final equations. The clever idea of the Lagrange multiplier is to notice that
the whole problem is symmetric with respect to the different components
of \( \Delta v \). Choosing one \( c \) value, as we did above, breaks this symmetry and
often complicates the algebra. To introduce the Lagrange multiplier, we
simply define it as

\[
\lambda = -\frac{[\nabla f]_c}{[\nabla g]_c}.
\]  
(A.57)

With this notation, the final set of equations (A.56) can be written as

\[
[\nabla f]_a + \lambda [\nabla g]_a = 0.
\]  
(A.58)

Before, we had to say that these equations held only for \( a \neq c \) because \( c \) was
treated differently. Now, however, notice that the above equation when \( a 
\)
is set to \( c \) is algebraically equivalent to the definition in equation A.57.
Thus, we can say that equation A.58 applies for all \( a \), and this provides a
symmetric formulation of the problem of finding an extremum that often
results in simpler algebra.

The final realization is that equation A.58 for all \( a \) is precisely what we
would have derived if we had set out in the first place to find an extremum
of the function \( f(v) + \lambda g(v) \) and forgotten about the constraint entirely. Of
course this lunch is not completely free. From equation A.58, we derive a
set of extremum points parameterized by the undetermined variable \( \lambda \).
To fix \( \lambda \), we must substitute this family of solutions back into \( g(v) \)
and find the value of \( \lambda \) that satisfies the constraint that \( g(v) \) equals the specified
value. This provides the solution to the constrained problem.

### A.3 Differential Equations

The most general differential equation we consider takes the form

\[
\frac{dv}{dt} = f(v),
\]  
(A.59)

where \( v \) is an \( N \)-component vector of time-dependent variables, and \( f \) is a
vector of functions of \( v \). Unless it is unstable, allowing the absolute value
of one or more of the components of \( v \) to grow without bound, this type
of equation has three classes of solutions. For one class, called stable fixed
points or point attractors, \( v(t) \) approaches a time-independent vector \( v_\infty \)
\( (v(t) \rightarrow v_\infty) \) as \( t \rightarrow \infty \). In a second class of solutions, called limit cycles,
\( v(t) \) becomes periodic at large times and repeats itself indefinitely. For
the third class of solutions, the chaotic ones, \( v(t) \) never repeats itself but
the trajectory of the system lies in a limited subspace of the total space
of allowed configurations called a strange attractor. Chaotic solutions are
extremely sensitive to initial conditions.

We focus most of our analysis on fixed point solutions, which are also
called equilibrium points. For \( v_\infty \) to be a time-independent solution
of equation A.59, we must have \( f(v_{\infty}) = 0 \). General solutions of equation A.59 when \( f \) is nonlinear cannot be constructed, but we can use linear techniques to study the behavior of \( v \) near a fixed point \( v_{\infty} \). If \( f \) is linear, the techniques we use and the solutions we obtain as approximations in the nonlinear case are exact. Near the fixed point \( v_{\infty} \), we write

\[ v(t) = v_{\infty} + \epsilon(t) \quad (A.60) \]

and consider the case when all the components of the vector \( \epsilon \) are small. Then, we can expand \( f \) in a Taylor series,

\[ f(v(t)) \approx f(v_{\infty}) + J \cdot \epsilon(t) = J \cdot \epsilon(t), \quad (A.61) \]

where \( J \) is the called the Jacobian matrix and has elements

\[ J_{ab} = \left. \frac{\partial f_a(v)}{\partial v_b} \right|_{v=v_{\infty}}. \quad (A.62) \]

In the second equality of equation A.61, we have used the fact that \( f(v_{\infty}) = 0 \).

Using the approximation of equation A.61, equation A.59 becomes

\[ \frac{d\epsilon}{dt} = J \cdot \epsilon. \quad (A.63) \]

The temporal evolution of \( v(t) \) is best understood by expanding \( \epsilon \) in the basis provided by the eigenvectors of \( J \). Assuming that \( J \) is real and has \( N \) linearly independent eigenvectors \( e_1, \ldots, e_N \) with different eigenvalues \( \lambda_1, \ldots, \lambda_N \), we write

\[ \epsilon(t) = \sum_{\mu=1}^{N} c_{\mu}(t)e_{\mu}. \quad (A.64) \]

Substituting this into equation A.63, we find that the coefficients must satisfy

\[ \frac{d c_{\mu}}{dt} = \lambda_{\mu} c_{\mu}. \quad (A.65) \]

This produces the solution

\[ \epsilon(t) = \sum_{\mu=1}^{N} c_{\mu}(0) \exp(\lambda_{\mu} t)e_{\mu}, \quad (A.66) \]

where \( \epsilon(0) = \sum_{\mu} c_{\mu}(0)e_{\mu} \). The individual terms in the sum on the right side of equation A.66 are called modes. This solution is exact for equation A.63, but is only a valid approximation when applied to equation A.59 if \( \epsilon \) is small. Note that the different coefficients \( c_{\mu} \) evolve over time, independently of each other. This does not require the eigenvectors to be orthogonal. If the eigenvalues and eigenvectors are complex, \( v(t) \) will nonetheless remain real if \( v(0) \) is real, because the complex modes come
in conjugate pairs that combine to form a real function. Expression A.66 is not the correct solution if some of the eigenvalues are equal. The reader should consult the references for the solution in this case.

Equation A.66 determines how the evolution of \( v(t) \) in the neighborhood of \( v_\infty \) depends on the eigenvalues of \( J \). If we write \( \lambda_\mu = \alpha_\mu + i \omega_\mu \),

\[
\exp(\lambda_\mu t) = \exp(\alpha_\mu t) (\cos(\omega_\mu t) + i \sin(\omega_\mu t)) .
\]  

(A.67)

This implies that modes with real eigenvalues (\( \omega_\mu = 0 \)) evolve exponentially over time, and modes with complex eigenvalues (\( \omega_\mu \neq 0 \)) oscillate with a frequency \( \omega_\mu \). Recall that the eigenvalues are always real if \( J \) is a symmetric matrix. Modes with negative real eigenvalues (\( \alpha_\mu < 0 \) and \( \omega_\mu = 0 \)) decay exponentially to 0, while those with positive real eigenvalues (\( \alpha_\mu > 0 \) and \( \omega_\mu = 0 \)) grow exponentially. Similarly, the oscillations for modes with complex eigenvalues are damped exponentially to 0 if the real part of the eigenvalue is negative (\( \alpha_\mu < 0 \) and \( \omega_\mu \neq 0 \)), and grow exponentially if the real part is positive (\( \alpha_\mu > 0 \) and \( \omega_\mu \neq 0 \)).

Stability of the fixed point \( v_\infty \) requires the real parts of all the eigenvalues to be negative (\( \alpha_\mu < 0 \) for all \( \mu \)). In this case, the point \( v_\infty \) is a stable fixed-point attractor of the system, meaning that \( v(t) \) will approach \( v_\infty \) if it starts from any point in the neighborhood of \( v_\infty \). If any real part is positive (\( \alpha_\mu > 0 \) for any \( \mu \)), the fixed point is unstable. Almost any \( v(t) \) initially in the neighborhood of \( v_\infty \) will move away from that neighborhood. If \( f \) is linear, the exponential growth of \( |v(t) - v_\infty| \) never stops in this case. For a nonlinear \( f \), equation A.66 determines what happens only in the neighborhood of \( v_\infty \), and the system may ultimately find a stable attractor away from \( v_\infty \), either a fixed point, a limit cycle, or a chaotic attractor. In all these cases, the mode for which the real part of \( \lambda_\mu \) takes the largest value dominates the dynamics as \( t \to \infty \). If this real part is equal to 0, the fixed point is called marginally stable.

As mentioned previously, the analysis presented above as an approximation for nonlinear differential equations near a fixed point is exact if the original equation is linear. In the text, we frequently encounter linear equations of the form

\[
\tau \frac{dv}{dt} = v_\infty - v .
\]  

(A.68)

This can be solved by setting \( z = v - v_\infty \), rewriting the equation as \( dz/z = -dt/\tau \), and integrating both sides:

\[
\tau \int_{z(0)}^{z(t)} \frac{1}{z'} = \ln \left( \frac{z(t)}{z(0)} \right) = -\frac{t}{\tau} .
\]  

(A.69)

This gives \( z(t) = z(0) \exp(-t/\tau) \) or

\[
v(t) = v_\infty + (v(0) - v_\infty) \exp(-t/\tau) .
\]  

(A.70)

In some cases, we consider discrete rather than continuous dynamics defined over discrete steps \( n = 1, 2, \ldots \) through a difference rather than a
differential equation. Linearization about equilibrium points can be used to analyze nonlinear difference equations as well as differential equations, and this reveals similar classes of behavior. We illustrate difference equations by analyzing a linear case,

\[ \mathbf{v}(n+1) = \mathbf{v}(n) + \mathbf{W} \cdot \mathbf{v}(n). \]  

(A.71)

The strategy for solving this equation is similar to that for solving differential equations. Assuming \( \mathbf{W} \) has a complete set of linearly independent eigenvectors \( \mathbf{e}_1, \ldots, \mathbf{e}_N \) with different eigenvalues \( \lambda_1, \ldots, \lambda_N \), the modes separate, and the general solution is

\[ \mathbf{v}(n) = \sum_{\mu=1}^{N} c_\mu (1 + \lambda_\mu)^n \mathbf{e}_\mu. \]  

(A.72)

where \( \mathbf{v}(0) = \sum_\mu c_\mu \mathbf{e}_\mu \). This has characteristics similar to equation A.66.

Writing \( \lambda_\mu = \alpha_\mu + i \omega_\mu \), mode \( \mu \) is oscillatory if \( \omega_\mu \neq 0 \). In the discrete case, stability of the system is controlled by the magnitude

\[ |1 + \lambda_\mu|^2 = (1 + \alpha_\mu)^2 + (\omega_\mu)^2. \]  

(A.73)

If this is greater than 1 for any value of \( \mu \), \( |\mathbf{v}(n)| \to \infty \) as \( n \to \infty \). If it is less than 1 for all \( \mu \), \( \mathbf{v}(n) \to 0 \) in this limit.

A.4 Electrical Circuits

Biophysical models of single cells involve equivalent circuits composed of resistors, capacitors, and voltage and current sources. We review here basic results for such circuits. Figures A.1A and A.1B show the standard symbols for resistors and capacitors, and define the relevant voltages and currents. A resistor (figure A.1A) satisfies Ohm's law, which states that the voltage \( V_R = V_1 - V_2 \) across a resistance \( R \) carrying a current \( I_R \) is

\[ V_R = I_R R. \]  

(A.74)

Resistance is measured in ohms (\( \Omega \)); 1 ohm is the resistance through which 1 ampere of current causes a voltage drop of 1 volt (1 V = 1 A \( \times \) 1 \( \Omega \)).

A capacitor (figure A.1B) stores charge across an insulating medium, and the voltage across it \( V_C = V_1 - V_2 \) is related to the charge it stores, \( Q_C \), by

\[ CV_C = Q_C. \]  

(A.75)

where \( C \) is the capacitance. Electrical current cannot cross the insulating medium, but charges can be redistributed on each side of the capacitor, which leads to the flow of current. We can take a time derivative of both sides of equation A.75 and use the fact that current is equal to the rate of