Feedback control toward tumor suppression

In the future work, we will integrate our clonal evolution estimation method and data assimilation to estimate the parameters in the time evolution model for the clonal evolution using the circulating tumor DNA (ctDNA) exome sequencing data. After that, we will apply optimal control theory to the identified time evolution model to optimize the anticancer drug dosage online based on the inferred abundance ratio and growth rate of each subtype using ctDNA sequencing data which is sampled at each time of the treatment.

The time evolution model of the tumor clonal evolution can be regarded as the system in which anticancer drug dosage affect the population of each tumor subtype. Putting the population of each subtype as $x(t) = \big(x_1(t), \dots, x_I(t)\big)$, dosage of each anticancer drug as $u(t) = \big(u_1(t), \dots, u_M(t)\big)$, the system can be described as $\dot{x}(t) = Fx(t) + Gu(t) + w(t)$, where $w(t)$ represents a white noise. After the estimation of F and G using data assimilation, we can optimize the dosage by the feedback control which modulate the dosage according to the estimated population of each subtype (Figure 1). The problem is the minimization of the expected loss function $J = E[x^T(t_f)x(t_f) + \int_{t_0}^{t_f}\big(x^T(t)x(t) + u^T(t)u(t)\big)dt]$ with respect to $u(t)$, where t_0 and t_f represents for the beginning and end of the chemotherapy. The optimal dosage can be represented as $u(t) = -G^T S(t)x(t)$ using the backward solution $S(t)$ of the Riccati equation $\dot{S}(t) = -F^T S(t) - S(t)F + S(t)GG^T S(t) - I$ under the end condition $S(t_f) = I$.

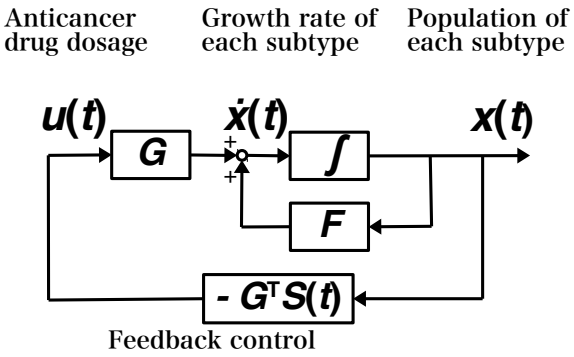

Figure 1. Optimal feedback control of anticancer drug dosage to suppress the tumor growth.