20.1 Definition

Consider a system whose states are described by a pair of stochastic variables \((X(t), M(t))\), where \(X(t) \in \Sigma \subset \mathbb{R}\) is a continuous variable and \(M(t)\) is a discrete stochastic variable taking values in the finite set \(\Gamma \equiv \{0, \ldots, M_0\}\). When the internal state is \(M(t) = m\), the system evolves according to the ordinary differential equation (ODE)

\[
\frac{dX}{dt} = F_m(X),
\]

(20.1)

Note that the nonlinear function \(F_m(X)\) depends on the discrete state \(m\). Let \(t_1, t_2, t_3, \ldots\) be the random times at which \(M(t)\) jumps starting from \(t = 0\), with \(M(t) = m\) for \(0 < t < t_1\), \(M(t) = m_1\) for \(t_1 < t < t_2\) etc. The variable \(X(t)\) then evolves as shown schematically in Fig. 72. The stochastic variable \(M(t)\) evolves according to the master equation for a Markov chain with transition rate matrix \(W\) and generator \(A\). (In general, \(W\) and hence \(A\) depend on the current state \(X\).)

Suppose that we decompose the transition matrix of the Markov chain as

\[
W_{nm}(x) = P_{nm}(x)\lambda_m(x),
\]

with \(\sum_{n \neq m} P_{nm}(x) = 1\) for all \(x\). Hence \(\lambda_m(x)\) determines the jump times from the state \(m\) whereas \(P_{nm}(x)\) determines the probability distribution that when it jumps the new state is \(n\) for \(n \neq m\). The hybrid evolution of the system with respect to \(X(t)\) and \(M(t)\) can then be described as follows, see Fig. 72. Suppose the system starts at time zero in the state \((x_0, m_0)\). Call \(x_0(t)\) the solution of (20.1) with \(m = m_0\) such that \(x_0(0) = x_0\). Let \(t_1\) be the random variable (stopping time) such that

\[
\mathbb{P}(t_1 < t) = 1 - \exp \left( - \int_0^t \lambda_{m_0}(x_0(t')) dt' \right).
\]

Figure 72: Schematic illustration of a stochastic hybrid system. Here \(t_1, t_2\) etc. are the random switching times of the discrete Markov process. In between these times, the continuous variable evolves smoothly.
Then in the random time interval $s \in [0, t_1)$ the state of the system is $(x_0(s), m_0)$. Now draw a value of $t_1$ from $\mathbb{P}(t_1 < t)$, choose an internal state $m_1 \in \Gamma$ with probability $P_{m_1m_0}(x_0(t_1))$, and call $x_1(t)$ the solution of the following Cauchy problem on $[t_1, \infty)$:

\[
\begin{cases}
    \dot{x}_1(t) &= F_{m_1}(x_1(t)), \quad t \geq t_1 \\
    x_1(t_1) &= x_0(t_1).
\end{cases}
\]

Iterating this procedure, one can construct a sequence of increasing jumping times $(t_k)_{k \geq 0}$ (setting $t_0 = 0$) and a corresponding sequence of internal states $(m_k)_{k \geq 0}$. The evolution $(X(t), M(t))$ is then defined as

$$(X(t), M(t)) = (x_k(t), m_k) \quad \text{if} \quad t_k \leq t < t_{k+1}. \tag{20.2}$$

Note that the path $X(t)$ is continuous and piecewise $C^1$.

### 20.2 Examples

Here we list some examples of stochastic hybrid systems, see Fig. 73.

(a) One example that we have already considered is the two-state gene regulatory network that switches between an active and inactive state with switching rates $k_{\pm}$. Here $X(t)$ represents protein concentration and $M(t)$ denotes the current state of the gene with $M(t) = 1$ (active) or $M(t) = 0$ (inactive). In the active state the gene produces protein at a rate $\kappa_p$ and protein degrades at a rate $\gamma_p$. We have

$$F_m(x) = \kappa_pm - \gamma_px, \tag{20.3}$$

b) A second example is a velocity jump process, where $X(t)$ is the position of a particle that switches between two or more velocity states:

$$\frac{dX}{dt} = v_m, \tag{20.4}$$

![Figure 73: Some examples of stochastic hybrid systems.](image-url)
where $v_m$ is the velocity when the particle is in velocity state $M(t) = m$. The generator $A$ specifies the transitions between the different velocity states. Examples include the following: i) bidirectional motor transport, where $X(t)$ is the position of the motor on a cytoskeletal filament track; ii) bacterial run-and-tumble with $X(t)$ the position of the bacterium is some chemotactic gradient; growth and shrinkage of a microtubule with $X(t)$ the location of the tip.

c) A third example is a conductance based model of a neuron, in which the number of open ion channels switches according to a birth-death process. Here $X(t)$ represents the membrane voltage, whereas $M(t)$ is the fraction of open ion channels. (There could be more than one type of ion channel.)

### 20.3 Chapman-Kolomogorov equation

The conditional probability density $p_m(x, t|x_0, m_0, 0)$ with
\[
P \{ X(t) \in (x, x + dx), M(t) = m|x_0, m_0 \} = p_m(x, t|x_0, m_0, 0)dx,
\]
evolves according to the differential Chapman-Kolmogorov (CK) equation
\[
\frac{\partial p_m}{\partial t} = -\frac{\partial}{\partial x}[F_m(x)p_m(x, t)] + \sum_{m'}A_{mm'}(x)p_{m'}(x, t).
\] (20.5)

For notational convenience we have dropped the explicit dependence on initial conditions. The first term on the right-hand side represents the probability flow associated with the piecewise deterministic dynamics for a given $n$ (Liouville equation), whereas the second term represents jumps in the discrete state $n$.

It remains to specify boundary conditions for the CK equation. For the sake of illustration, suppose that $\Sigma = [0, L]$. No-flux boundary conditions at the ends $x = 0, L$ take the form $J(0, t) = J(L, t) = 0$ with
\[
J(x, t) = \sum_{m=0}^{M_0-1} F_m(x)p_m(x, t).
\] (20.6)

On the other hand an absorbing boundary condition at $x = L$, say, is
\[
p_m(L, t) = 0, \quad \forall m \text{ such that } F_m(L) < 0.
\]
In general, it is difficult to obtain an analytical steady-state solution of (20.5), assuming it exists, unless $M_0 = 2$.

In the two-state case ($M_0 = 2$),

$$A(x) = \begin{pmatrix} -\alpha(x) & \beta(x) \\ \alpha(x) & -\beta(x) \end{pmatrix},$$

for a pair of transition rates $\alpha(x), \beta(x)$, so that the steady-state version of (20.14) reduces to the pair of equations

$$0 = -\frac{\partial}{\partial x} (F_0(x)p_0(x)) + \beta(x)p_1(x) - \alpha(x)p_0(x),$$

(20.7)

$$0 = -\frac{\partial}{\partial x} (F_1(x)p_1(x)) - \beta(x)p_0(x) + \alpha(x)p_1(x).$$

(20.8)

Adding the pair of equations yields

$$\frac{\partial}{\partial x} (F_0(x)p_0(x) + F_1(x)p_1(x)) = 0,$$

(20.9)

that is,

$$F_0(x)p_0(x) + F_1(x)p_1(x) = c,$$

for some constant $c$. The reflecting boundary conditions imply that $c = 0$. Since $F_n(x)$ is non-zero for all $x \in \Sigma$, we can express $p_1(x)$ in terms of $p_0(x)$:

$$p_1(x) = -\frac{F_0(x)p_0(x)}{F_1(x)}. \quad (20.10)$$

Substituting into equation (20.7) gives

$$0 = \frac{\partial}{\partial x} (F_0(x)p_0(x)) + \left(\frac{\beta(x)}{F_1(x)} + \frac{\alpha(x)}{F_0(x)}\right) F_0(x)p_0(x).$$

(20.11)

This yields the solutions

$$p_m(x) = \frac{1}{Z|F_m(x)|} \exp \left( -\int_{x_*}^x \left( \frac{\beta(y)}{F_1(y)} + \frac{\alpha(y)}{F_0(y)} \right) dy \right),$$

(20.12)

where $x_* \in \Sigma$ is arbitrary and assuming that the normalization factor $Z$ exists.

**Fast switching limit.** Suppose that for fixed $x$ the discrete Markov process has a steady-state distribution $\rho_m$, which implies that

$$\sum_k A_{mk}(x)\rho_k(x) = 0, \quad \text{for all } m. \quad (20.13)$$

Typically the dynamics of the continuous variable(s) $x$ are much slower than the rate of switching between the different discrete states $m$. This can be incorporated into the model by introducing a small positive parameter $\epsilon$ and rescaling the transition matrix so that equation (20.5) becomes

$$\frac{\partial p_m}{\partial t} = -\frac{\partial}{\partial x} [F_m(x)p_m(x, t)] + \frac{1}{\epsilon} \sum_{k \in \Gamma} A_{mk}(x)p_k(x, t),$$

(20.14)
The fast switching limit then corresponds to the case $\varepsilon \rightarrow 0$. Define the averaged function
\[ F(x) = \sum_m \rho_m(x) F_m(x). \] (20.15)

It can be shown that the stochastic hybrid system (20.1) reduces to the deterministic dynamical system
\[
\begin{aligned}
\dot{x}(t) &= F(x(t)) \\
x(0) &= x_0
\end{aligned}
\] (20.16)
in the fast switching limit $\varepsilon \rightarrow 0$.

### 20.4 QSS reduction

For small but non-zero $\varepsilon$, one can use perturbation theory to derive lowest order corrections to the deterministic mean field equation, which leads to a Langevin equation with noise amplitude $O(\sqrt{\varepsilon})$. More specifically, perturbations of the mean-field equation (20.16) can be analyzed using a quasi-steady-state (QSS) diffusion or adiabatic approximation, in which the CK equation (20.14) is approximated by a Fokker-Planck (FP) equation for the total density $C(x,t) = \sum_m p_m(x,t)$. The basic steps of the QSS reduction are as follows:

1. Decompose the probability density as
\[ p_m(x,t) = C(x,t) \rho_m(x) + \varepsilon w_m(x,t), \] (20.17)
where $\sum_m p_m(x,t) = C(x,t)$ and $\sum_m w_m(x,t) = 0$. Substituting into the CK equation yields
\[
\frac{\partial C}{\partial t} \rho_m(x) + \varepsilon \frac{\partial w_m(x,t)}{\partial t} = - \frac{\partial}{\partial x} F_m(x)[C(x,t)\rho_m(x) + \varepsilon w_m(x,t)] + \frac{1}{\varepsilon} \sum_{m'} A_{mm'}(x)[C(x,t)\rho_{m'}(x) + \varepsilon w_{m'}(x,t)]
\]

Summing both sides with respect to $m$ then gives
\[ \frac{\partial C}{\partial t} = - \frac{\partial F(x)C}{\partial x} - \varepsilon \sum_{m=1}^{M_0} \frac{\partial F_m(x)w_m(x,t)}{\partial x}. \] (20.18)

2. Using the equation for $C$ and the fact that $A\rho = 0$, we have
\[
\varepsilon \frac{\partial w_m}{\partial t} = \sum_{m'=1}^{M_0} A_{mm'}(x)w_{m'}(x,t) - \frac{\partial F_m(x)\rho_m(x)C}{\partial x} + \rho_m(x) \frac{\partial F(x)C}{\partial x} - \varepsilon \sum_{m'=1}^{M_0} [\delta_{m,m'} - \rho_m(x)] \frac{\partial F_{m'}(x)w_{m'}(x,t)}{\partial x}
\]
3. Introduce the asymptotic expansion

\[ w \sim w^0 + \epsilon w^1 + \epsilon^2 w^2 + \ldots \]

and collect \( O(1) \) terms:

\[
\sum_{m=1}^{M_0} A_{mm'}(x) w^0_{m'}(x,t) = \frac{\partial F_m(x) \rho_m(x) C(x,t)}{\partial x} - \rho_m(x) \frac{\partial F(x) C(x,t)}{\partial x}.
\] (20.19)

The Fredholm alternative theorem show that this has a solution, which is unique on imposing the condition \( \sum_m w^0_m(x,t) = 0 \).

4. Combining equations (20.19) and (23.4) shows that \( C \) evolves according to the FP equation

\[
\frac{\partial C}{\partial t} = -\frac{\partial}{\partial x}(F(x)C) + \epsilon \frac{\partial}{\partial x} \left( D \frac{\partial C}{\partial x} \right)
\] (20.20)

with the diffusion coefficient \( D \) given by

\[
D(x) = \sum_{m=1}^{M_0} Z_m(x) F_m(x),
\] (20.21)

where \( Z_m(x) \) is the unique solution to

\[
\sum_{m'=1}^{M_0} A_{mm'}(x) Z_{m'}(x) = [F(x) - F_m(x)] \rho_n(x)
\] (20.22)

with \( \sum_m Z_m(x) = 0 \). We have dropped \( O(\epsilon) \) corrections to the drift term.

For \( M_0 > 2 \) one typically has to solve equation (20.22) numerically in order to find the pseudo-inverse of \( A \). However, in the special case of a two-state discrete process \( (n = 0,1) \), one has the explicit solution

\[
D(x) = \frac{\beta(x)[F_0(x) - \overline{F}(x)]F_0(x) + \alpha(x)[F_1(x) - \overline{F}(x)]F_1(x)}{[\alpha(x) + \beta(x)]^2}.
\] (20.23)

At a fixed point \( x_* \) of the deterministic equation \( \dot{x} = F(x) \), we have \( \overline{F}(x_*) = 0 \) and \( \beta(x_*) F_0(x_*) = -\alpha(x_*) F_1(x_*) \). This gives the reduced expression

\[
D(x_*) = \frac{|F_0(x_*) F_1(x_*)|}{\alpha(x_*) + \beta(x_*)}.
\] (20.24)