Pf tent

(inspired by PfLOME)

By Cassia

I gave up on PfLOME

- Wayyy too much for our use case, which made it difficult to to learn what was relevant for me.
- Coded in R in R6 objects, which are private access objects that I was not familiar with and kept getting confused by.
- Type-specific immunity was not actually implemented, and I had to recode it in anyway and fit it into their immune framework.

Presenting Pf tent!

Retains the key features of PfLOME:

- Infections defined by tent function.
- Tent function modified by existing immunity.
- Strains defined by specific alleles at some number of loci.
- Immunity can be “general” or “type-specific”

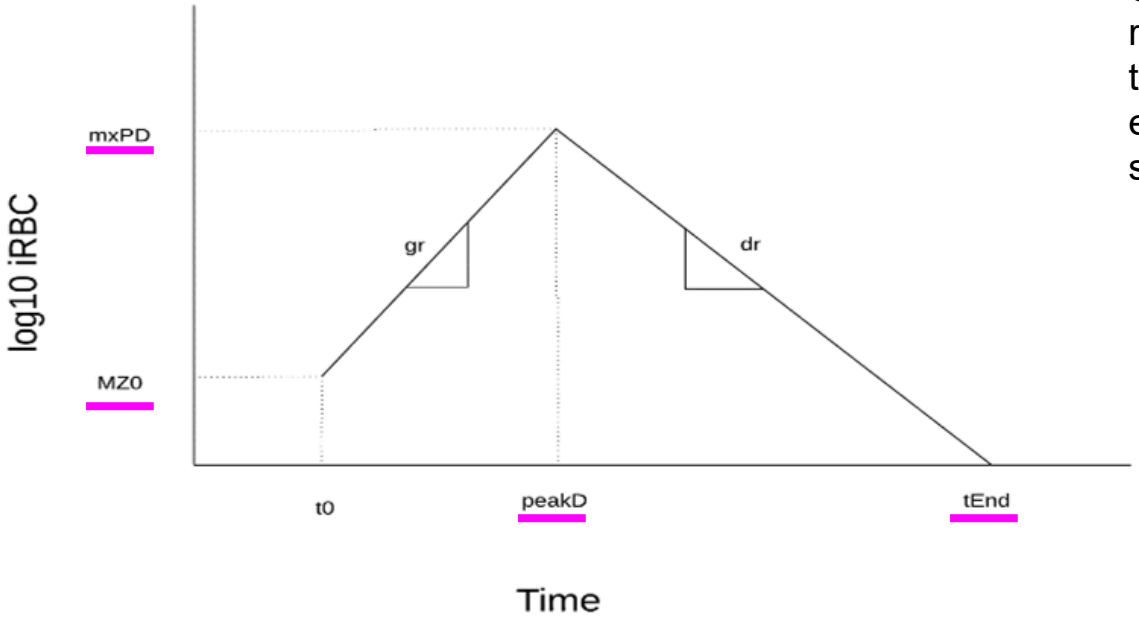
Bites

Time between bites is pulled from an exponential distribution with a rate k. I've been using k = 0.11 per day, which corresponds to 40 bites/year.

At each bite time, a person is infected with a parasite strain defined by a vector of alleles at loci. The shape (length, height) of that infection are determined by tent params that are modulated by immunity (type-specific cross immunity and/or general immunity).

Infections

As in PfLOME, infections are defined by 4 params:



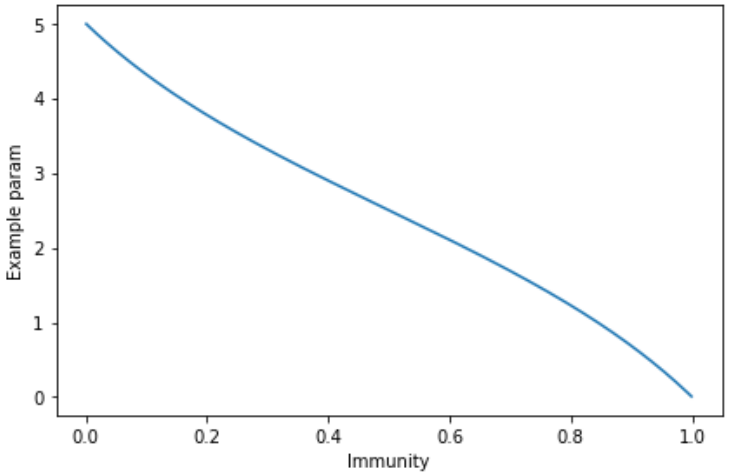
Unlike in PfLOME, I got rid of the fancy math that will smooth out the edges too keep things simple.

Params are pulled from distributions, so includes some limited stochasticity:

- Mz0 & pmax pulled from log normal distributions
- Peak time & duration pulled from normal distributions.
- I thought this was how PfLOME works but when I dove into code. Params were just values they were not pulled from a distribution.

Immunity modulates params via a sigmoid:

- This immunity modulation is pulled directly from PfLOME
- Immunity is defined on scale from 0 to 1.
- I'll explain how immunity is calculated in a hot sec.



Strains

Strains are defined by vector specifying allele at each loci.

[0 2 5]

The strain is defined by 3 loci. In the first loci, you have allele 0. In the second loci, you have allele 2. In third loci, you have allele 5.

Different loci can have different potential number of alleles.

Parasite density is tracked by loci at each allele.

Parasite density at time t

Alleles

Loci

```
[ 298, 1323,  996,    0,    0,    0]
[ 285, 1251,  671,  409,    0,    0]
[   0, 1080,    0, 1199,    0,  337]
```

Sum along any row = total parasite density

When you get infected anew, simply add the “tent” of parasites densities at the strain’s alleles at each loci.

Immunity

Strain immunity

Alleles

Loci

```
[1.   , 1.   , 1.   , 0.   , 0.   , 0.   ]
[0.736, 1.   , 1.   , 0.6  , 0.   , 0.   ]
[0.   , 1.   , 0.228, 1.   , 0.   , 1.   ]
```

If parasite density at allele is > immune threshold, immunity is gained at rate gamma.
If parasite density at allele is < immune threshold, immunity is lost at rate delta.

General immunity

If total parasite density > immune threshold, immunity is gained at rate alpha
If total parasite density < immune threshold, immunity lost at rate beta.

Both strain & general immunity can only be gained up to 1, and then it plateaus.

(This is how PfLOME works, they just did some fancy smoothing that I did not add in for simplicity.)

How immunity works in practice:

(cool because can apply different weights to general immunity & specific alleles)

Infection with strain [1,3,0]

```
[1.   , 1.   , 1.   , 0.   , 0.   , 0.   ]
[0.736, 1.   , 1.   , 0.6  , 0.   , 0.   ]
[0.   , 1.   , 0.228, 1.   , 0.   , 1.   ]
```

New param = Σ Sigmoid((Immunity vector) 0.2 / 0.1 / 0.6 / 0 , Param x (weight vector) 0.2 / 0.1 / 0.3 / 0.4)

0.2 ← general

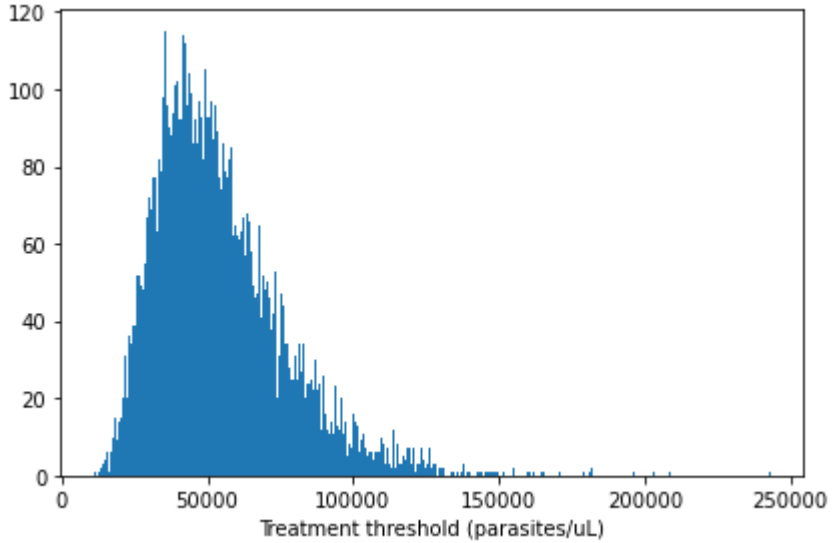
0.1 / 0.3 / 0.4 ← Strain specific

Treatment

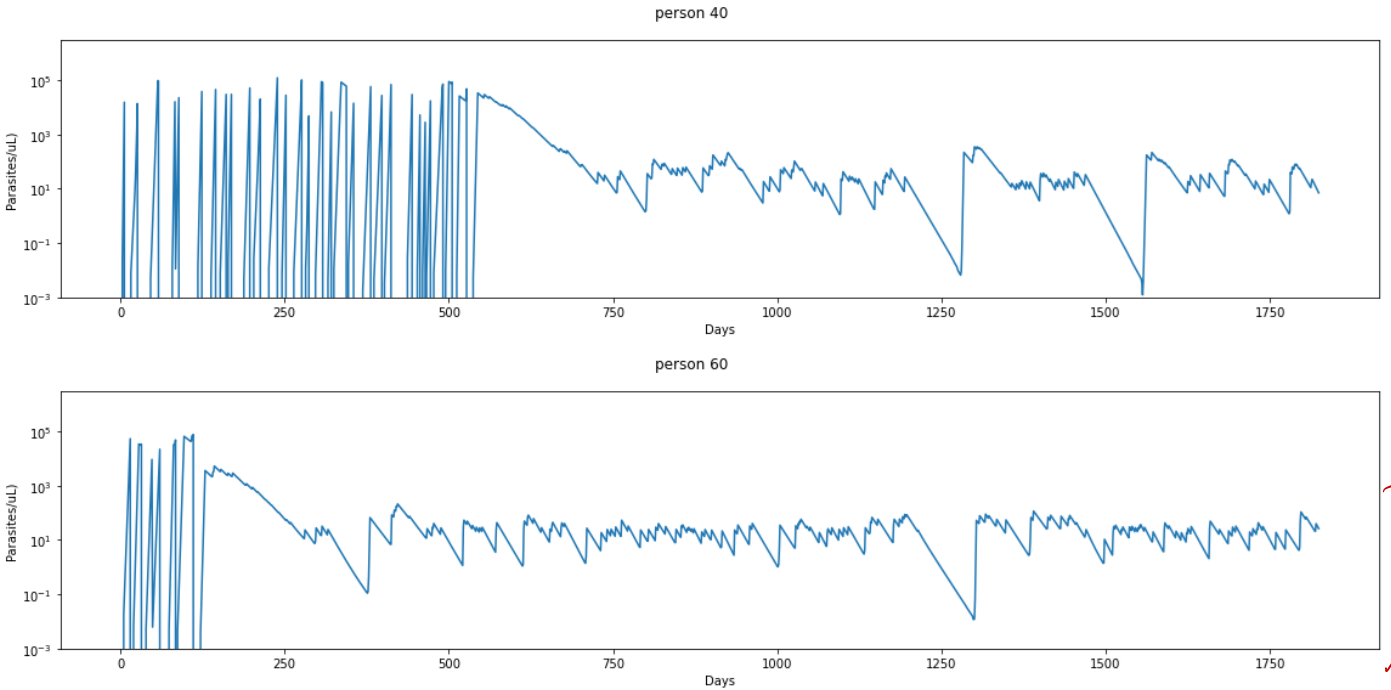
Varied by age + exposure?

When parasitemia goes above some threshold, all parasites are wiped out.

Threshold is pulled from log normal distribution.



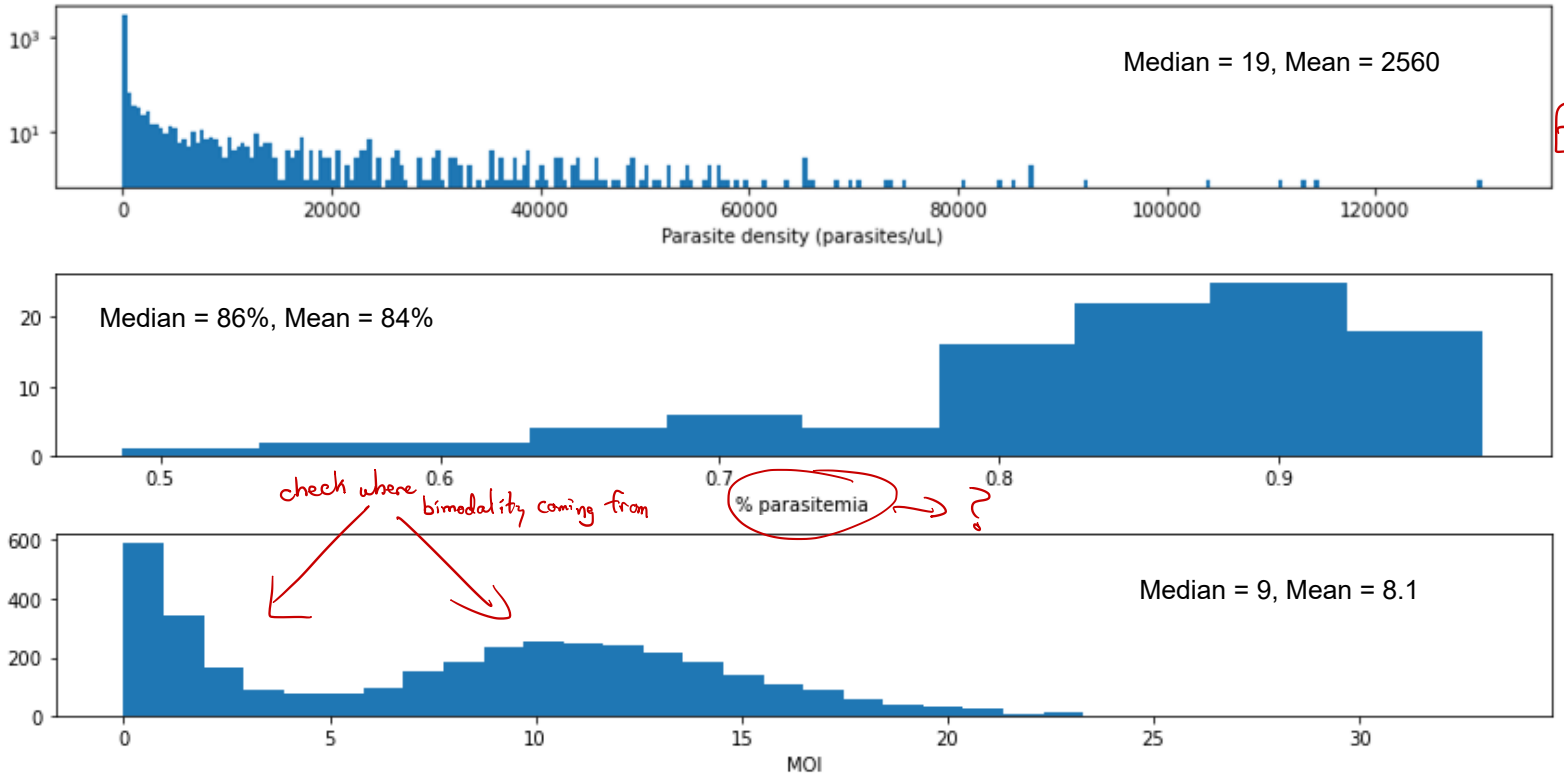
Simulations from 0-3 years: Example trajectories



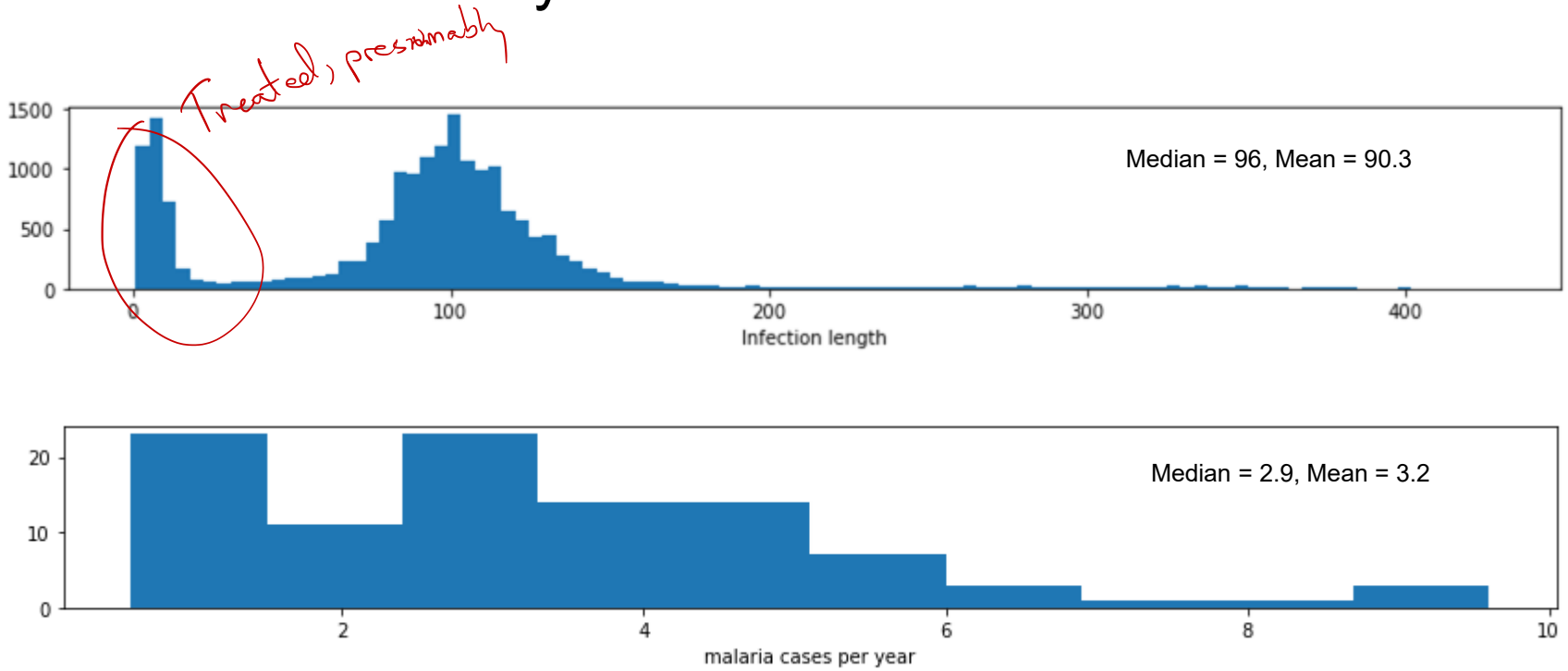
Parasite densities high enough to cause fever only happen when young. Then get one infection that builds up a lot of immunity & mostly steady parasitemia from then on.

Simulation from 0-3 years: Results from 100 kids

Parasitemia & MOI measured every 30 days:



Simulation from 0-3 years: Results from 100 kids



Thoughts

- I think overall trajectories are a bit weird in that they don't allow for symptomatic malaria when older. And this is kind of a problem inherent to how immunity impacts infection parameters in Pf Tent.
- However, summary stats that I care about (parasite densities, malaria cases, infection length, MOI) are all reasonable and within the range of expected.
- I think I should use this to move on & start looking for signals of antigenic loci.

+1!

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