Simulating compound non-homogeneous Poisson process for cell proliferation process (in this simulation I start with the simple case where there is no non-viable stem cell, i.e $p_4 = 0$. The simulation is similar to what we have done with the differential equation model, with a different way to simulate the event time

- Use the package **nhppp** to simulate the event times (non-homogeneous Poisson process) based on the intensity function $\lambda(t) = rS(t) = r \cdot S_0 \exp\{r \int_0^t [p_1(v) - p_3(v)] dv\}$.
  The package **nhppp** offers 3 different methods to simulate the event: thinning, time inversion and ordered statistics. The time inversion and ordered statistics uses the cumulative intensity function $\Lambda(t) = \int_0^t \lambda(v) dv$ and its inverse (preimage) $\Lambda^{-1}(t)$. However, since our function $\Lambda(t)$ involves integrals and no closed form for the inverse, I use the thinning algorithm.
  The thinning algorithm simulates the target non-homogeneous Poisson process with intensity $\lambda(t)$ by first drawing events from an easy-to-sample non-homogeneous Poisson process with intensity $\lambda_1(t) > \lambda(t)$, then accepts sample i with probability $\lambda(Z_i)/\lambda_1(Z_i)$. In this simulation, I choose $\lambda_1(t) = \exp(a + bt)$.

- At each of the generated event time, sample a division event (divide into 2 stem cells (p_1), divide into 1 stem cell and 1 ependymal cell (p_2), and divide into 2 ependymal cell (p_3)) based on the proliferation function
  $$q(t) = p_2(t) + 2p_3(t) = 2 - \frac{1}{a_0 + a_1 t + a_2 t^2}.$$
  The probabilities are determined as follows
  $$p_1(t) = \frac{2 - q(t)}{k},$$
  $$p_2(t) = \max\left(0, \frac{(k-2) * \left(2 - q(t)\right)}{k}\right),$$
  $$p_3(t) = \max\left(0, \frac{2 - k + (k-1) * q(t)}{k}\right).$$

I tried to run the simulation with the following parameters: starting stem cells $S_0 = 200$, division rate $r = 0.2$, and the proliferation parameter $a_0 = 1.2,\ a_1 = -0.106,\ a_2 = 0.005$. Figure 1 is the intensity function $\lambda(t)$ with the given parameters. Figure 2 is simulated cell counts of 1 replication and the expected cell counts with the given parameters. I will simulate more replications as well as with different parameter setting.

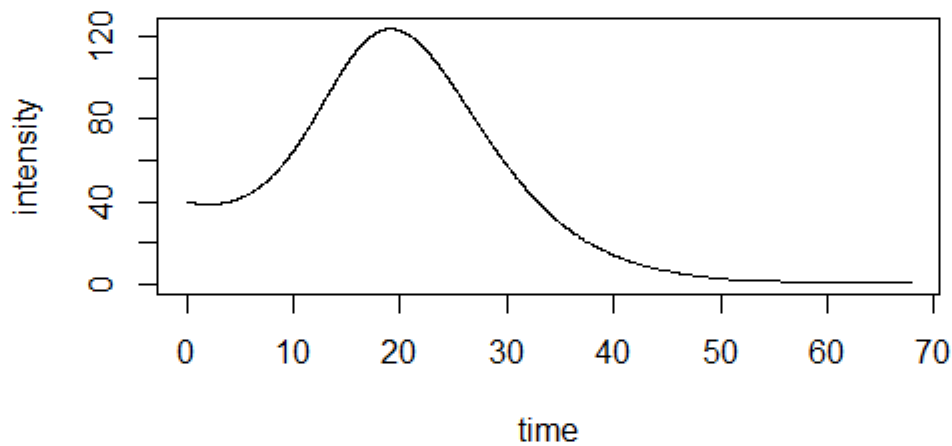

Figure 1. Intensity function

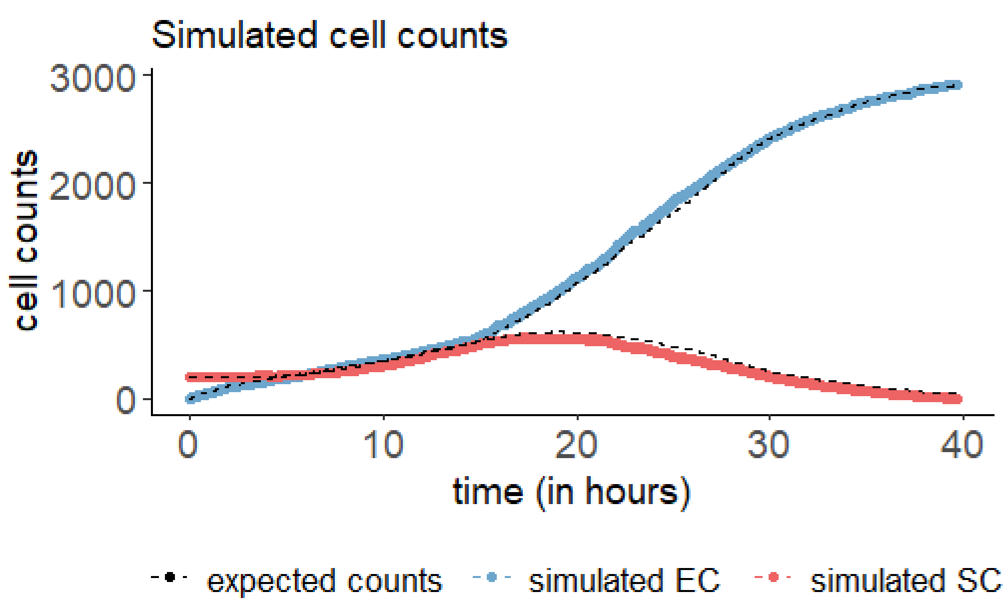

Figure 2. Simulated cell counts