coinf_model

August 20, 2018

1 STH co-infection model

In [1]:
```
using Distributions #Package contaning negative binomial distribution
```

1.0.1 Global parameters

In [2]:
```
const ts = 1/73 #time step in years; 5 days
const halflife = 8.1/365 * ts #halflife of immunity in hosts in days
const av_age = 18.2 #Initial average age in years in population - used very roughly
const pc_dr = 8/1000 * ts #per capita death rate
const stool_samp = 0.054 #Stool sample used in measuring egg deposition
```

Out[2]: 0.054

Age specific death rates Source: Table 7 in http://www.statistics.gov.lk/PopHouSat/Life%20Table%20Report

In [3]:
```
age_specific_death_rates = vcat(
        repeat([0.00045 * ts], inner = 5),
        repeat([0.00078 * ts], inner = 10),
        repeat([0.00320 * ts], inner = 15),
        repeat([0.00429 * ts], inner = 10),
        repeat([0.00890 * ts], inner = 10),
        repeat([0.01946 * ts], inner = 10),
        repeat([0.04245 * ts], inner = 10),
        repeat([0.09133 * ts], inner = 10),
        repeat([0.22017 * ts], inner = 10),
        repeat([1],inner = 100))
# ### Worm species specific parameters
# Defining a data structure with parameter values that are specific to worm species, w
# Can access elements in the structure using '.', e.g `N_a.b`
# T means type, e.g. Int, Float64.
# The struct is mutable so that parameters can vary if necessary
mutable struct Par{T}
  b                    ::T   # 1.rate of exposure per day - has to be v v low
  Imme_activation      ::T   # 2.to fit - activation of immunity per worm
  Immf_activation      ::T   # 3.as above but for anti fecundity immunity
  WfN                  ::T   # 4.max eggs per day per female worm
  mu_le                ::T   # 5.death rate of early larvae per day
```

```
    mu_ll                ::T   # 6.death rate of late larvae per day
    mu_adults            ::T   # 7.death rate of adult worms per day
    M_le                 ::T   # 8.rate of maturation of early larvae per day
    M_ll                 ::T   # 9.rate of maturation of late larvae per day
    pool_egg_loss        ::T   # 10.rate of loss of eggs from field per day
    pool_egg_maturation  ::T   # 11.rate of maturation of eggs in field oer day
    pool_infectives_loss ::T   # 12.rate of loss of infective larvae from field per day
    dens_effect          ::T   # 13.density dependent effect on per worm fecundity
    k                    ::T   # 14.k of negative binomial distribution (mean, k)
    weightings           ::T   # 15.relative weight of worms
    est_modulation       ::T   # 16.modulation of antiestablishment immunity
    fec_modulation       ::T   # 17.modulation of antifecundity immunity
    init_mean            ::T   # 18.mean of initial distribution of worms in pop.
end
```

Inputting parameters for each species

```
In [4]: N_a = Par{Float64}(
            5e-10,
            0.00, 0.00, #1,2,3
            20000 * 365 * ts, 0.067 * 365 * ts, 0.00182 * 365 * ts, #4,5,6
            0.00182 * 365 * ts, 0.07 * 365 * ts, 0.0467 * 365 * ts, #7,8,9
            0.011 * 365 * ts, 0.11 * 365 * ts, 0.15 * 365 * ts, #10,11,12
            0.019, 0.27, 0.037, 0, 0, 16.34) #13,14,15,16,17,18


        A_l = Par{Float64}(
            01e-11,
            0.00, 0.00, #1,2,3
            200000 * 365 * ts, 0.067 * 365 * ts, 0.00183 * 365 * ts, #4,5,6
            0.00183 * 365 * ts, 0.10 * 365 * ts, 0.0714 * 365 * ts, #7,8,9
            0.0085 * 365 * ts, 0.0286 * 365 * ts, 0.03 * 365 * ts, #10,11,12
            0.00425, 0.34, 1, 0, 0, 434) #13,14,15,16,17,18

        T_t = Par{Float64}(
            01e-10,
            0.00, 0.00, #1,2,3
            20000 * 365 * ts, 1, 0.00182 * 365 * ts, #4,5,6
            0.00182 * 365 * ts, min(0.4 * 365 * ts, 1), 0.0133 * 365 * ts, #7,8,9
            0.00192 * 365 * ts, 0.0286 * 365 * ts, 0.05 * 365 * ts, #10,11,12
            0.001, 0.21, 0.0148, 0, 0, 38.79) #13,14,15,16,17,18
        # Can keep these three Pars structs in an array, accessing as SpPars[1] etc
        SpPars = [N_a, A_l, T_t]

Out[4]: 3-element Array{##728.Par{Float64},1}:
         ##728.Par{Float64}(5.0e-10, 0.0, 0.0, 100000.0, 0.335, 0.0091, 0.0091, 0.35, 0.2335, 0
         ##728.Par{Float64}(1.0e-11, 0.0, 0.0, 1.0e6, 0.335, 0.00915, 0.00915, 0.5, 0.357, 0.04
         ##728.Par{Float64}(1.0e-10, 0.0, 0.0, 100000.0, 1.0, 0.0091, 0.0091, 1.0, 0.0665, 0.00
```

1.0.2 Host infections data structures

Each host has infections attributes per species in a data structure:

```
In [5]: struct Infection{T}
            Imme    ::T #Anti-establishment immunity strength
            Immf    ::T #Anti-fecundity immunity strength
            PEL     ::T #Pre establishment larvae
            EL      ::T #Established larvae
            AW      ::T #Adult worms
            EOut    ::T #Egg output
        end
```

Define a method so that we can easily make an empty structure.

```
In [6]: Infection{T}() where T = Infection{T}(0,0,0,0,0,0)
```

1.0.3 Pool attributes data structre

```
In [7]: struct Soil{T}
            PIS ::T #Pre-infective stages
            IS  ::T #Infective stages
        end

        Soil{T}() where T = Soil{T}(0,0)
```

1.0.4 Model functions

Update infections Arguments are: individual, worm burden, infective stages in pool, halflife, parameters. We assume everything is happening sequentially rather than simultaneously - therefore: - Imme and Immf calculation uses WB from the previous time step and are only calculated once - New eggs uses this time step's adult worms even though Imme and Immf are using *last* timestep's WB.

```
In [8]: function update_Infection(i, WB, IS, halflife, p, risk)
            #New infections
            #mean = 5 #fixed acquisition
            mean = p.b * IS * risk#Non fixed acquisition
            #mean = 5 * risk #gamma risk

            if mean > 0
                exposure = mean
                #exposure = float(rand(Poisson(mean)))
                #exposure = float(rand(NegativeBinomial(1, (mean/(mean+p.k)))))
            else
                exposure = 0.0
            end

            #New pre-establishment larvae
```

```
        newPEL = ((1-p.mu_le) * i.PEL) + exposure
        PEL = newPEL * (1-p.M_le)
        @assert PEL >= 0 "PEL < 0"

        #Anti establishment immunity
        activation = newPEL * p.Imme_activation
        if p.est_modulation > 0
          modulation = exp(-(p.est_modulation * WB))
        else
          modulation = 1
        end
        Imme = ((0.5^(1/halflife) * i.Imme) + activation) * modulation

        #New established larvae
        newEL = ((1-p.mu_ll) * i.EL) + (p.M_le * newPEL * exp(-Imme))
        EL = newEL * (1-p.M_ll)
        @assert EL >= 0 "EL < 0"

        #Anti fecundity immunity
        activation = newEL * p.Immf_activation
        if p.fec_modulation > 0
          modulation = exp(-(p.fec_modulation * WB))
        else
          modulation = 1
        end
        Immf = ((0.5^(1/halflife) * i.Immf) + activation) * modulation

        #New adults
        AW = float(rand(Poisson(((1-p.mu_adults) * i.AW) + (p.M_ll * newEL))))
        #AW = ((1-p.mu_adults) * i.AW) + (p.M_ll * newEL))
        @assert AW >= 0 "AW < 0"

        #New eggs
        modulation = exp(-(Immf + (p.dens_effect * AW/2)))
        EOut = AW/2 * p.WfN * modulation

        Infection{Float64}(Imme, Immf, PEL, EL, AW, EOut)
    end
```

```
Out[8]: update_Infection (generic function with 1 method)
```

Calculate worm burdens (WB)

```
In [9]: function update_WBs(pop, pars, n_hosts)
          [sum([x.AW for x in pop[i,:]] .* [p.weightings for p in pars]) for i in 1:n_hosts]
        end
```

```
Out[9]: update_WBs (generic function with 1 method)
```

Deposit eggs in soil Arguments: soil, population of infections, parameters

```
In [10]: function update_pool(S, pop, p)
             Eggs = sum([x.EOut for x in pop])
             PIS = ((1 - (p.pool_egg_loss + p.pool_egg_maturation)) * S.PIS) + Eggs
             IS = ((1-p.pool_infectives_loss) * S.IS) + (p.pool_egg_maturation * S.PIS)
             #IS = ((1-p.pool_infectives_loss) * (1 - (p.b * length(pop[:,1]))) * S.IS)
                       + (p.pool_egg_maturation * S.PIS)

             Soil{Float64}(PIS, IS)
         end

Out[10]: update_pool (generic function with 1 method)
```

Birth and death process Select all individuals over 80 years old and randomly select from the rest of the population - reset ages and infections so population size remains constant

```
In [11]: function get_age_index(age) ifelse(age <= 0.5, 1, Int(round(age))) end

         function reset_inds_sys(population, ages, risk, death_rates, pars)
           for i = 1:length(ages)
             #@assert ages[i] < 100 "age > 100"
             if rand(Binomial(1, death_rates[get_age_index(ages[i])])) == 1
               population[i, 1:3] .= Infection{Float64}()
               ages[i] = 0
               risk[i, 1:3] = [rand(Gamma(p.k, 1/p.k)) for p in pars]
             end
           end
           return population, ages, risk
         end

         function update_ages(ages, ts)
             [a += ts for a in ages]
         end

Out[11]: update_ages (generic function with 1 method)
```

1.0.5 Set up and model run functions

```
In [12]: function initworms(init_mean, k)
           if init_mean == 0
             Infection{Float64}()
           else
             Infection{Float64}(0, 0, 0, 0, float(rand(NegativeBinomial(k, (k)/(init_mean + k)))
           end
         end

         function SystemSetUp(n_hosts, pars, av_age)
```

```
        #Initialise ages, assume exponential type population structure
        ages = [rand(Uniform(0, 80)) for i in 1:n_hosts]

        #New and exciting: gamma distributed risk
        risk = [rand(Gamma(p.k, 1/p.k)) for i in 1:n_hosts, p in pars]

        #Initialise pool with eggs and infective stages
        Pool = [Soil{Float64}(100, 100) for sp in 1:3]

        #Initialise worms with n. binom draw for adults
        pop_infections = [initworms(p.init_mean, p.k) for i in 1:n_hosts, p in pars]

        #Initialise worms burdens based on initial adult burdens
        WBs = update_WBs(pop_infections, pars, n_hosts)
        return ages, risk, Pool, pop_infections, WBs
    end


    function run_mod(n_hosts, pars, ts, halflife, pop_infections, Pool, ages, WBs, death_

        #Update ages and remove some individuals
        ages = update_ages(ages, ts)
        pop_infections, ages, risk = reset_inds_sys(pop_infections, ages, risk, death_rate

        #Species specific calculations
        for sp in 1:3

            #Per host calculations
            for i in 1:n_hosts
                pop_infections[i, sp] = update_Infection(pop_infections[i, sp], WBs[i],
                                                Pool[sp].IS, halflife, SpPars[sp], risk[i, sp
            end

            #Update pool
            Pool[sp] = update_pool(Pool[sp], pop_infections[:, sp], SpPars[sp])
        end

        #Update worm burdens
        WBs = update_WBs(pop_infections, SpPars, n_hosts)

        return ages, pop_infections, Pool, WBs
    end
```

```
Out[12]: run_mod (generic function with 1 method)
```

Note on order in run_mod function: WB happens outside of the species and host loop because it needs information from all species in the whole population

```
In [13]: function main(n_runs, n_hosts; pars = SpPars, av_age = 18.2, ts_ = ts, halflife_ = hal
```

```
                death_rates = age_specific_death_rates,
                record_run = 0, record_final = 1)

    #Set arrays up
    ages, risk, Pool, pop_infections, WBs = SystemSetUp(n_hosts, pars, av_age)

    #For storing summary statistics
    stages = [:Imme, :Immf, :PEL, :EL, :AW, :EOut, :prev, :soil]
    if record_run > 0
      run_record = Dict(s => zeros(Float64, n_runs, 3) for s in stages)
    else
      run_record = 0
    end

    #Loop through the runs
    for r in 1:n_runs
      ages, pop_infections, Pool, WBs = run_mod(n_hosts, pars, ts_, halflife_,
          pop_infections, Pool, ages, WBs, death_rates, risk)

      #Get records for whole run
      if record_run > 0
        for sp in 1:3
          for s in 1:6
            run_record[stages[s]][r,sp] = mean([getfield(x, s) for x in pop_infections[
          end
          run_record[stages[7]][r, sp] = count(i -> i > 0.0, x.AW for x in pop_infectio
          run_record[stages[8]][r,sp] = Pool[sp].IS
        end
      end

    end

    #Get final distributions
    if record_final > 0
      final_record = Dict(s => zeros(Float64, n_hosts, 3) for s in stages[1:6])
      for sp in 1:3
        for s in 1:6
          final_record[stages[s]][:,sp] = [getfield(x, s) for x in pop_infections[:,sp]
        end
      end
    else
      final_record = 0
    end

    return run_record, final_record, ages, pop_infections
  end
```

```
Out[13]: main (generic function with 1 method)
```

1.1 Example run

```
In [14]: @time run_record, final_record, ages, pop_infections = main(1000, 2000, record_run = 
```

```
  6.591756 seconds (148.38 M allocations: 7.799 GiB, 19.17% gc time)
```

```
Out[14]: (Dict(:soil=>[80.0 99.3 89.3; 5.02901e8 1.08165e10 4.9125e8;  ; 1.25776e9 3.46117e11 8
```

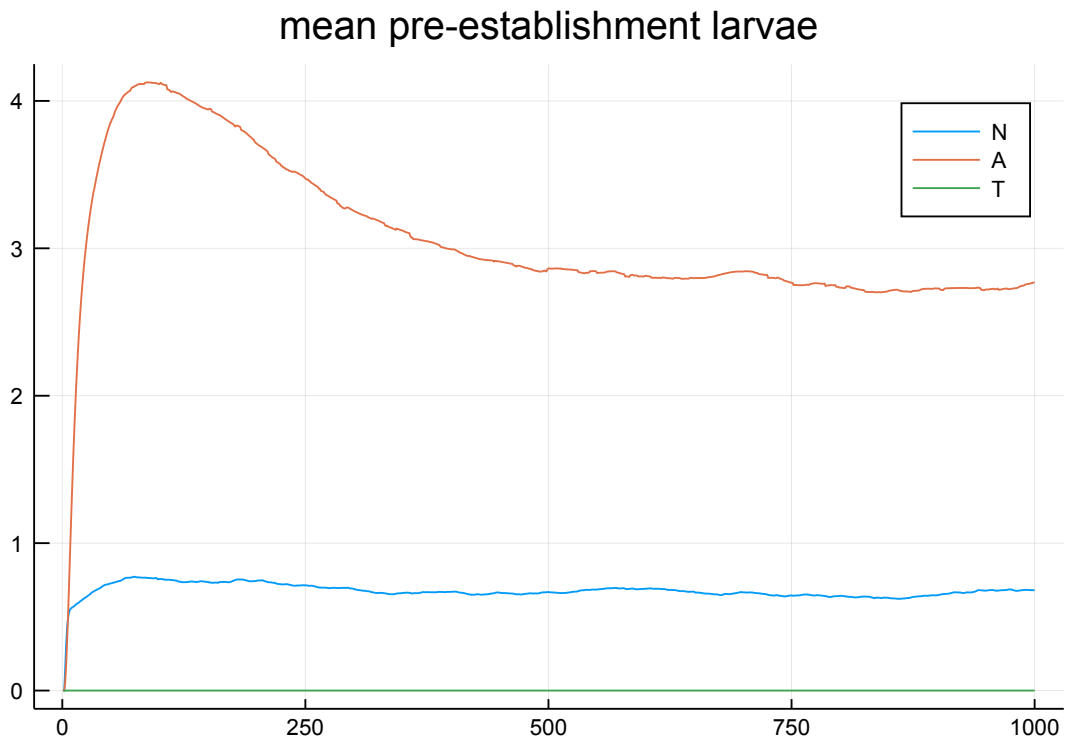
1.1.1 Plot output

```
In [15]: using Plots
```

Plots of each time step. y1 = Na, y2 = Al, y3 = Tt
Pre-established larvae

```
In [16]: plot(1:1000, run_record[:PEL][1:1000,:], title = "mean pre-establishment larvae", labe
```

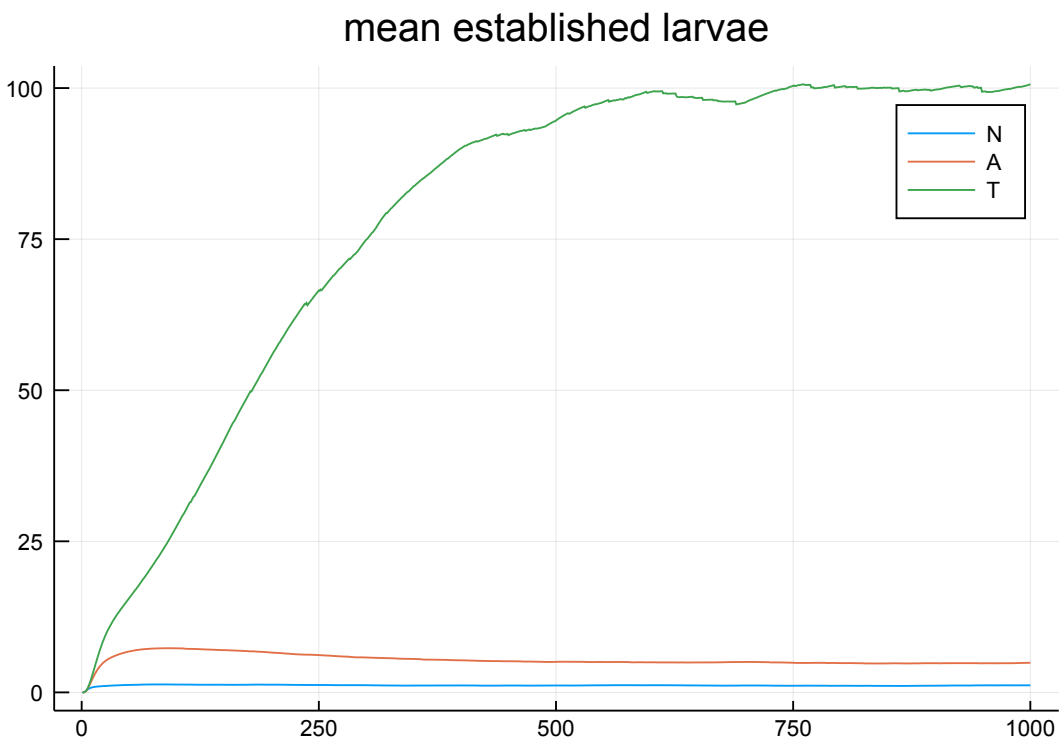
Out[16]:



Established larvae

```
In [17]: plot(1:1000, run_record[:EL][1:1000,:], title = "mean established larvae", label = ["
```

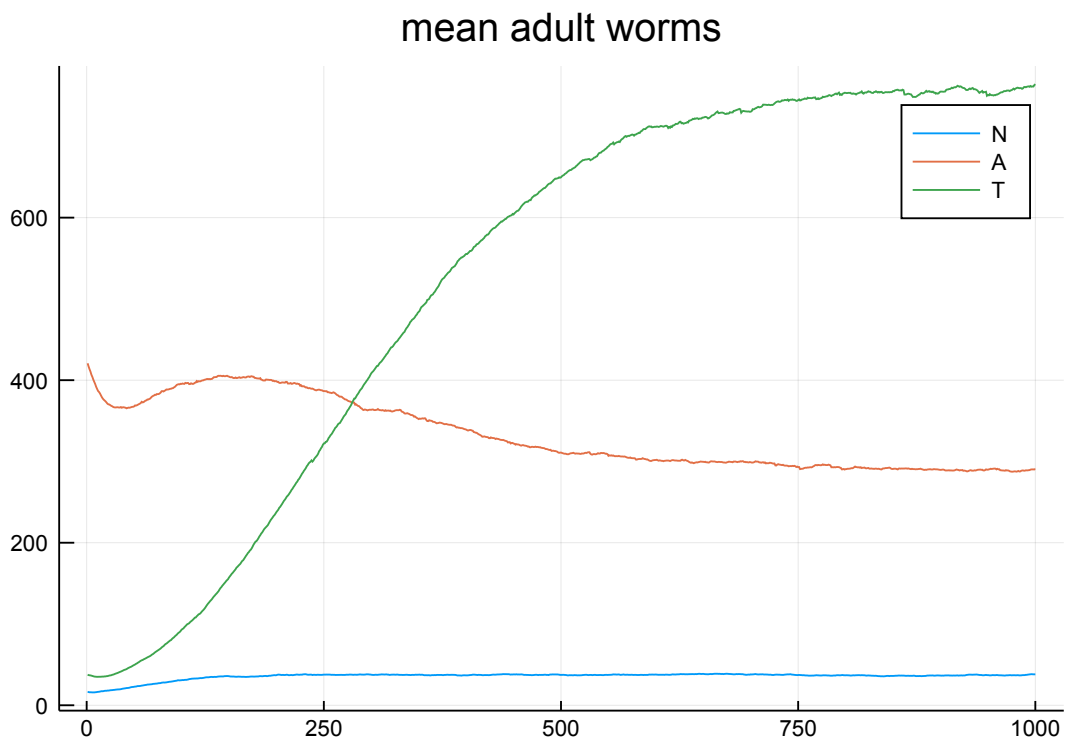
Out[17]:



Adult worms - the poisson draw now happens to as worms enter the adult phase

```
In [18]: plot(1:1000, run_record[:AW][1:1000,:], title = "mean adult worms", label = ["N", "A"
```

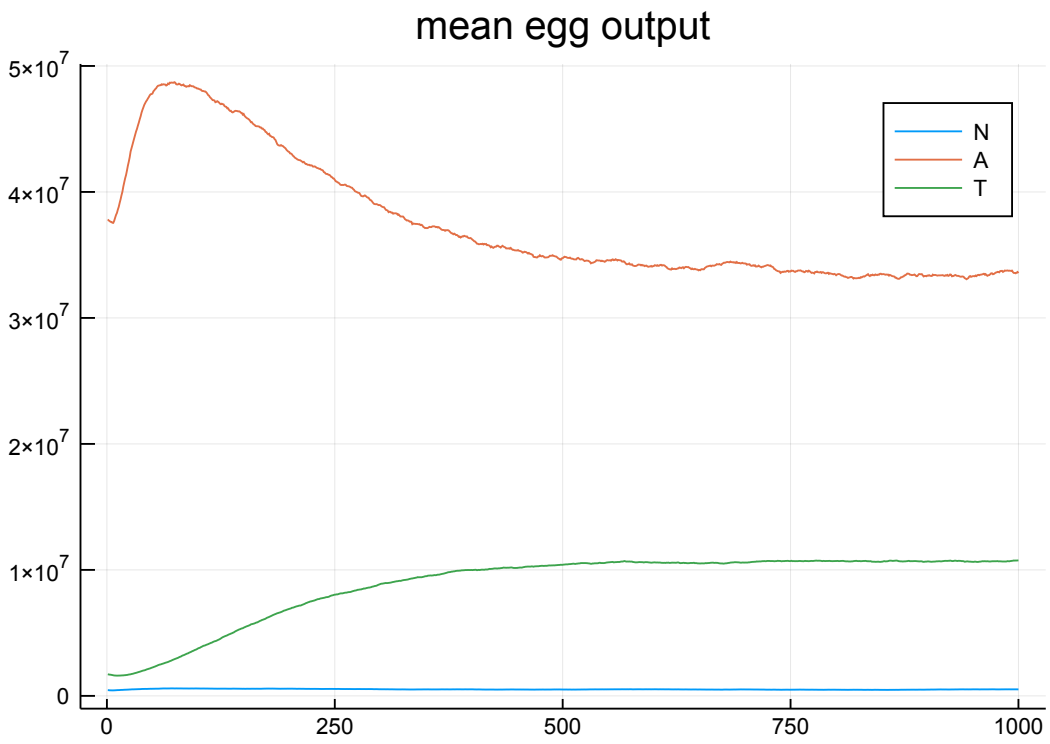
```
Out[18]:
```



All eggs per host

```
In [19]: plot(1:1000, run_record[:EOut][1:1000,:], title = "mean egg output", label = ["N", "A
```

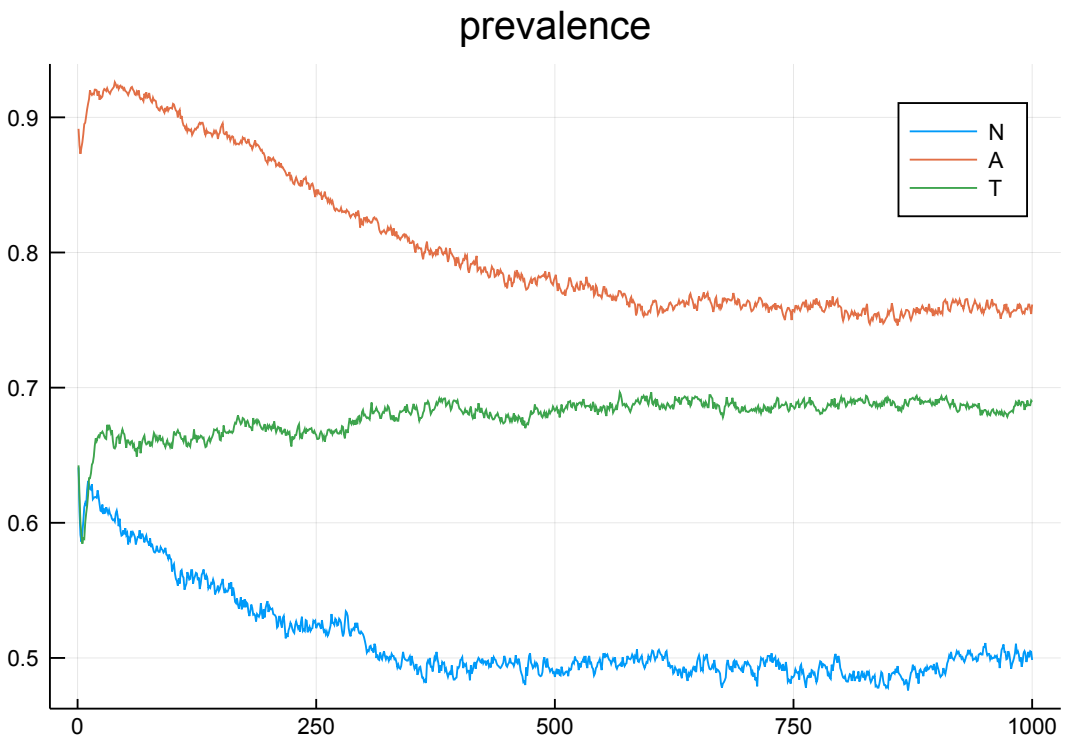
```
Out[19]:
```



Prevalence - positives numbers of adult worms

```
In [20]: plot(1:1000, run_record[:prev][1:1000,:], title = "prevalence", label = ["N", "A", "T
```

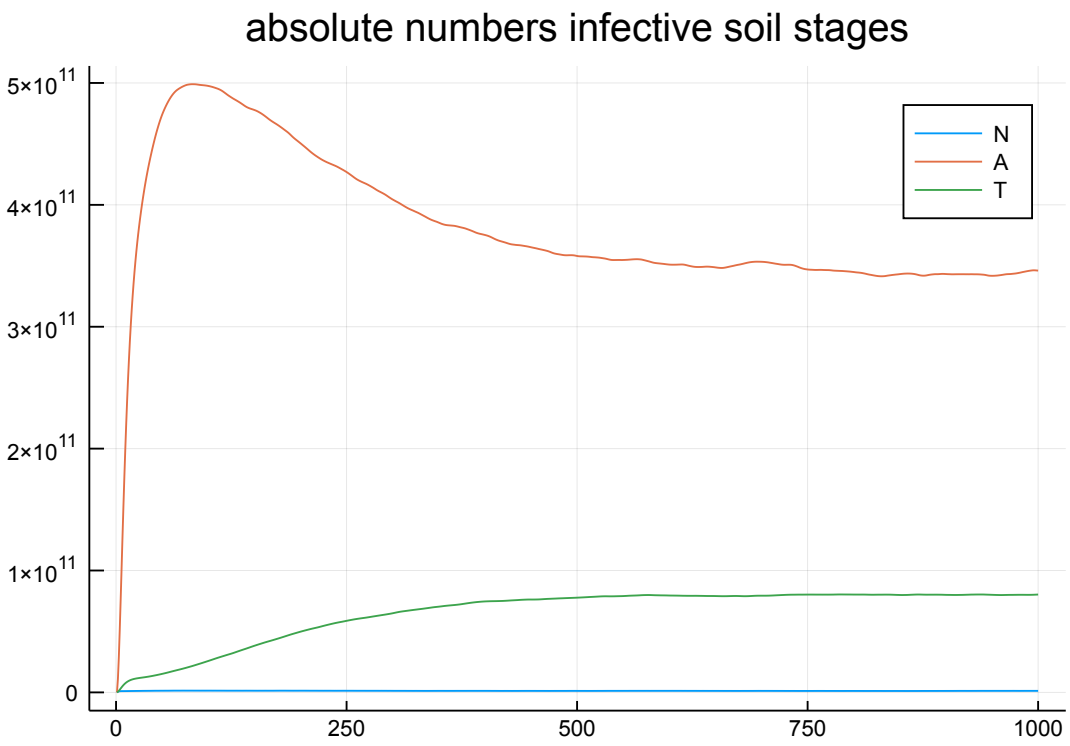
```
Out[20]:
```



Infective stages in the soil, absolute numbers

```
In [21]: plot(1:1000, run_record[:soil][1:1000,:], title = "absolute numbers infective soil sta
```

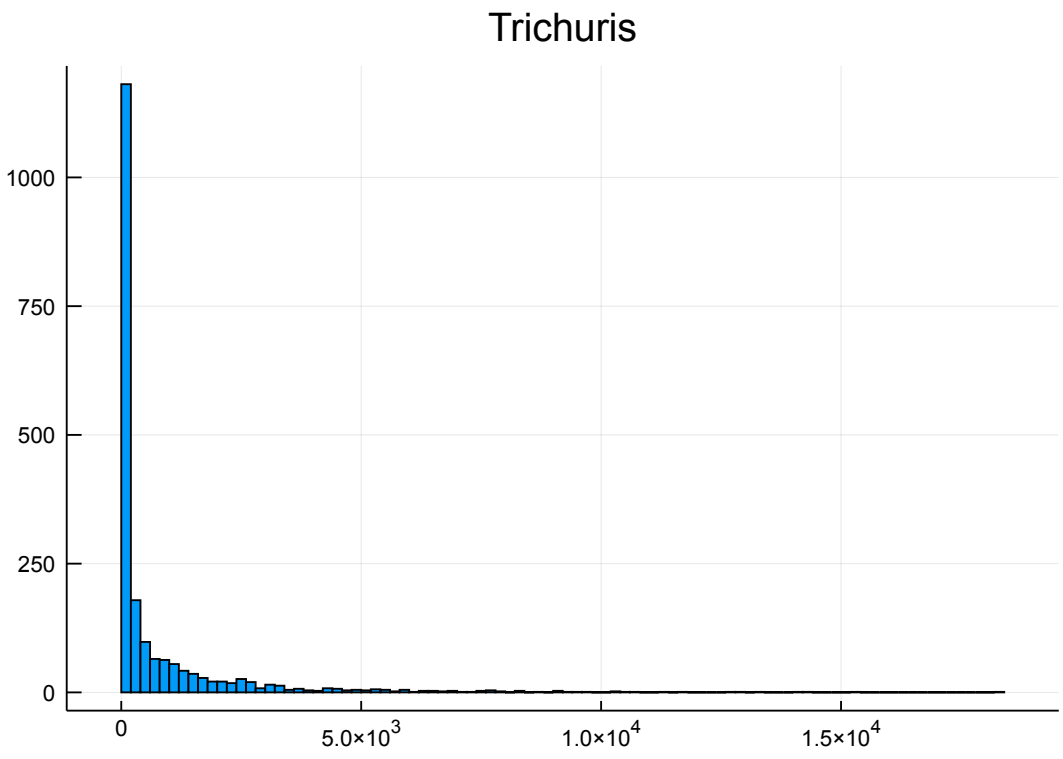
```
Out[21]:
```



Histograms of final time step (should be stedy) - reassuringly these are all negative binomial looking. Printed below on the notebook is the histogram of Trichuris adult worms in the population at the end of the simulation.

```
In [22]: histogram(final_record[:AW][:,1], legend = false, title = "N.americanus")
         histogram(final_record[:AW][:,2], legend = false, title = "Ascaris")
         histogram(final_record[:AW][:,3], legend = false, title = "Trichuris")
```

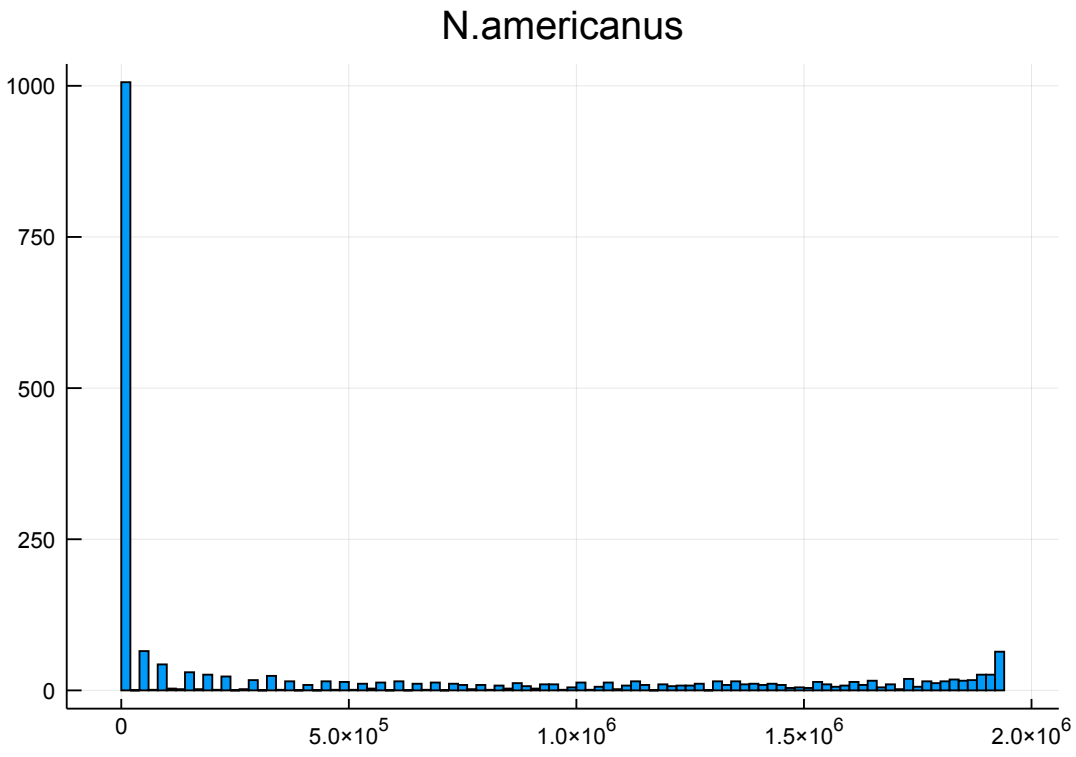
Out[22]:



The histogram of the eggs per individual at the end of the simulation is not as nicely negative binomial.

```
In [23]: histogram(final_record[:EOut][:,2], legend = false, title = "Ascaris")
         histogram(final_record[:EOut][:,3], legend = false, title = "Trichuris")
         histogram(final_record[:EOut][:,1], bins = 100, legend = false, title = "N.americanus"
```

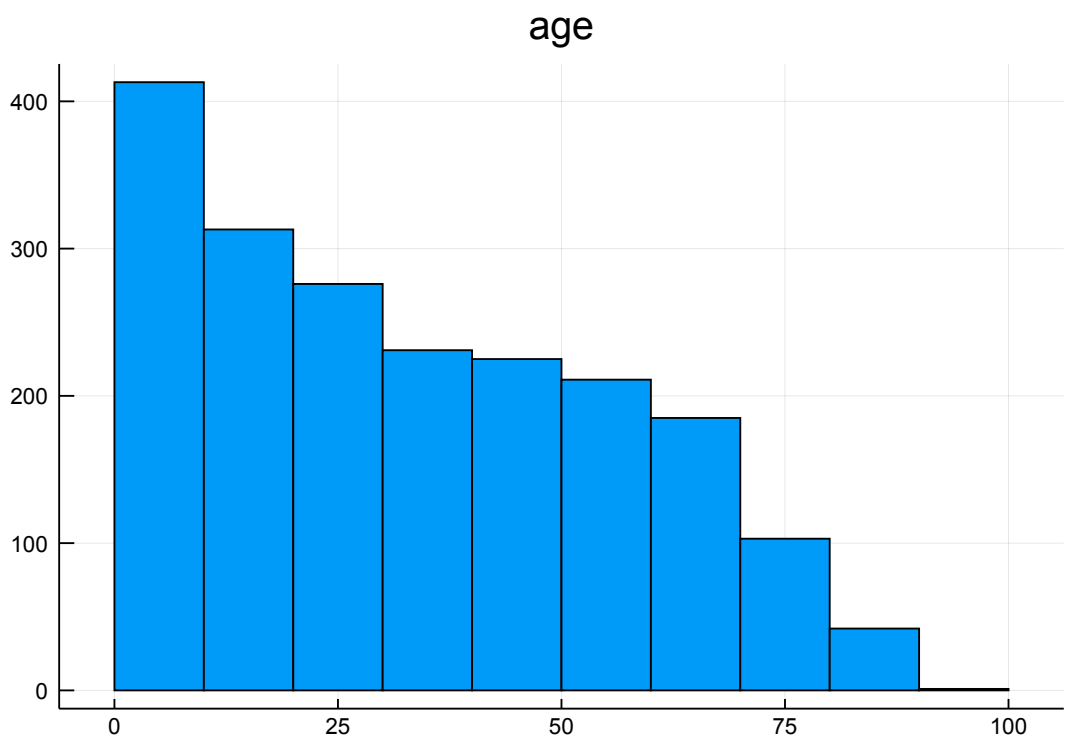
Out[23]:



I am not sure what is caugin this - it may be do do with the birth-death process, which is not maintaining an exponential distribution. To demonstrate, a histogram of ages in the population at the end of the simulation.

```
In [24]: histogram(ages, legend = false, title = "age")
```

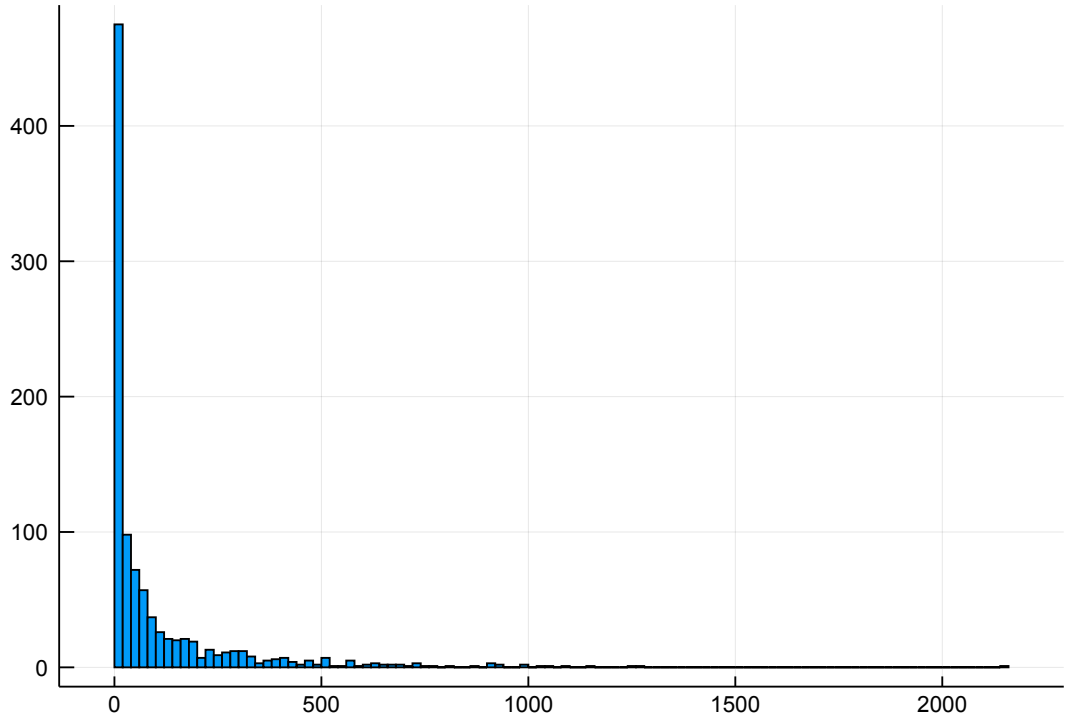
```
Out[24]:
```



It may also be to do with the density dependent process. A quick test of what happens if there is density dependence in a Poisson process:

```
In [25]: risk = rand(Gamma(0.3, 1/0.3), 1000)
         acquisition = map(i -> rand(Poisson(100 * i)), risk)
         histogram(acquisition, legend = false)
```

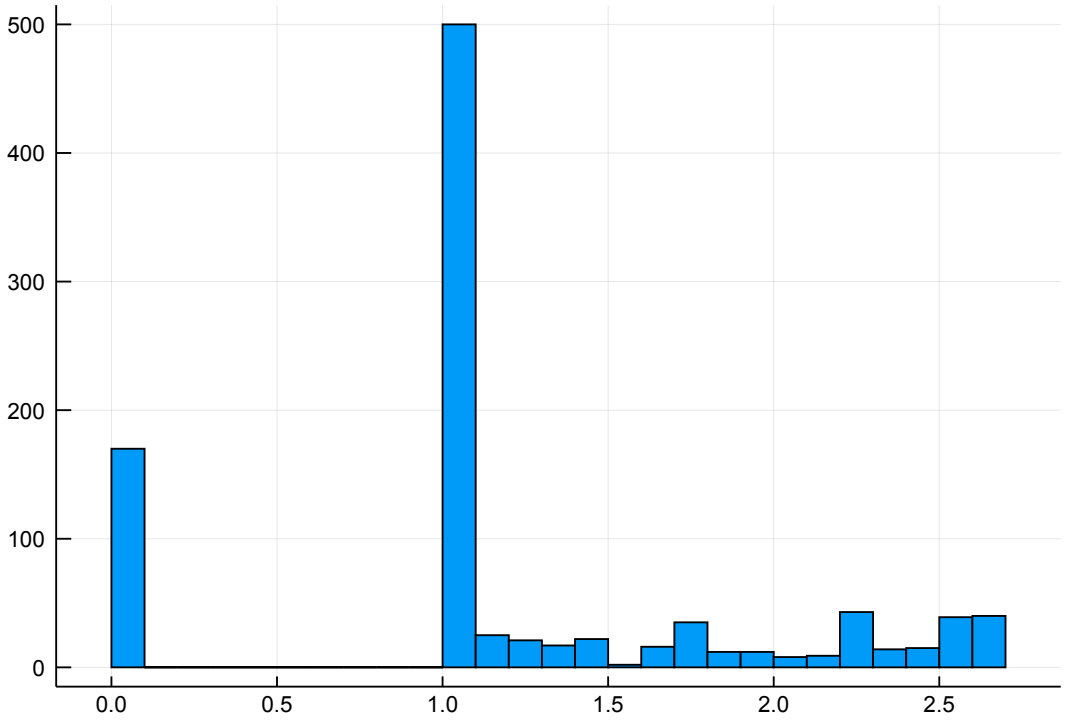
Out[25]:



Now we try the density dependent component

```
In [26]: acquisition_density_dependent = map(i -> i^exp(-(i * 0.1)), acquisition)
         histogram(acquisition_density_dependent, legend = false)
```

Out[26]:



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