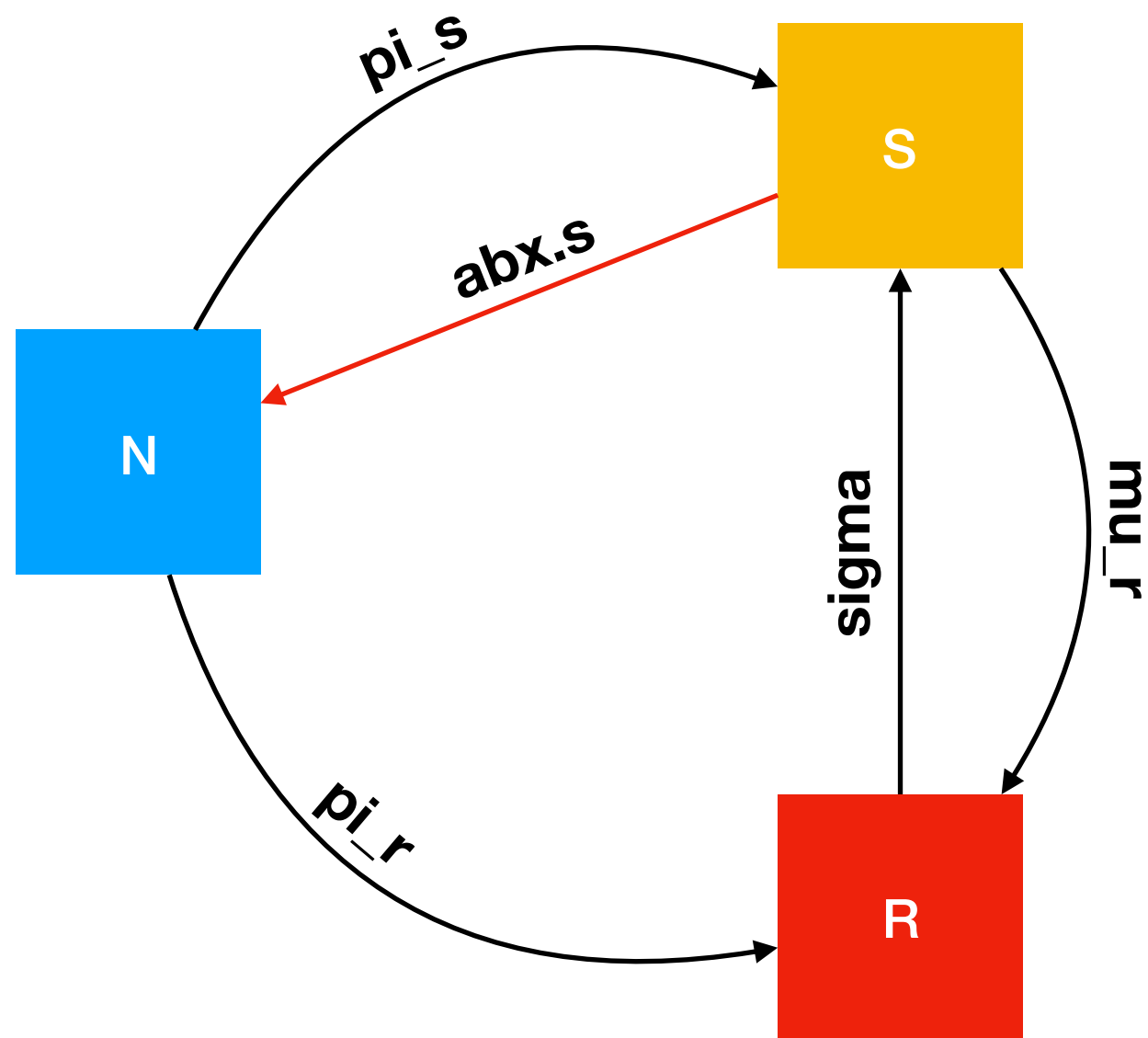


Duration of antibiotic treatment on resistance emergence in hospital setting

10 October 2018

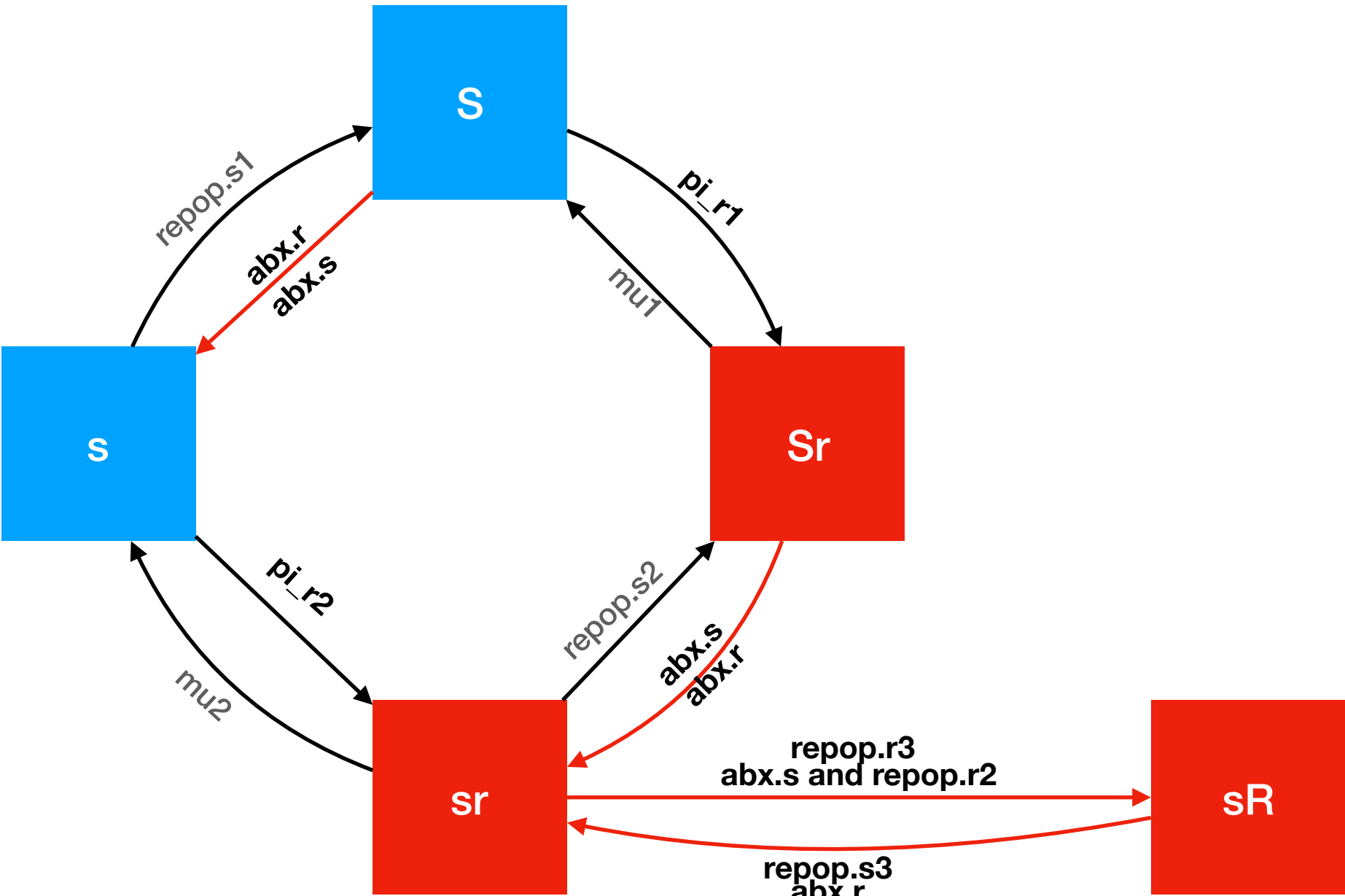
Ben, Fai, Cherry, Jet, Ana, Patrick, Ricardo, Mo Yin

Model 1



Parameters		
abx.s		probability of clearing S to become N
π_s		probability of regrowth of S
π_r		probability of being transmitted R
sigma		probability of being decolonised
μ_r		probability of being transmitted R

Model 2



Parameters		Parameters	
p.s	probability of being prescribed narrow spectrum antibiotic	repop.r3	probability of regrowth of s (sR→ sr)
p.r	probability of being prescribed broad spectrum antibiotic	abx.s	probability of clearing S to become s
pi_r1	probability of being transmitted r to S (S→ Sr)	abs.r	probability of clearing R to become r
pi_r2	probability of being transmitted r to s (s→ sr)	mu1	probability of being decolonised to S (Sr→ S)
repop.s1	probability of regrowth of S (s→ S)	mu2	probability of being decolonised to S (sr→ s)
repop.s2	probability of regrowth of S (sr→ Sr)	bif	bacterial interference factor (pi_r2 = pi_r1 * bif)
repop.s3	probability of transmission of r to S (s→ Sr)	bif1	bacterial interference factor 1 (repop.r3=repop.r2*bif1)
repop.r2	probability of transmission of r to S (s→ Sr)		

	S	s	Sr	sr	sR
S	- (abx.r or abx.s + pi_r1)	abx.r or abx.s	pi_r1	0	0
s	repop.s1	- (repop.s1 + pi_r2)	0	pi_r2	0
Sr	mu1	0	- (abx.r or abx.s + mu1)	abx.r or abx.s	0
sr	0	mu2	repop.s2	-(repop.s2 +repop.r3 or abx.s and repop.r2)	repop.r3 or abx.s and repop.r2
sR	0	0	0	repop.s3 or abx.r	- (repop.s3 or abx.r)

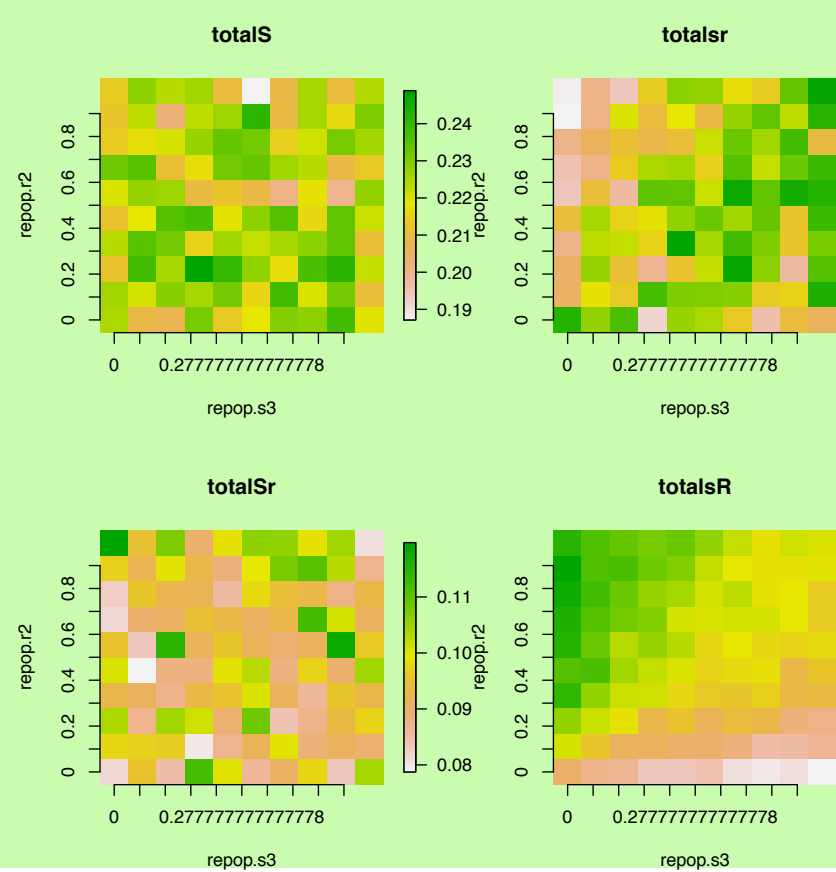
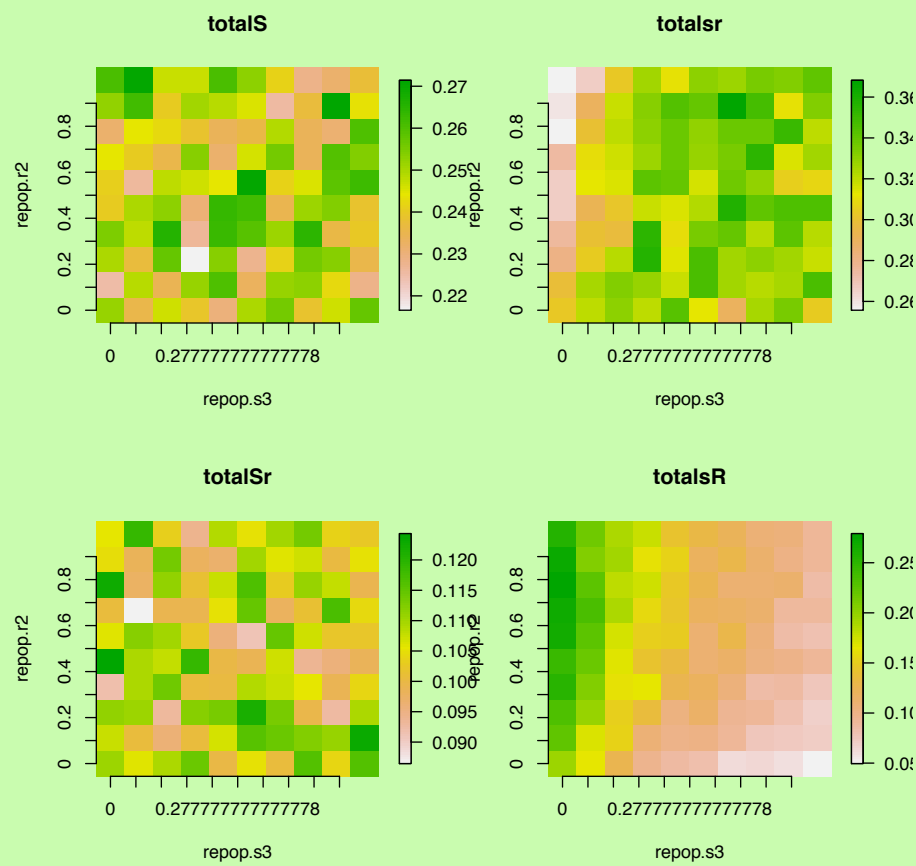
Model 2 exploration

Parameters		Values explored	Baseline value
p.s	probability of being prescribed narrow spectrum antibiotic	0.1-0.9	0.4
p.r	probability of being prescribed broad spectrum antibiotic	0.01-0.05	0.05
abx.s	probability of clearing S to become s	0.2-0.9	0.5
abx.r	probability of clearing R to become r	0.2-0.9	0.5
pi_r1	probability of being transmitted r to S ($S \rightarrow Sr$)	0.003-0.5	0.003
pi_r2	probability of being transmitted r to s ($s \rightarrow sr$)		depends on bif
repop.s1	probability of regrowth of S ($s \rightarrow S$)		0
repop.s2	probability of regrowth of S ($sr \rightarrow Sr$)		0
repop.s3	probability of transmission of r to S ($s \rightarrow Sr$)	0-0.5	0.05
repop.r2	probability of transmission of r to S ($s \rightarrow Sr$)	0-0.9	0.5
repop.r3	probability of regrowth of s ($sR \rightarrow sr$)		depends on bif1
mu1	probability of being decolonised to S ($Sr \rightarrow S$)	0-0.5	0
mu2	probability of being decolonised to S ($sr \rightarrow s$)		0
bif	bacterial interference factor ($pi_r2 = pi_r1 * bif$)	1-500	20
bif1	bacterial interference factor 1 ($repop.r3 = repop.r2 * bif1$)	0-1	0.2
n.bed	number of beds		20
mean.max.los	mean of length of stay (normal distribution)		20
n.days	number of days of observation		100
prob_StartBact	probability of initial carriage		S = 0.5, Sr = 0.2, sR=0.1, sr=0.05
mean_dur	mean duration of antibiotics (normal distribution)		4 vs 14

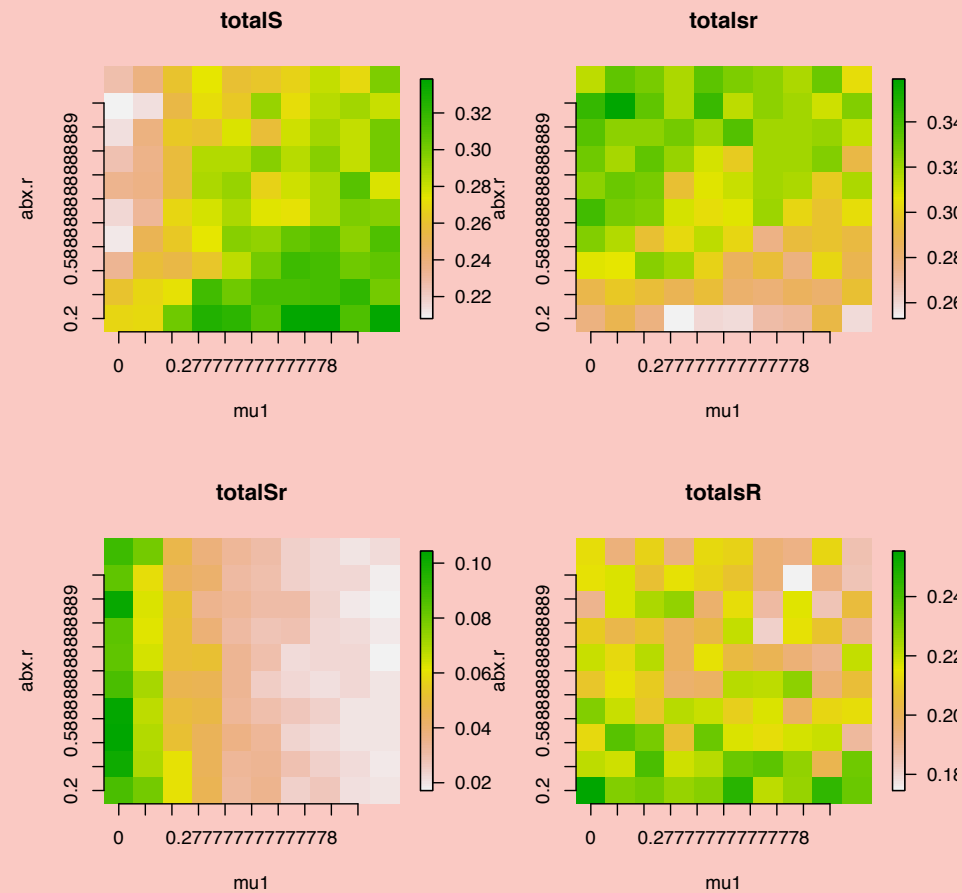
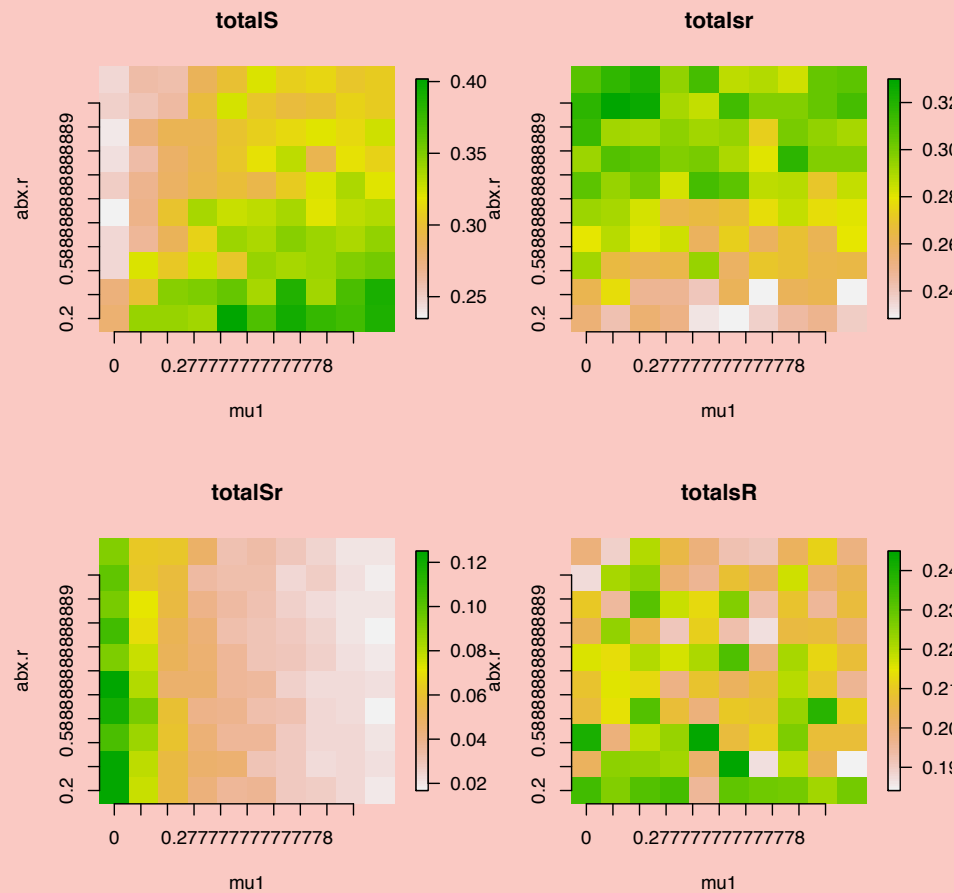
Model 2 exploration

Pairs of parameters explored to determine the effect of each parameter on resistance

repo.r2 vs repo.s3



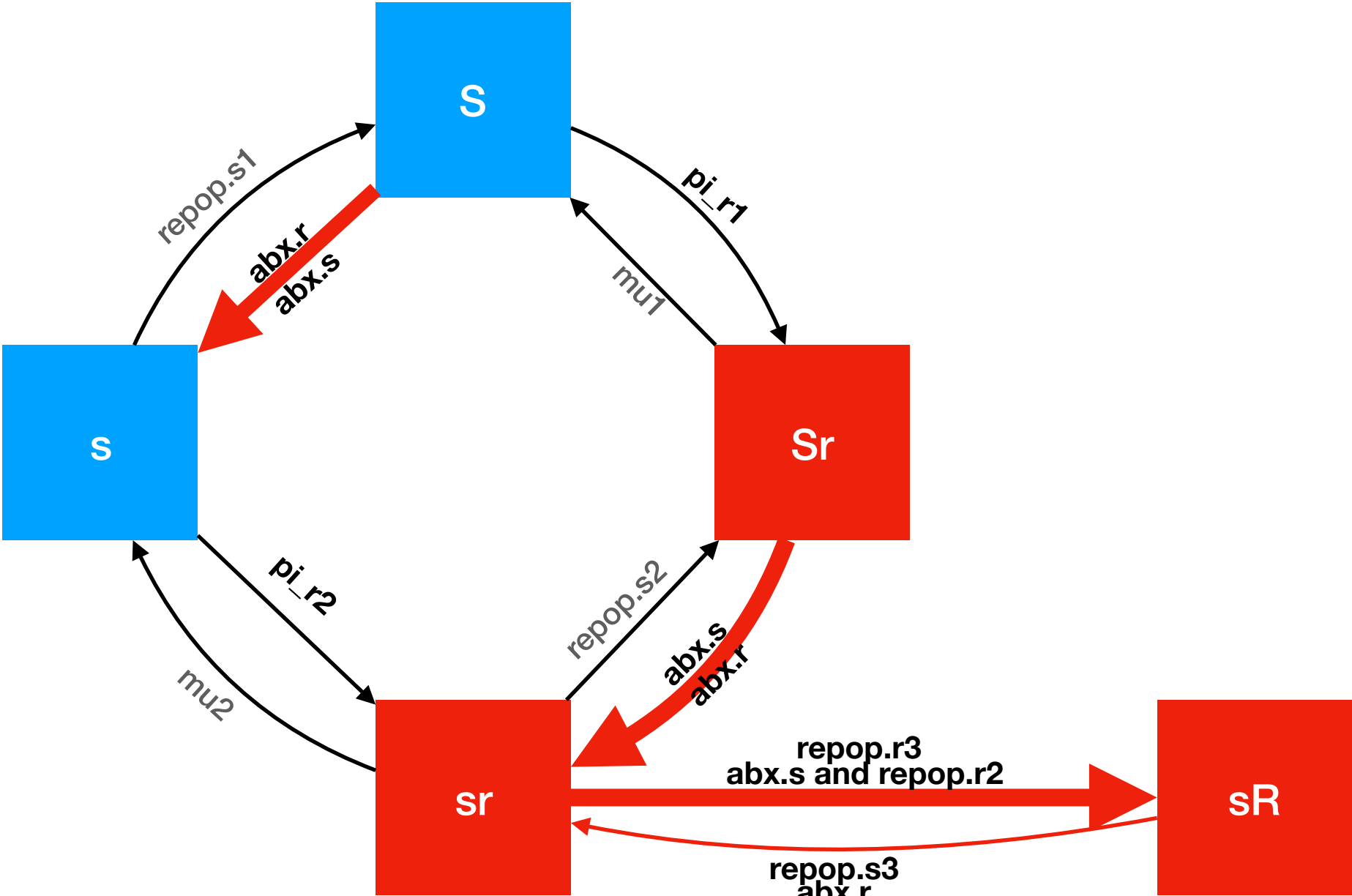
abx.r vs mu1



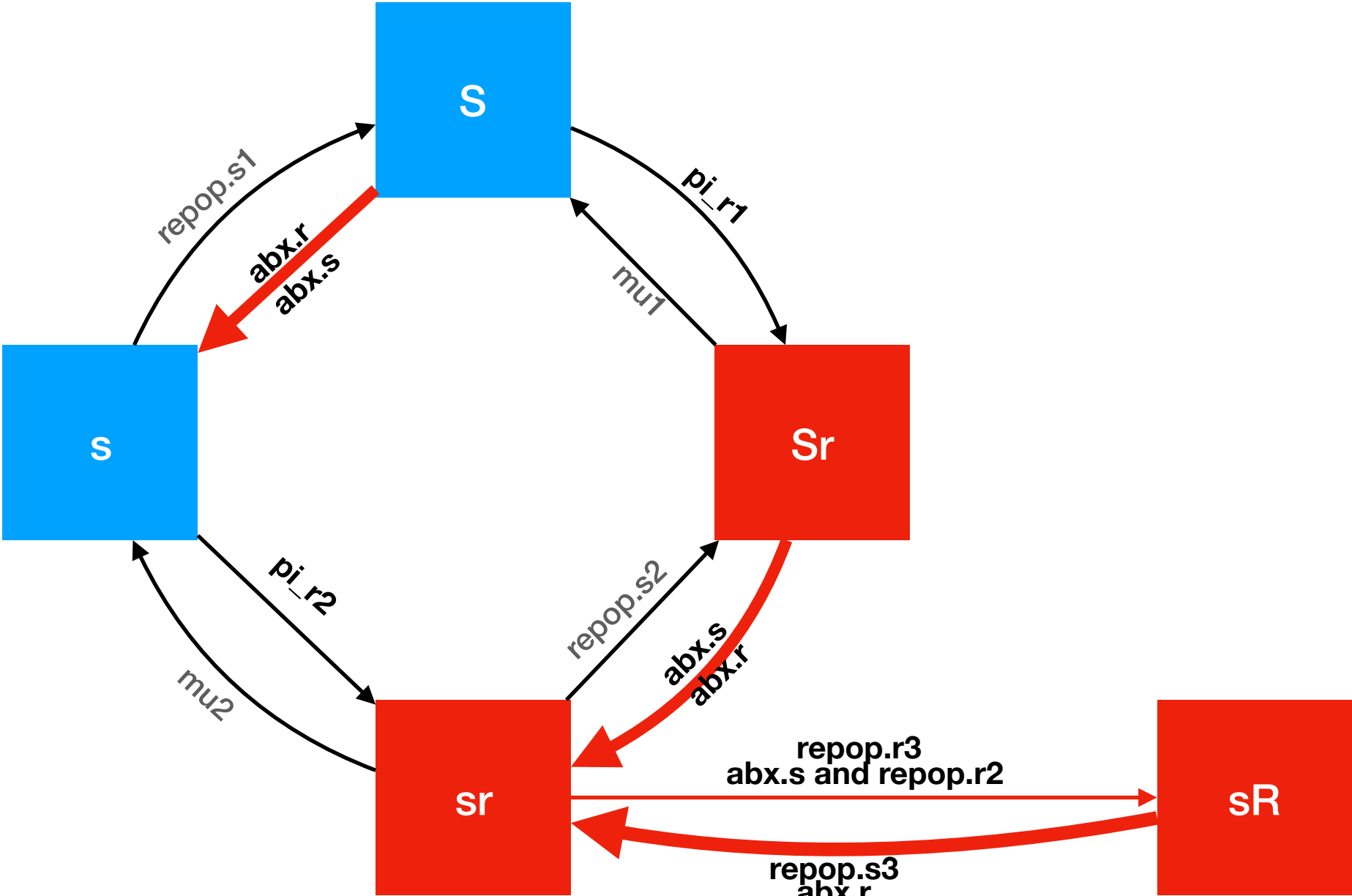
Model 2 exploration

Parameters		Values explored	Baseline value	Increase resistance
p.s	probability of being prescribed narrow spectrum antibiotic	0.1-0.9	0.4	increasing
p.r	probability of being prescribed broad spectrum antibiotic	0.01-0.05	0.05	decreasing
abx.s	probability of clearing S to become s	0.2-0.9	0.5	None
abx.r	probability of clearing R to become r	0.2-0.9	0.5	None
pi_r1	probability of being transmitted r to S ($S \rightarrow Sr$)	0.003-0.5	0.003	None
pi_r2	probability of being transmitted r to s ($s \rightarrow sr$)	depends on bif		
repop.s1	probability of regrowth of S ($s \rightarrow S$)		0	
repop.s2	probability of regrowth of S ($sr \rightarrow Sr$)		0	
repop.s3	probability of transmission of r to S ($s \rightarrow Sr$)	0-0.5	0.05	decreasing
repop.r2	probability of transmission of r to S ($s \rightarrow Sr$)	0-0.9	0.5	increasing
repop.r3	probability of regrowth of s ($sR \rightarrow sr$)	depends on bif1		
mu1	probability of being decolonised to S ($Sr \rightarrow S$)	0-0.5	0	None
mu2	probability of being decolonised to S ($sr \rightarrow s$)		0	
bif	bacterial interference factor ($pi_r2 = pi_r1 * bif$)	1-500	20	increasing
bif1	bacterial interference factor 1 ($repop.r3 = repop.r2 * bif1$)	0-1	0.2	increasing
n.bed	number of beds		20	
mean.max.los	mean of length of stay (normal distribution)		20	
n.days	number of days of observation		100	
prob_StartBact	probability of initial carriage		S = 0.5, Sr = 0.2, sR=0.1, sr=0.05	
mean_dur	mean duration of antibiotics (normal distribution)		4 vs 14	

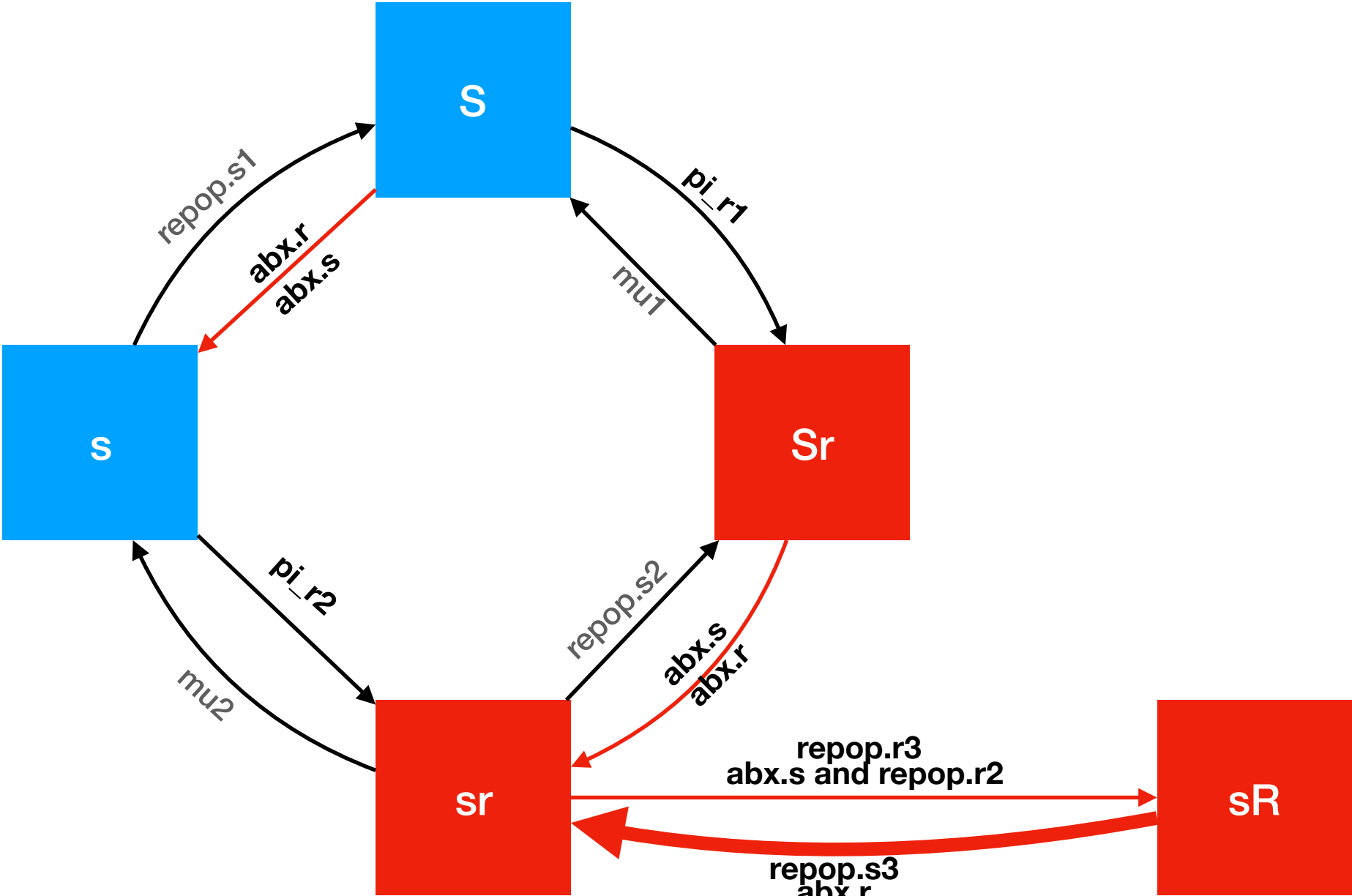
Increasing p.s



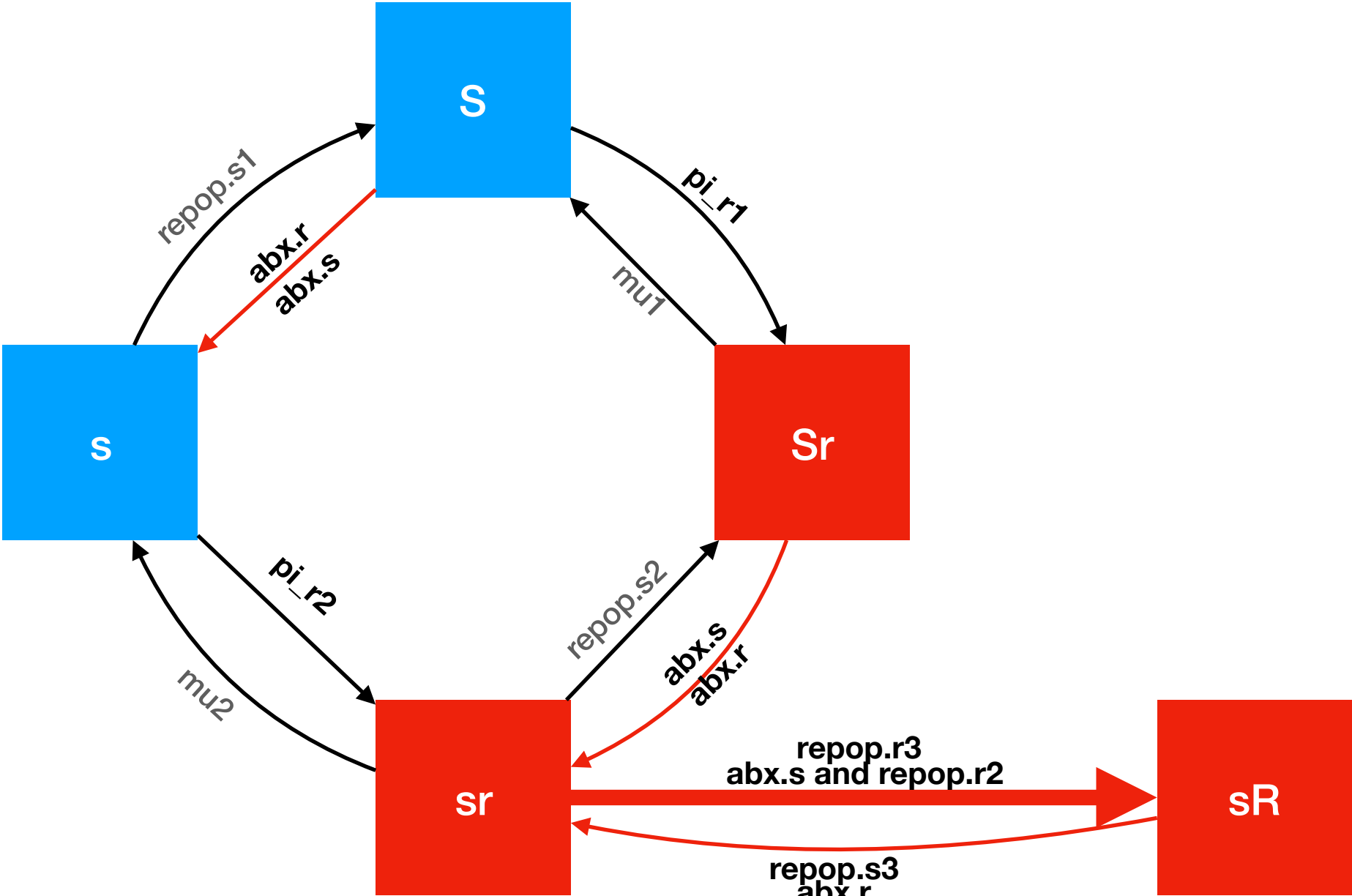
Increasing p.r
($p.r \ll p.s$)



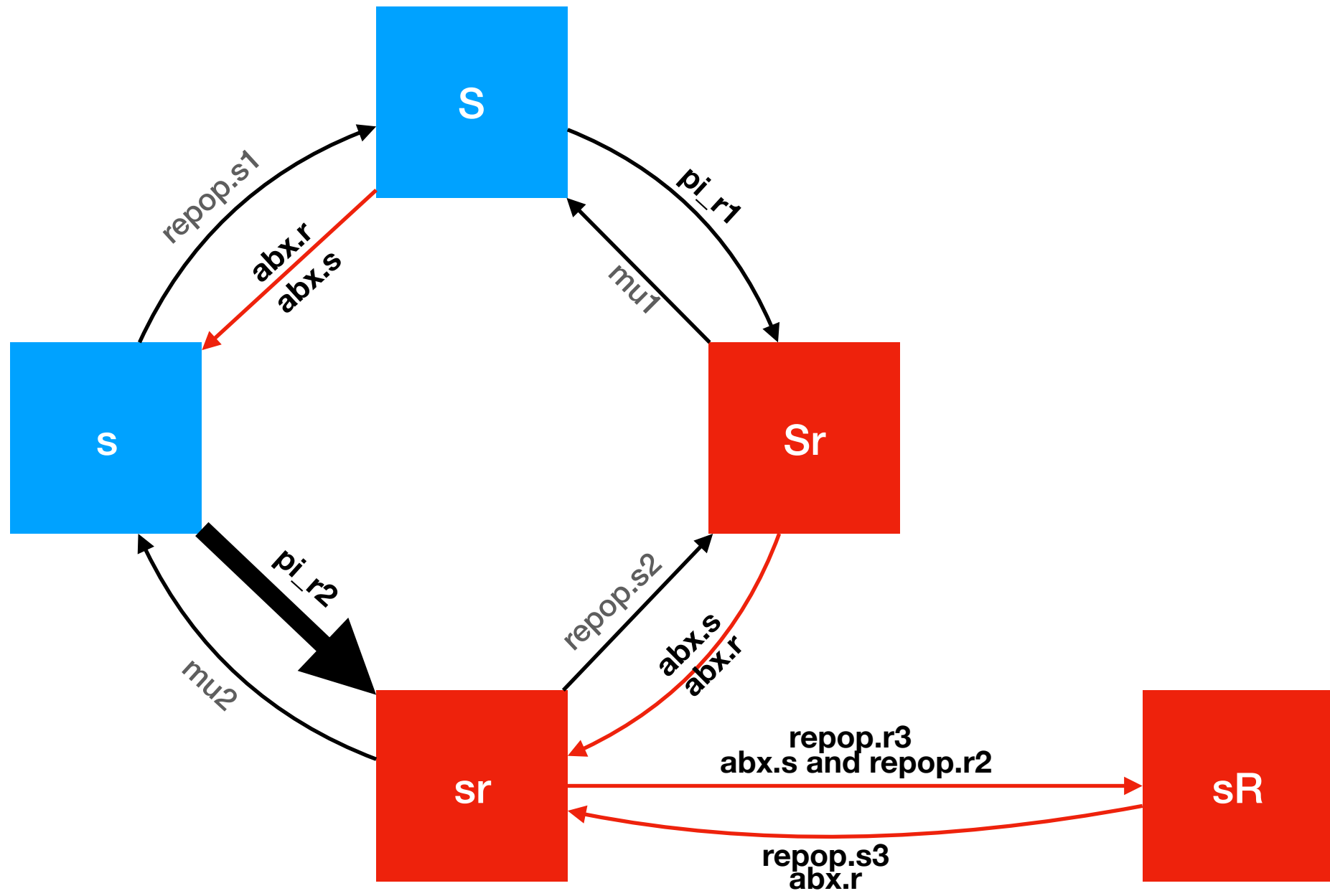
Increasing repop.s3



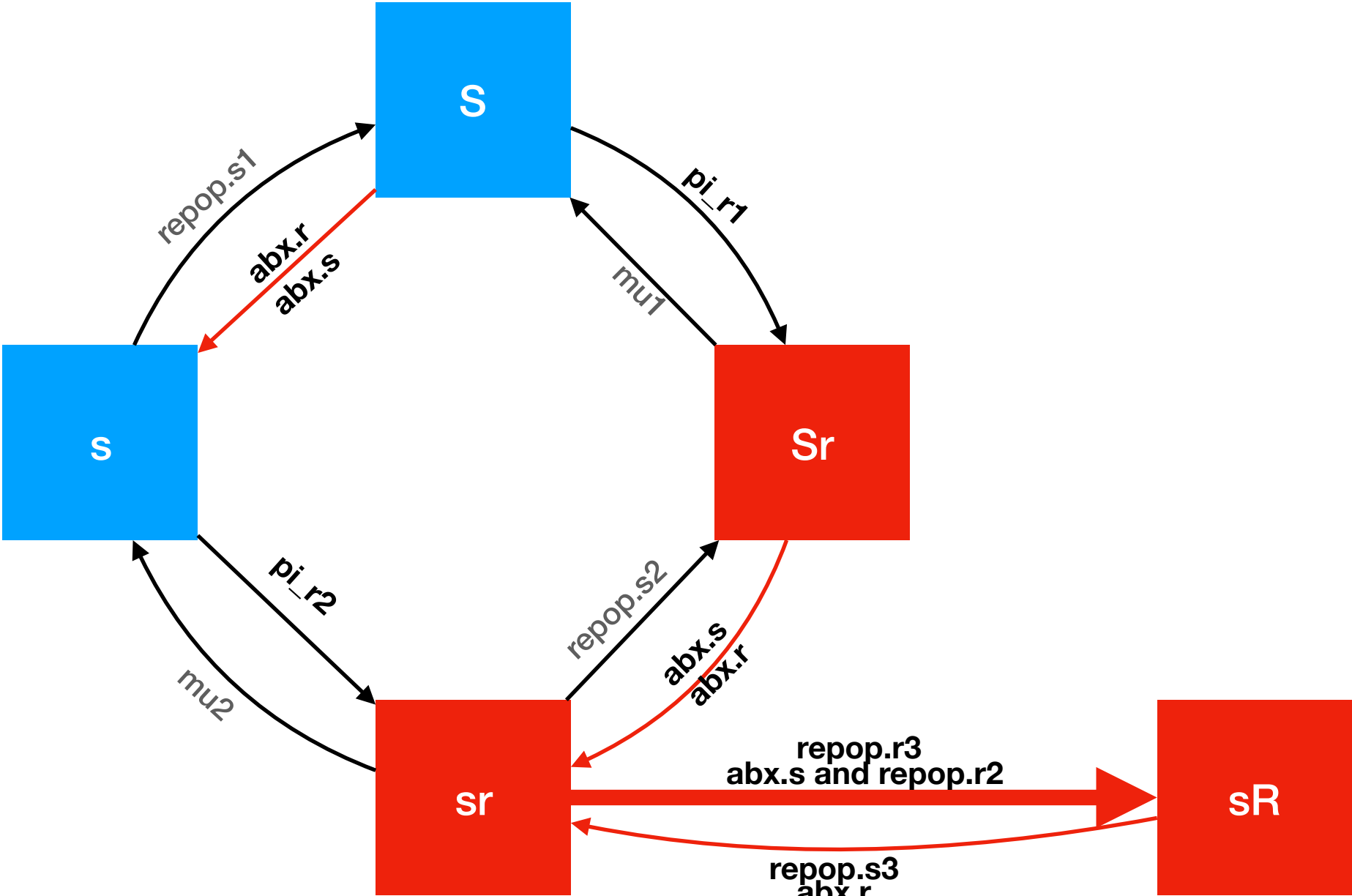
Increasing repop.r2



Increasing bif



Increasing bif1



p.s

p.r

repop.s3

repop.r2

bif

bif1

Short Long Short Long Short Long Short Long Short Long Short Long

p.s

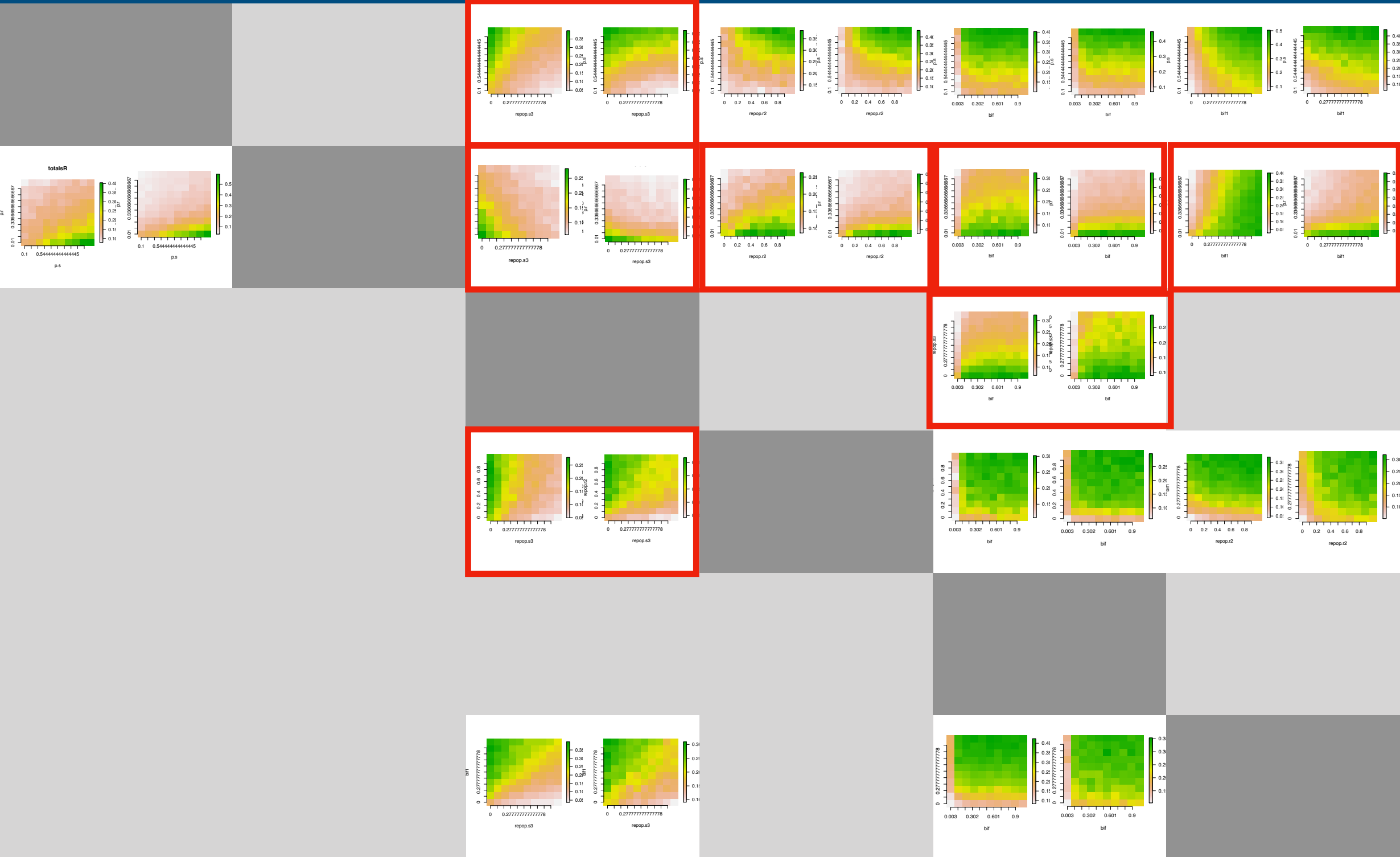
p.r

repop.s3

repop.r2

bif

bif1



Model 3

- Within host model
- Gut bacterial population is made up of S, R, E (empty)

Population growth

Antibiotic
against S

Antibiotic
against R

Transmission

Random death

$\frac{dN_s}{dt}$

$r(N_s + N_r)(1 - (N_s + N_r)/K)$	$-\gamma_s N_s$	$-\gamma_r N_s$	$+m_r p_r$	$-\beta$
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$\frac{dN_r}{dt}$

$r(N_s + N_r)(1 - (N_s + N_r)/K)$	$+\epsilon N_r$	$-\gamma_r N_r$		$-\beta$
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