negative selection pressure from unnecessary burden of gene expression. I think the ATP burn from these ABC transporters would fit with that nicely.
https://www.biorxiv.org/content/10.1101/2024.05.09.593358v1.full

Also a selection of other papers which I've expect you've read Albi but pasting here just in case. Perhaps most interesting is the one about the hyperpolyploid which has a very similar genome in the various environments from which it has been isolated.

https://academic.oup.com/mbe/article/38/3/1040/5970467
https://academic.oup.com/genetics/article/222/2/iyac121/6663764
https://www.mdpi.com/2076-2607/11/9/2267
https://journals.plos.org/plosgenetics/article?id=10.1371/journal.pgen.1010829
https://www.nature.com/articles/s41564-021-01034-3
https://journals.asm.org/doi/10.1128/mbio.00510-19
https://academic.oup.com/gbe/article/13/6/evab037/6156627

From: Christopher J. Howe <ch26@cam.ac.uk>
Sent: 06 June 2024 13:59
To: Joshua Lawrence <jml203@cam.ac.uk>; Alberto Scarampi del Cairo di Prunetto <as2945@cam.ac.uk>
Subject: Re: Presubmission enquiry

PS Or you can have a polymorphism with both alleles being neutral at high frequency and beneficial at low.

On 06/06/2024 14:57, Christopher Howe wrote:

> Another way of maintaining a polymorphism is -ve frequency dependent selection, ie an allele is advantageous at low frequency, but disadvantageous at high.
>
> Maybe the MV-R allele pumps out something nasty, but pumps out useful things as well when there is more of it, or wastes ATP when pumping nasty things out which gets to be a problem if there is a lot of it. That might give the frequency dependent selection.
>
> Best wishes,
> Chris
>
> On 06/06/2024 13:44, Christopher Howe wrote:
>
> > Thanks - they look very useful.
> >
> > I'm sure there has to be some kind of balancing selection to maintain the kind of polymorphism we see. So if there are occasionally conditions under which the MV resistance mutations can be beneficial (assuming populations aren't routinely exposed to MV) that would allow them to be maintained.
> >
> > C
> >
> > On 06/06/2024 13:37, Joshua Lawrence wrote:
> >
> > > Also this paper just appeared in my inbox. Very relevant! It's a model showing how heterozygosity of plasmids in bacteria can be maintained, but only with strong fitness advantage in the heterozygote to combat genetic drift.
> > >
> > > https://www.biorxiv.org/content/10.1101/2024.05.29.596466v1.abstract
> > >
> > > They also reference this paper which has experimental evidence to show that this genetic drift actually limits the rate of mutations in plasmids relative to a haploid chromosome. So it could be that actually the Cyanobacteria have a slower rate of new mutations, but benefits from the heterozygous advantage. I think this is consistent with measurements of cyanobacterial mutation rates relative to E. coli, and anecdotally Tanai told me in his LTE experiments with Cyanobacteria they were barely changing over many generations.
> > >
> > > https://academic.oup.com/mbe/article/38/12/5610/6373903
> > >
> > > It also references this (brilliant) paper where they show that heterozygous plasmids can be maintained under fluctuating selection pressures- either with and without or switching between two different selection pressures. I think this nicely explains how cyanos maintain these mutations. They could provide heterozygous fitness over a day-night cycle, or even over longer periods (e.g. seasons). Also raises the questions if allele frequencies fluctuate between seasons.
> > >
> > > https://www.nature.com/articles/s41559-018-0529-z

@Alberto Scarampi del Cairo di Prunetto I think these papers should help a lot with the discussion. I'd recommend reading them and digging into their references when you're back from your holidays to help with writing this. These are all on plasmid systems, but I think they give a strong theoretical basis to our observations in Cyanobacteria.

Best wishes,

Josh

From: Christopher J. Howe <ch26@cam.ac.uk>
Sent: Wednesday, June 5, 2024 5:04:06 PM
To: Alberto Scarampi del Cairo di Prunetto <as2945@cam.ac.uk>; Joshua Lawrence <jml203@cam.ac.uk>
Subject: Re: Fwd: Presubmission enquiry

Dear Both,
Just to let you know Curr Biol have said submission by the end of June is fine.
Best wishes,
Chris

On 05/06/2024 07:15, Christopher Howe wrote:

> Dear Albi and Josh,
> This is encouraging.
> Can we discuss the follow-up after the lab meeting today?
> Thanks,
> Chris
>
> -------- Forwarded Message --------
> **Subject:** RE: Presubmission enquiry
> **Date:** Tue, 4 Jun 2024 20:30:04 +0000
> **From:** Cosma, Christine (ELS-HBE) <ccosma@cell.com>
> **To:** Christopher Howe <ch26@cam.ac.uk>
>
> Dear Chris,
>
> Many thanks again for sending us your presubmission enquiry, and for your patience. I've now had a chance to consult with some expert advisers, and have discussed your manuscript with my colleagues. We will be happy to consider your manuscript for publication in Current Biology. When we send your manuscript out for review, we will be asking referees specifically for their thoughts on the extent of the advance, the strength of the evidence in support of your claims, and the suitability of your paper for publication in a general biology journal.
>
> **Please note that as you are preparing your manuscript for submission, we ask that you be mindful of the audience. As we strive to appeal to a very wide readership, the manuscript should be accessible to non-specialists, as well as being of sufficient depth for specialists in your field.
>
> **Please confirm by email to me the approximate date on which you plan to submit your manuscript.** When you submit the paper, please also be sure, in your covering letter, to refer to this presubmission exchange, mentioning my name and the date you received this message.
>
> Please note that you should submit your manuscript via our online submission and review system at http://www.editorialmanager.com/current-biology. When your manuscript is ready, please go to the site and follow the instructions on the homepage.
>
> If you have any questions, please let me know.
>
> Best Wishes,
>
> Christine Cosma
> Senior Editor, Current Biology
>
> ---
>
> **From:** Christopher Howe <ch26@cam.ac.uk>
> **Sent:** Friday, May 31, 2024 5:17 AM
> **To:** Cosma, Christine (ELS-HBE) <ccosma@cell.com>
> **Subject:** Re: Presubmission enquiry
>
> Dear Christine,
>
> Sorry for the delay.
>
> I suggest the following:

Dr Tanai Cardona t.cardona@qmul.ac.uk Evolution of photosynthetic microorganisms

Prof Alistair McCormick alistair.mccormick@ed.ac.uk Adaptive laboratory evolution of microorganisms

Prof Saul Purton s.purton@ucl.ac.uk Molecular genetics of photosynthetic microorganisms

Prof Pramod Wangikar pramodwangikar@gmail.com (IIT, Bombay) Adaptive laboratory evolution, metabolomics

Prof Tom Bibby tsb@soton.ac.uk Polyploidy in cyanobacteria

Prof Anna Amtmann Anna.Amtmann@glasgow.ac.uk Stress response in photosynthetic organisms, including cyanobacteria

Thanks,
Chris

On 29/05/2024 19:52, Cosma, Christine (ELS-HBE) wrote:

> Dear Chris,
> Thank you for your presubmission inquiry to Current Biology. We are potentially interested in you
>
> Best wishes,
> Christine
>
> Christine Cosma, Ph.D.
> Senior Editor, Current Biology
>
> -----Original Message-----
> From: Christopher Howe <ch26@cam.ac.uk>
> Sent: Tuesday, May 28, 2024 6:00 AM
> To: ELS-LON Current Biology Mailbox <cbiol@current-biology.com>
> Subject: Presubmission enquiry
>
> [You don't often get email from ch26@cam.ac.uk. Learn why this is important at https://aka.ms/Lear
>
> Dear Editors,
>
> Please find attached a presubmission enquiry for Current Biology. We show that the high ploidy lev
>
> Please let me know if you require any further information. I look forward to hearing from you.
>
> Yours,
>
> Chris Howe