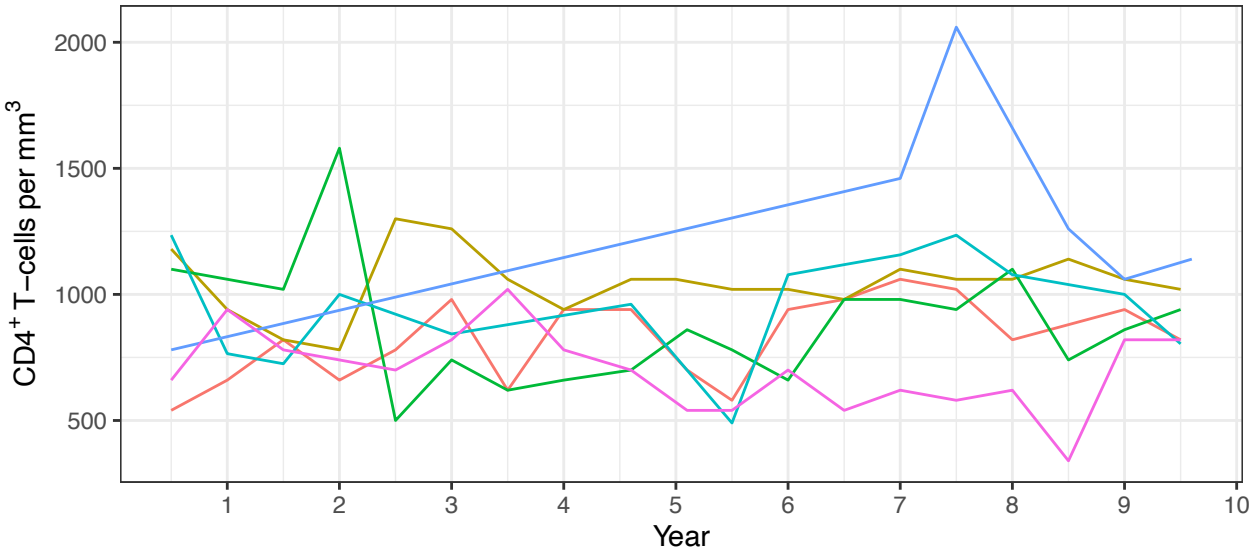
Numerical improvements and workarounds

- Only solve timepoints where there is data for speed up
  - Must also solve the "zero" timepoint to correspond to the initial conditions
  - 5 year offset to compare simulation "steady state" to data
- Solver errors mitigated by limiting iteration and reducing precision:

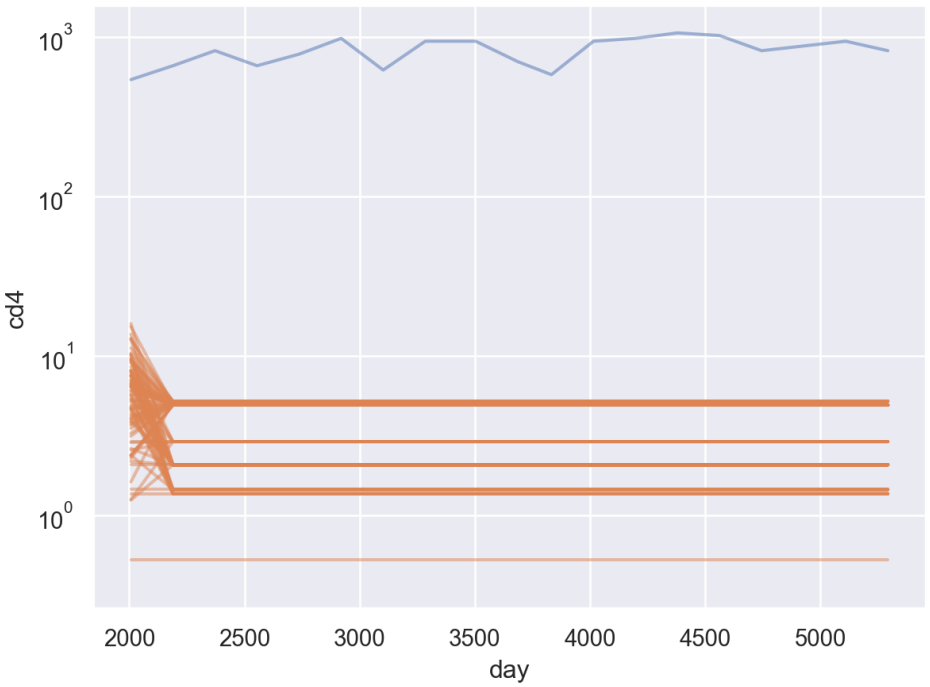
```
odeint(hiv, Y0, times, args=*params,
       mxstep=100, rtol=0.1)
```

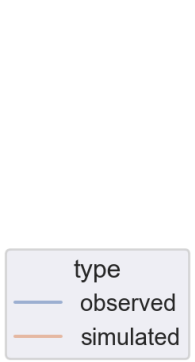


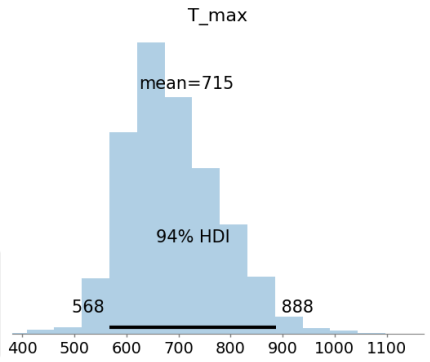

```
lsoda--  warning..internal t (=r1) and h (=r2)
are such that in the machine, t + h = t on the
next step (h = step size). solver will continue
anyway
```

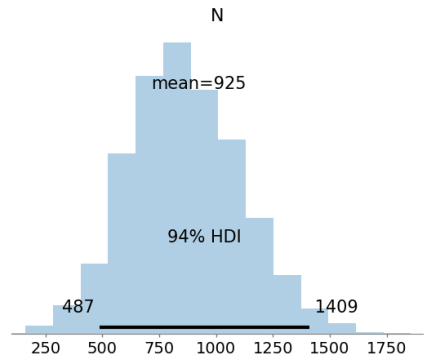
```
.../scipy/integrate/_odepack_py.py:248:
ODEintWarning: Excess work done on this call
(perhaps wrong Dfun type). Run with full_output
= 1 to get quantitative information.
  warnings.warn(warning_msg, ODEintWarning)
```

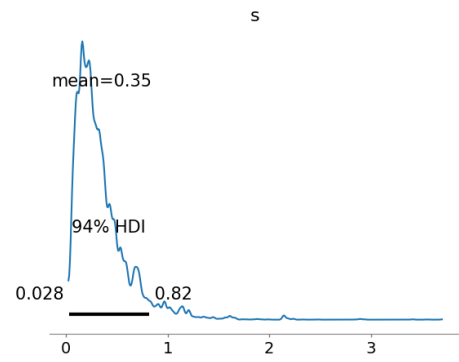
ABC-SMC fit is off by 10^2. Parameters are unimodal

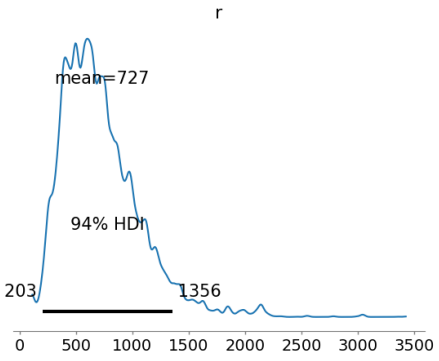


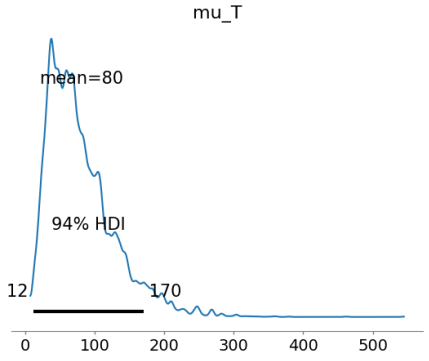


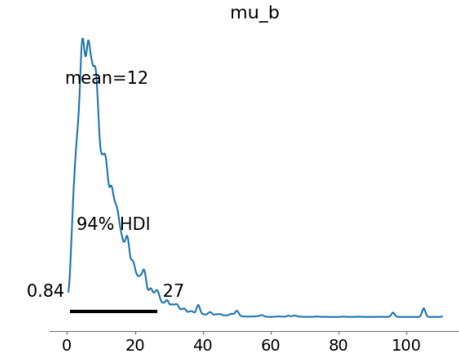


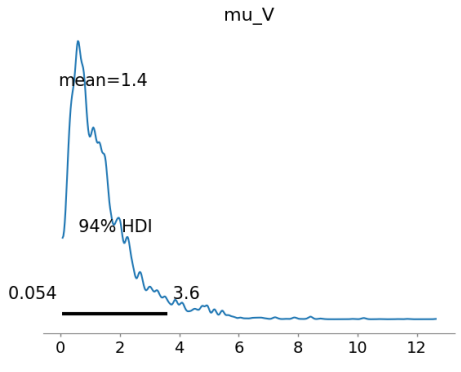


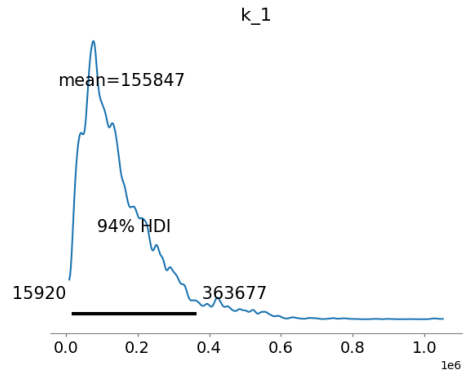


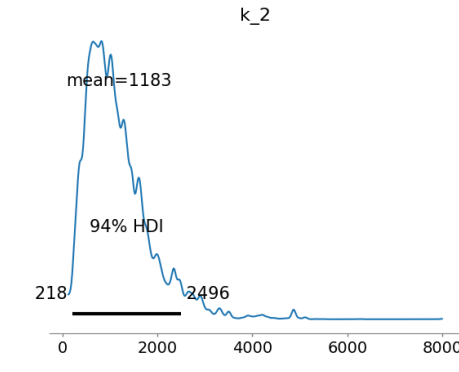




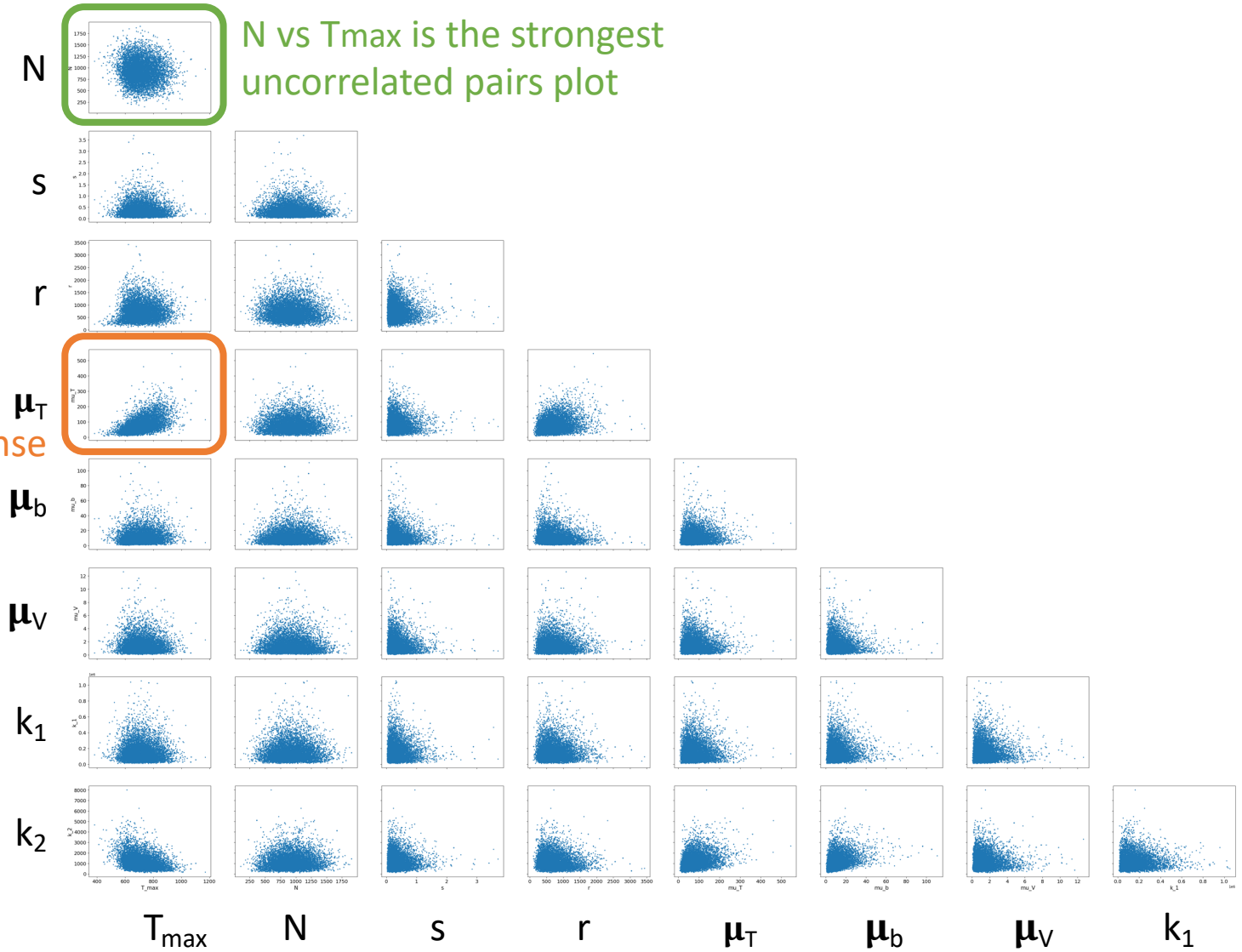








Pairs plot shows no strong collinearity or multiplicative (banana-shape) relationships



N vs Tmax is the strongest uncorrelated pairs plot

More correlated than others, but makes sense that they would be

r-hat is close to 1, but from varying weights rather than initial conditions between chains

	mean	sd	hdi 3%	hdi 97%	mcse mean	mcse sd	ess bulk	ess tail	r-hat
T_{max}	715.477	90.586	568.000	888.000	2.500	1.808	1376.0	886.0	1.01
N	924.761	248.180	487.000	1409.000	6.106	4.328	1665.0	1694.0	1.01
s	0.346	0.280	0.028	0.815	0.006	0.004	1952.0	1472.0	1.00
r	726.696	352.081	203.136	1355.833	9.366	6.624	1304.0	1311.0	1.01
μ_T	80.200	48.967	11.847	169.950	1.265	0.895	1362.0	1216.0	1.01
μ_b	11.590	10.579	0.835	26.578	0.375	0.350	1603.0	1371.0	1.01
μ_V	1.435	1.203	0.054	3.606	0.037	0.026	1006.0	896.0	1.01
k_1	155846.658	114677.442	15920.121	363677.189	2876.308	2034.230	1498.0	1173.0	1.01
k_2	1183.134	715.702	218.344	2495.619	18.205	13.694	1551.0	797.0	1.01

Parameter range quantiles [3%, 97%] changes with calibration (rounded to 2 significant digits)

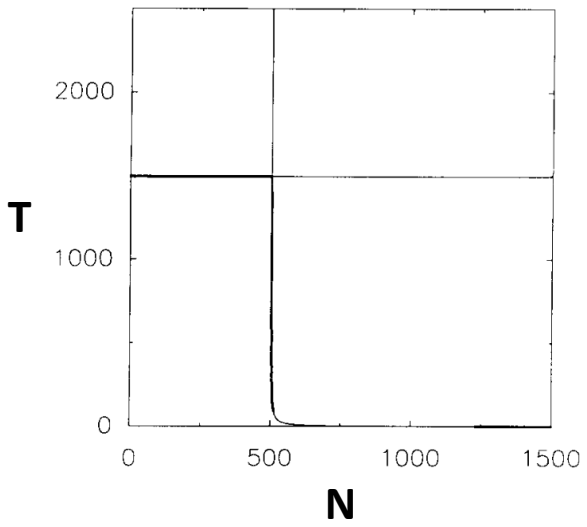
	T_{max}	N	s	r	μ_T	μ_b	μ_V	k_1	k_2
Before	312, 880	1400, 1400	1.5, 30.3	.01, .06	.003, .06	.03, .72	.35, 7.3	3.6e-6, 7.3e-5	3e-4, 9e-3
After	570, 890	490, 1410	.03, .82	200, 1360	12, 170	.84, 27	.05, 3.7	1.6e4, 3.6e5	220, 2500

shift

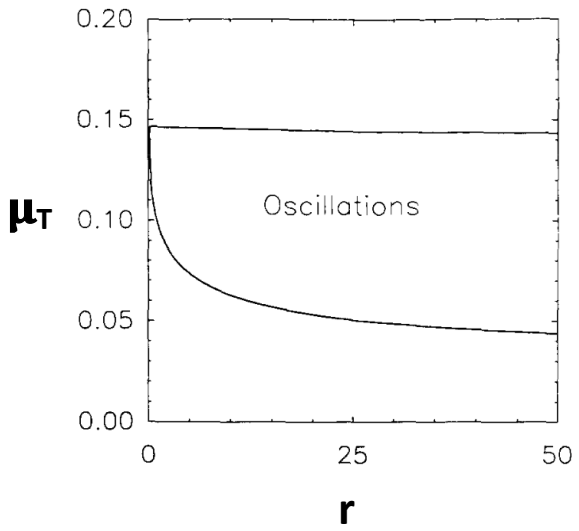
bifurcation

shrinkage

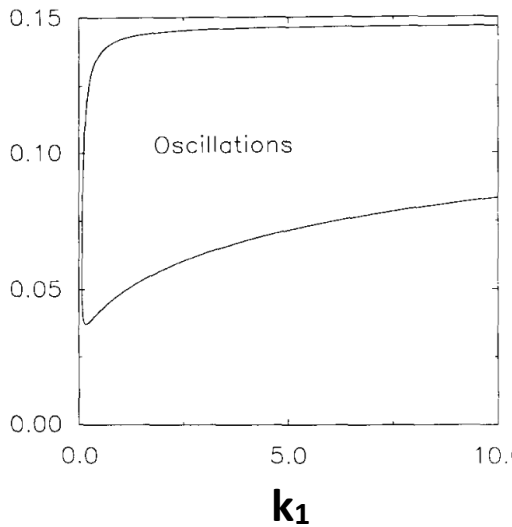
Hopf Bifurcation:
$502 < \mathbf{N_{crit}} > 1230$



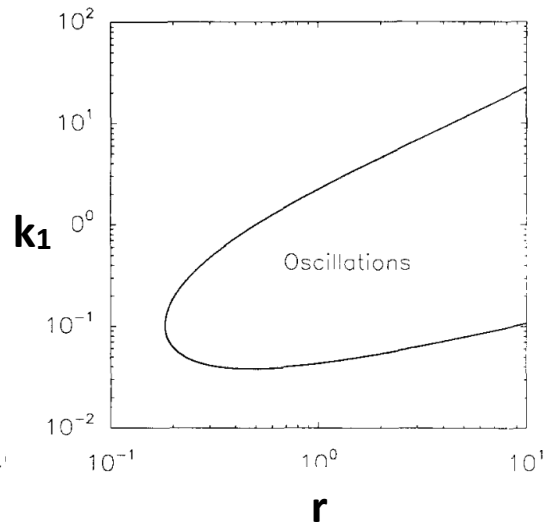
$\mu_T = 1\ d^{-1}$ & $r = 1.04$



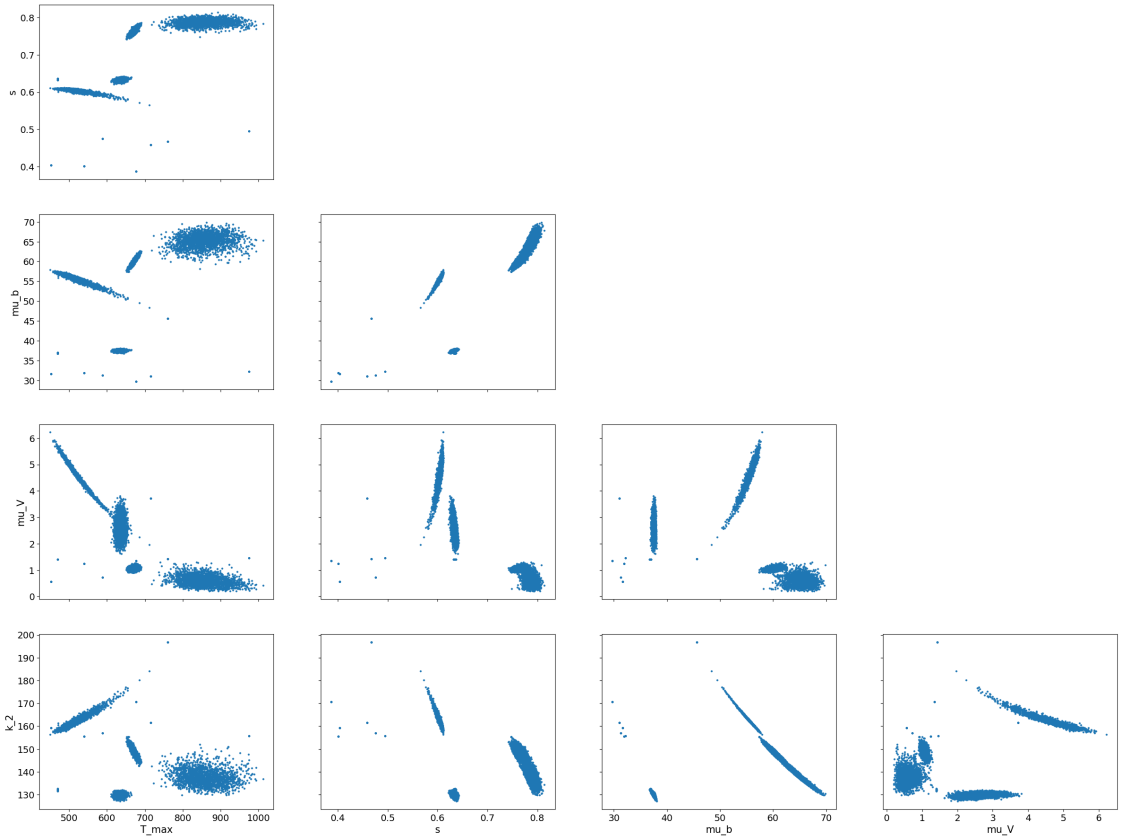
μ_T & k_1

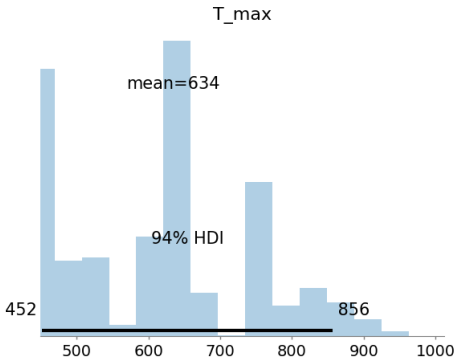


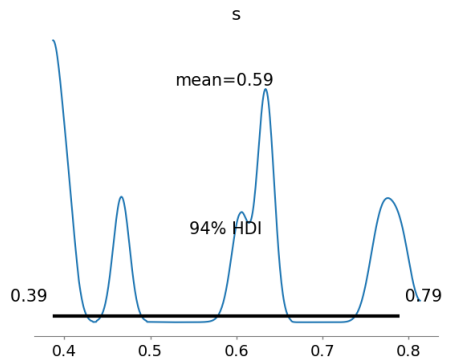
r & k_1

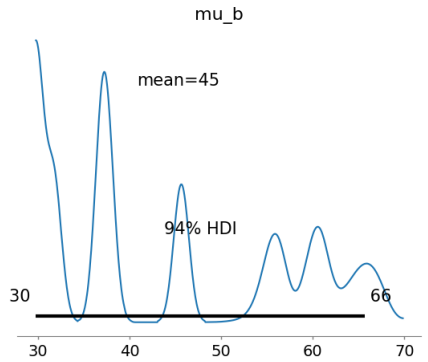


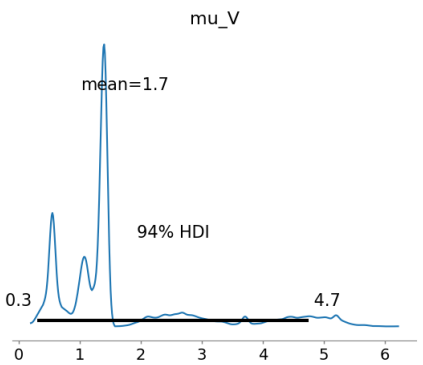
Fixed parameters to non-oscillatory regions:
(N=1400, μ_T=0.2, r=0.1, k_1=1) but ΣCD4 crashes to 0

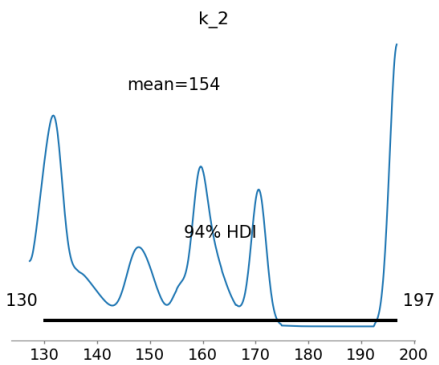










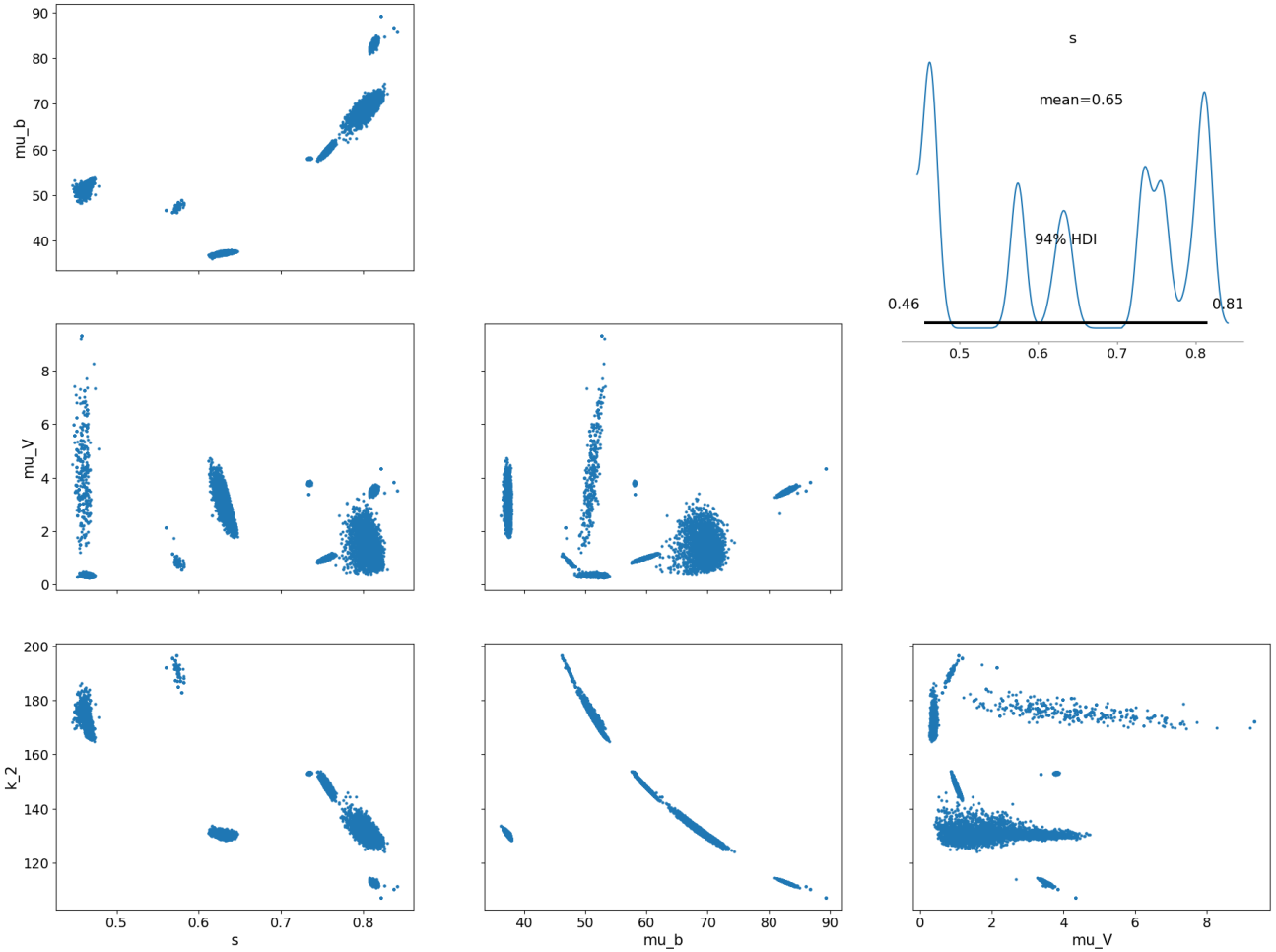


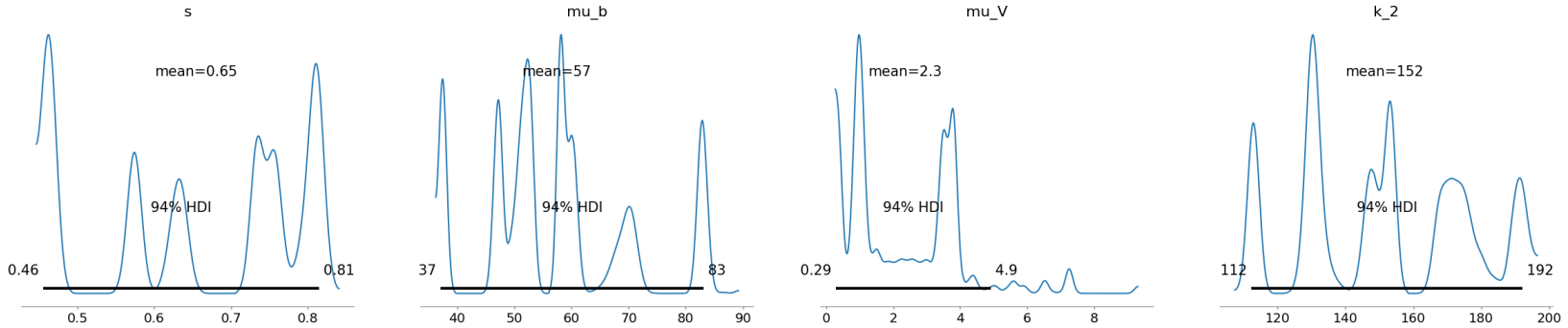

```
odeint(hiv, Y0, times, args=*params,
       mxstep=100, rtol=0.01)
```

Stages: 10

	T_{max}	s	μ_b	μ_V	k_2
Before	312, 880	1.5, 30.3	.03, .72	.35, 7.3	3e-4, 9e-3
After	450, 860	.38, .80	30, 66	.3, 4.8	130, 200

Fixed T_{max} hyperprior to value used in Perelson 1993 paper: (N=1400 , T_{max}=1500, μ_T=0.2, r=0.1, k_1=1) no improvement



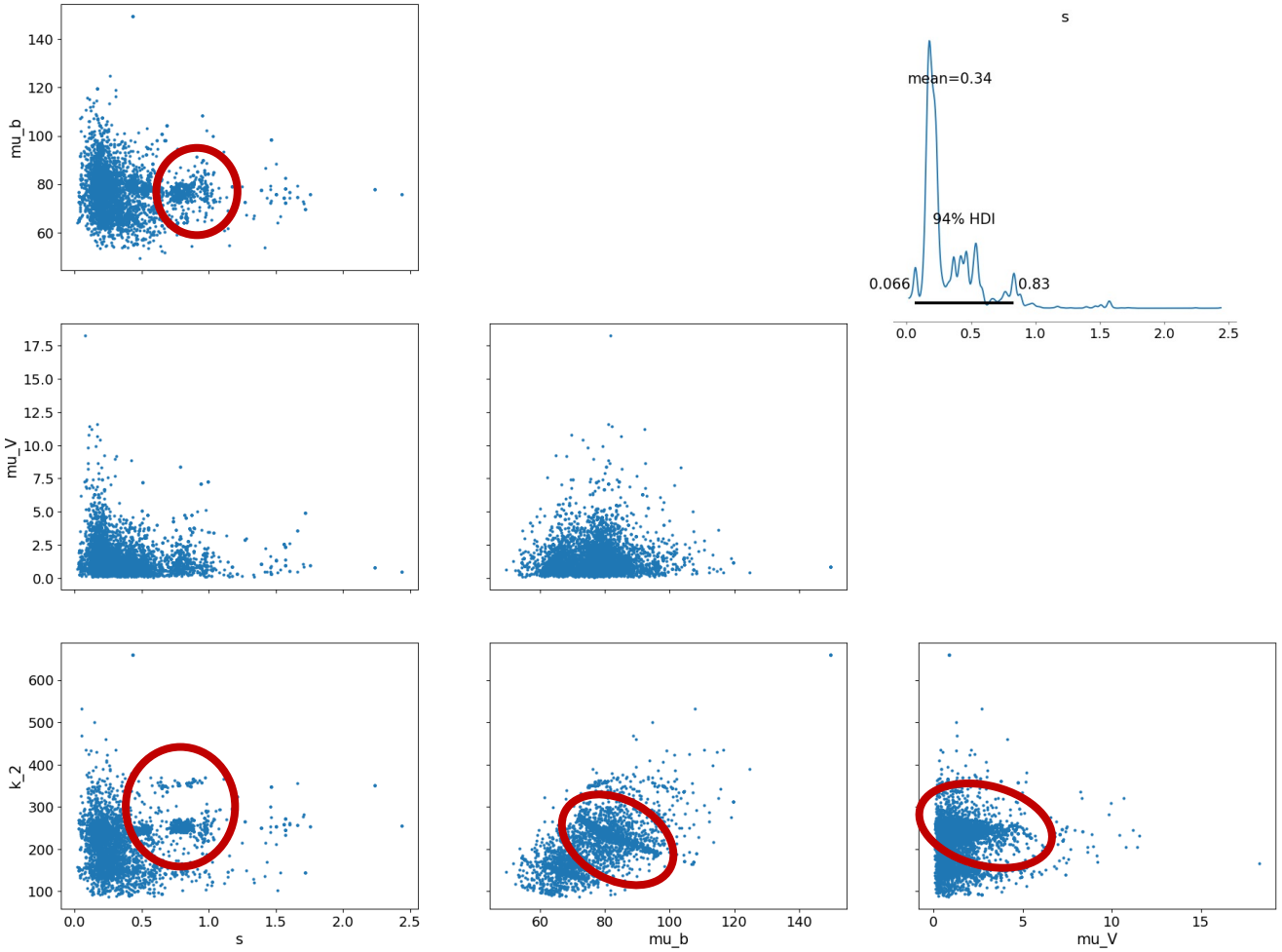


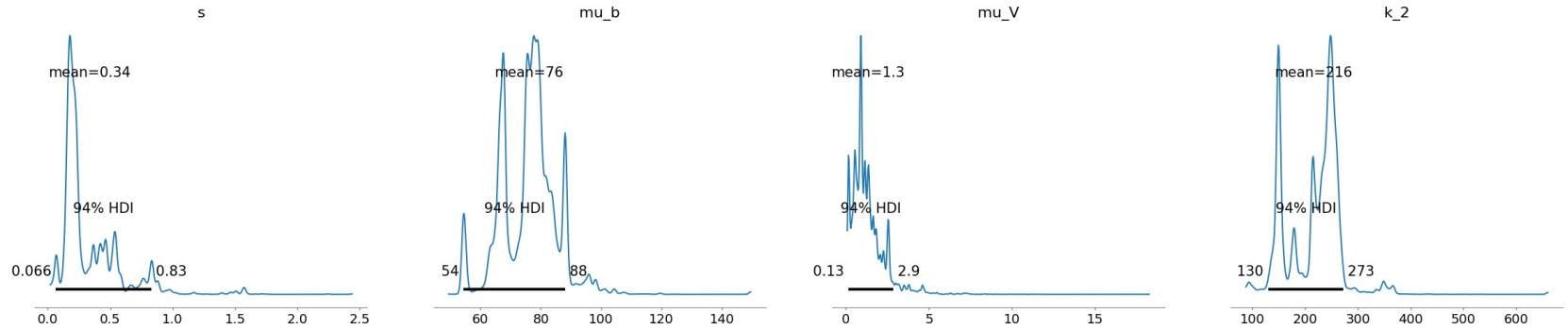

```
odeint(hiv, Y0, times, args=*params,
       mxstep=100, rtol=0.01)
```

Stages: 11

	s	μ_b	μ_V	k_2
Before	1.5, 30.3	.03, .72	.35, 7.3	3e-4, 9e-3
After	.46, .82	37, 83	.3, 4.9	110, 190

Reduced N below 502 bifurcation:
(N=400, T_{max}=1500, $\boldsymbol{\mu}_T$=0.2, r=0.1, k_1=1) less disjoint

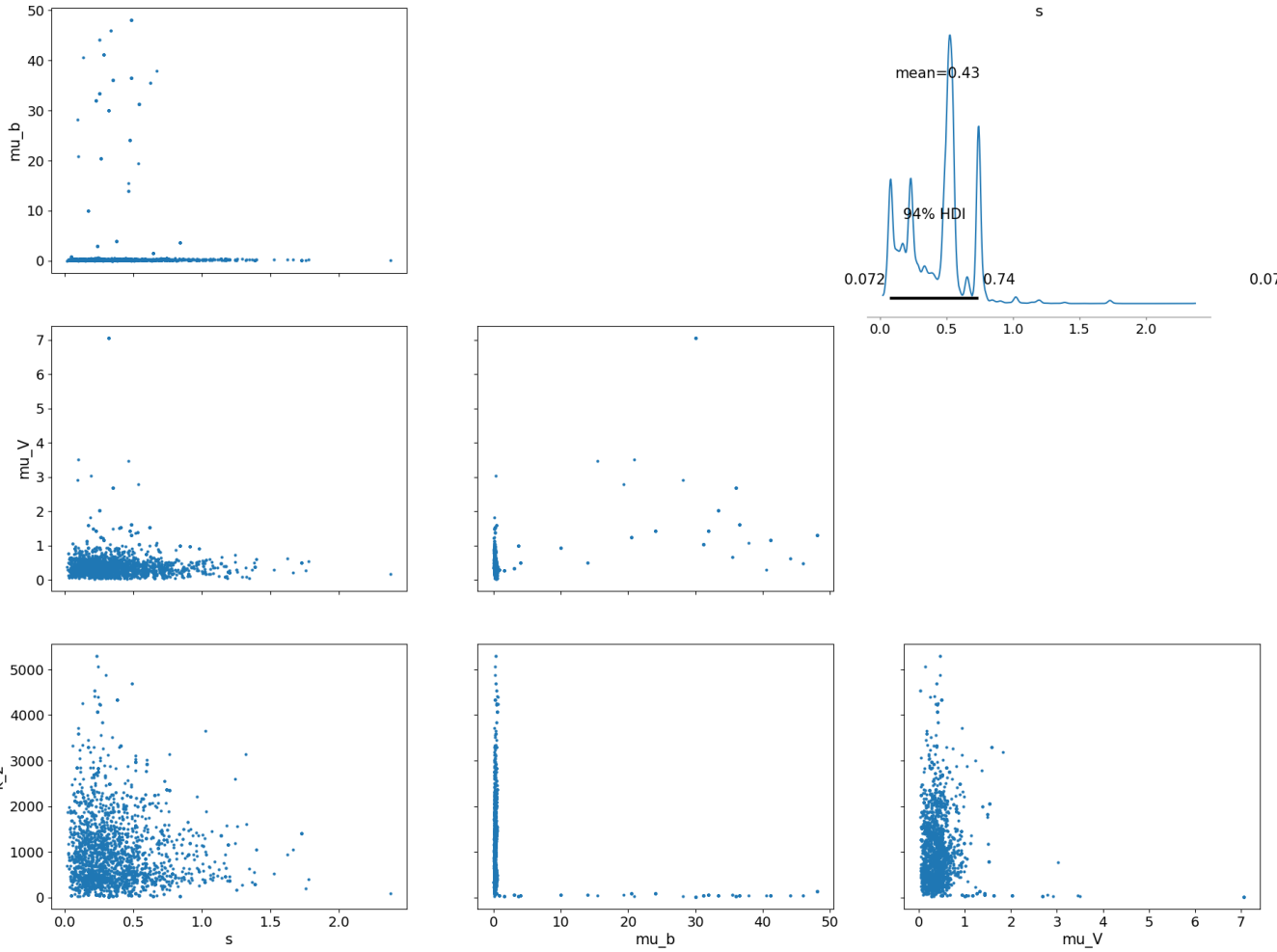


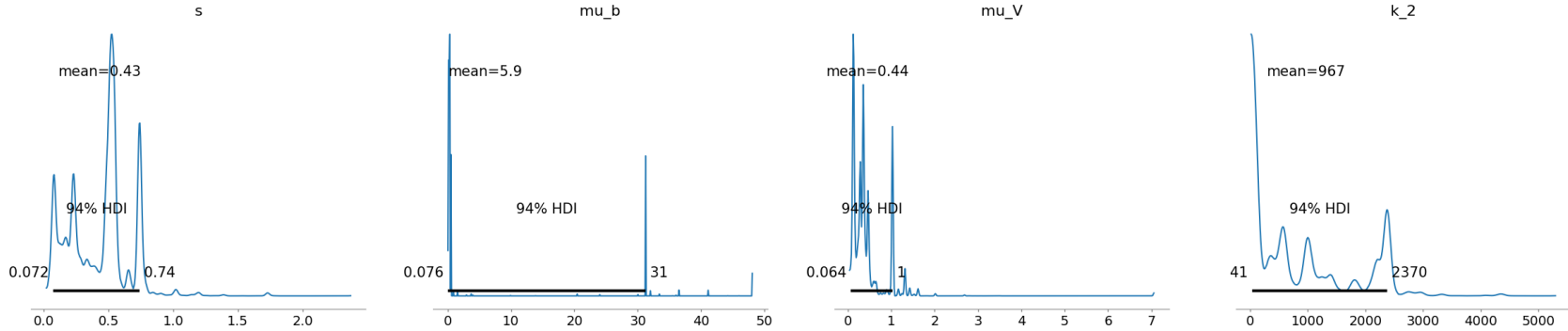



```
odeint(hiv, Y0, times, args=*params,
       mxstep=100, rtol=0.01)
```

	s	μ_b	μ_V	k_2
Before	1.5, 30.3	.03, .72	.35, 7.3	3e-4, 9e-3
After	.07, .83	54, 88	.13, 2.9	130, 270

Used exact values from the Perelson 1993 paper:
(N=774, T_{max}=1500, μ_T=0.02, r=0.03, k_1=2.4e-5) μ_b is better



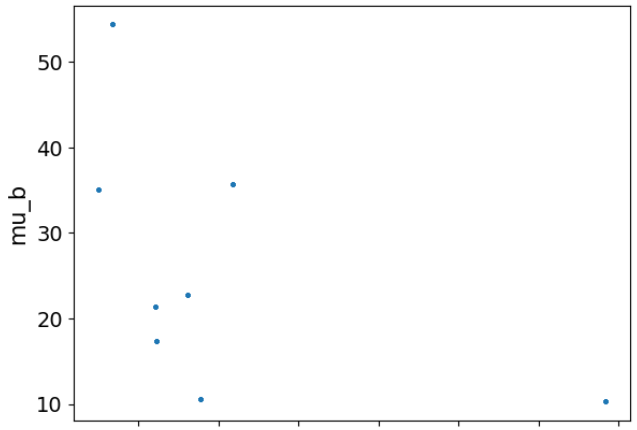


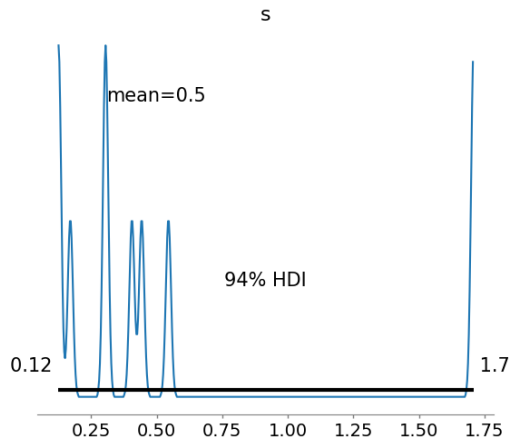

```
odeint(hiv, Y0, times, args=*params,
       mxstep=100, rtol=0.01)
```

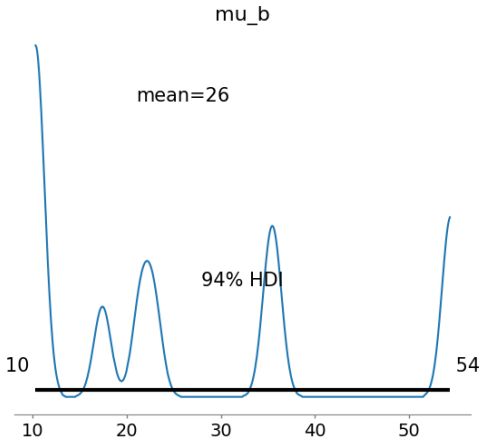
Stages: 7

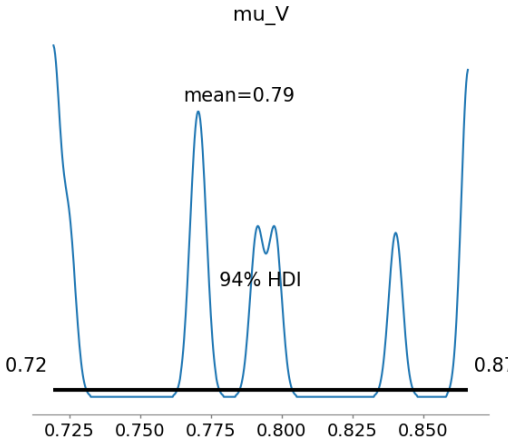
	s	μ_b	μ_V	k_2
Before	1.5, 30.3	.03, .72	.35, 7.3	3e-4, 9e-3
After	.07, .74	.08, 31	.06, 1.0	40, 2400

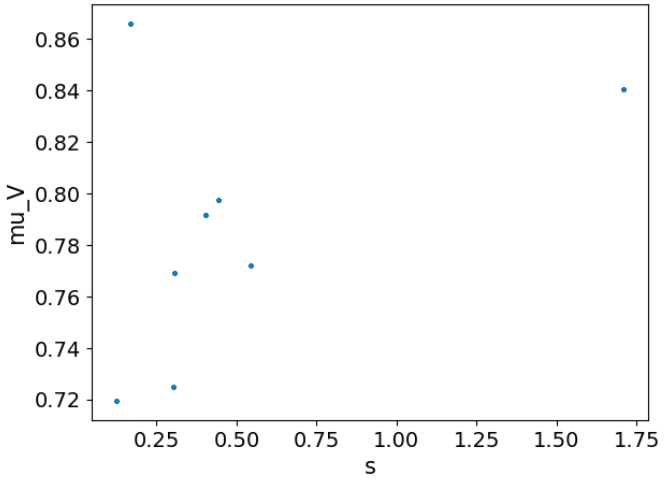
Fixed k_2 to value in Perelson 1993 paper:
(N=774, T_{max}=1500, μ_T=0.02, r=0.03, k_1=2.4e-5, k2=3e-3) μ_b is worse

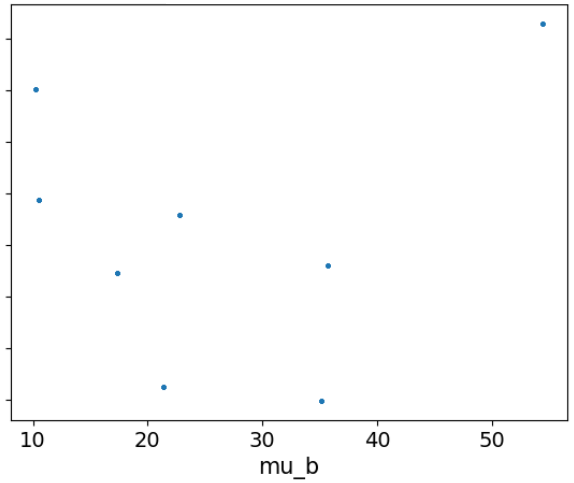










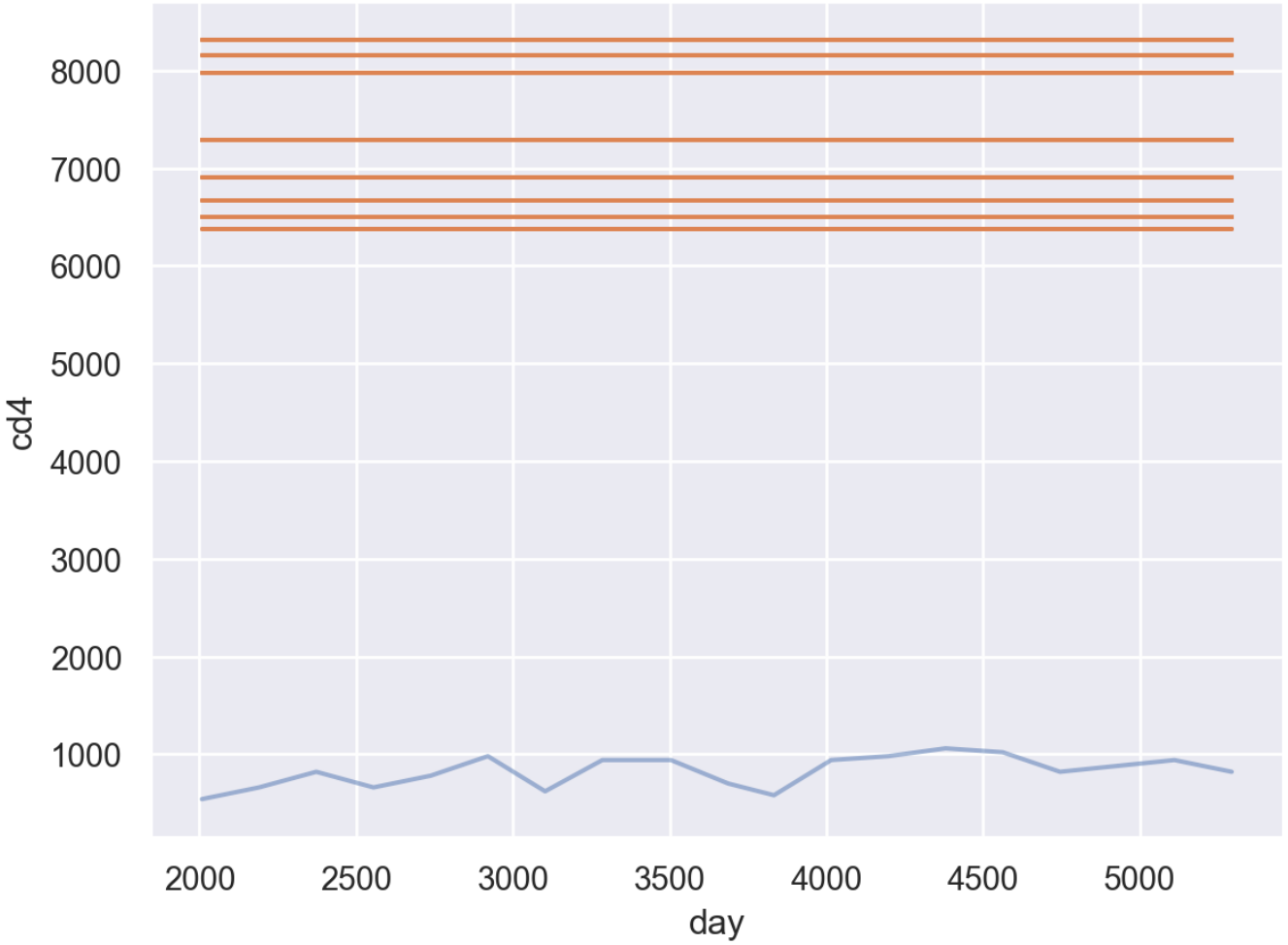


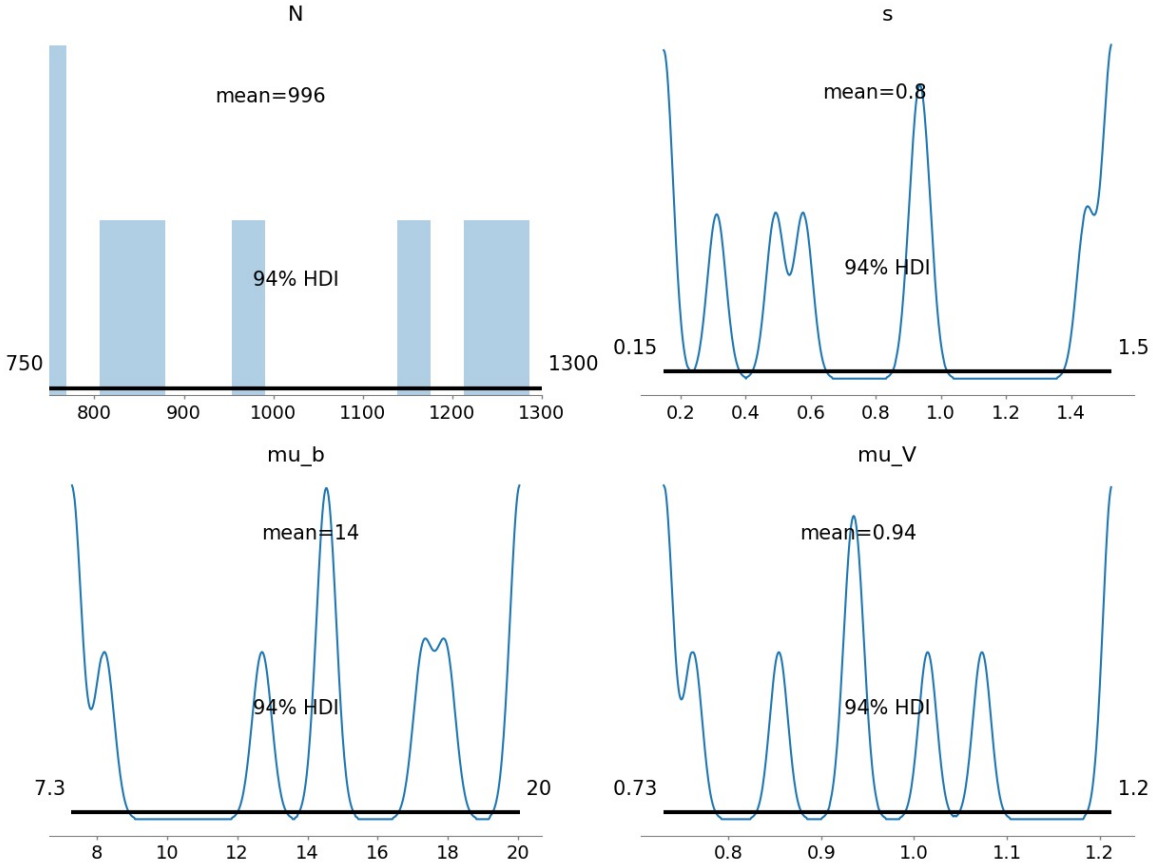

```
odeint(hiv, Y0, times, args=*params,
    mxstep=100, rtol=0.01)
```

Stages: 9

	s	μ_b	μ_V
Before	1.5, 30.3	.03, .72	.35, 7.3
After	.13, 1.7	10, 54	.71, 0.9

Varied N:
(T_{max}=1500, μ_T=0.02, r=0.03, k_1=2.4e-5, k2=3e-3) ΣCD4 no longer 0






```
odeint(hiv, Y0, times, args=*params,
       mxstep=100, rtol=0.01)
```

Stages: 8

	N	s	μ_b	μ_V
Before	490, 1410	1.5, 30.3	.03, .72	.35, 7.3
After	750, 1300	.15, 1.5	7.3, 20	0.7, 1.2

Fixed $\boldsymbol{\mu}_b$ to the value in the Perelson 1993 paper:
(T_{max}=1500, $\boldsymbol{\mu}_T$=0.02, $\boldsymbol{\mu}_b$=0.24, r=0.03, k_1=2.4e-5, k2=3e-3) solver crashes

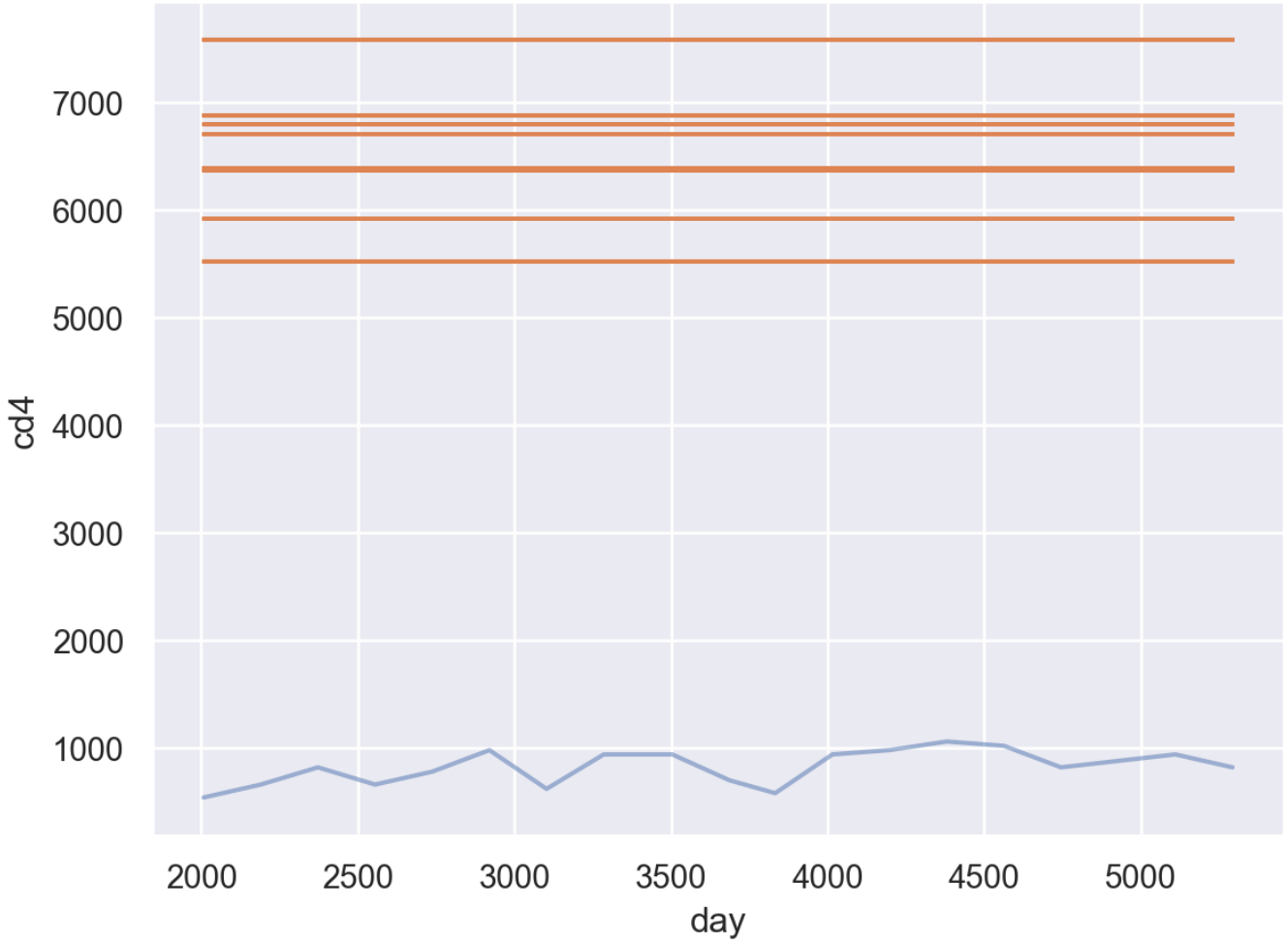
```
  File "../scipy/stats/_multivariate.py", line 172, in __init__
    raise np.linalg.LinAlgError(msg)
numpy.linalg.LinAlgError: When `allow_singular is False`, the input
matrix must be symmetric positive definite.
```

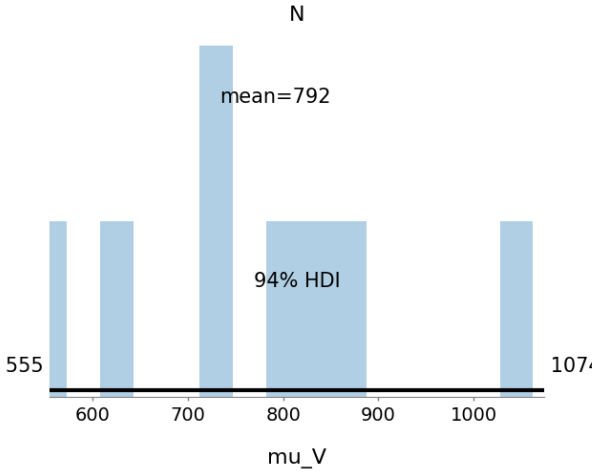
But then succeeds after re-running 2x more times

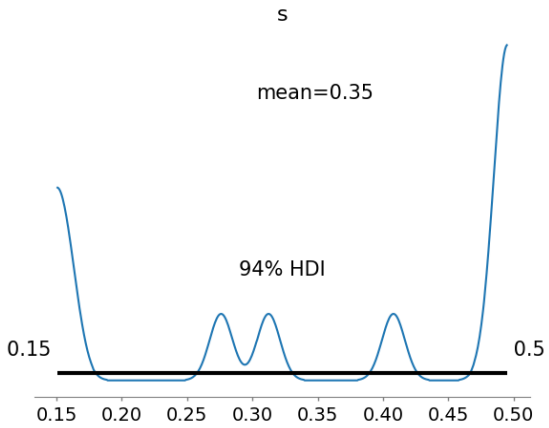
NB: Couldn't fix this with a "try" "except" clause, so I've reported the issue upstream as a possible problem with the sampler kernel:
https://github.com/pymc-devs/pymc/issues/6786
Update: Using a simpler sampling kernel no longer creates the crash!

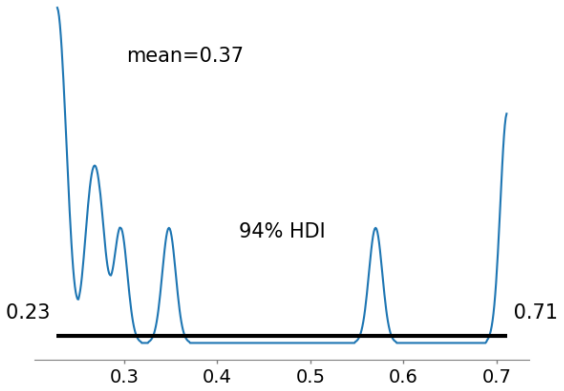
Stages: 7 (then crashes)

Fixed μ_b to the value in the Perelson 1993 paper:
(T_{max}=1500, μ_T=0.02, **μ_b=0.24**, r=0.03, k_1=2.4e-5, k2=3e-3) about the same










```
odeint(hiv, Y0, times, args=*params,
       mxstep=100, rtol=0.01)
```

Stages: 8

	N	s	μ_V
Before	490, 1410	1.5, 30.3	.35, 7.3
After	555, 1074	0.15, 0.50	0.23, 0.71