

Quantum counting: Operator methods for discrete population dynamics with applications to cell division

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Abstract

The set of natural numbers may be identified with the spectrum of eigenvalues of an operator (quantum counting), and the dynamical equations of populations of discrete, countable items may be formulated using operator methods. These equations take the form of time dependent operator equations, involving Hamiltonian operators, from which the statistical time dependence of population numbers may be determined. The quantum operator method is illustrated by a novel approach to cell population dynamics. This involves Hamiltonians that mimic the process of stimulated cell division. We evaluate two different models, one in which the stimuli are expended in the division process and one in which the stimuli act as true catalysts. While the former model exhibits only bounded cell population variations,

the latter exhibits two distinct regimes; one has bounded population fluctuations about a mean level and in the other, the population can undergo growth to levels that are orders of magnitude above threshold levels, through an instability that could be interpreted as a cancerous growth phase.

Keywords: quantum counting, quantum operator; population dynamics; cell division; oncogenic mutation

1 Introduction

Mathematical models incorporating differential equations have been in common use to investigate the dynamical behaviour of populations of systems of living things ever since Lotka [1] and Volterra [2] introduced their model of predator-prey competition in the 1920s. The nature of these models is often heuristic and it is usually taken for granted that the number continuum on the real number line can be used to model systems of discrete, countable entities like people, animals, plants, bacteria, cells, etc. Ecological systems [3], the spread of epidemics [4], and cancer cell population growth [5, 6] are just a few examples of what has been modelled in this way.

The continuum approach does lead to simplifications, since we can use continuous, scalar-valued functions and ordinary differential calculus for rates of change of such populations. This approximation is often justified by arguing that if one is only interested in averages, as is usually the case in population models, then real numbers and not just counting numbers, are justifiable in most cases, especially when large populations are involved. Then, also, the minimum change in population number, being one, is a small fraction of the population as a whole, so any errors incurred should be small. However, it remains unclear whether modelling the average is the same thing as averaging a model, in the case of natural number valued populations, especially when population numbers are not large. Bagarello [7] has recently shown how the number operator that is widely used in quantum theory can also be used to model discrete populations in social science and ecological contexts, and has pioneered a new approach to population dynamics based on this idea. The method is particularly relevant to closed ecosystems [8], where conservation rules play an important role in constraining the dynamics.

Such an approach might well be considered far fetched when endeavouring to persuade non-physicists that quantum tools are relevant to situations like predator-prey competition, that do not involve the often counterintuitive behaviour of quantum phenomena. Furthermore, number operators

and associated creation and annihilation operators that are ubiquitous in quantum field theory, especially where this deals with the many-body problem in condensed matter physics, were developed from the quantum theory of mechanical oscillators, as part of a procedure called *second quantization*. *First quantization* refers to the replacement of the scalar dynamical variables of classical physics by operators that operate on scalar wavefunctions. Second quantization refers to the procedure whereby the wavefunctions of the first quantization are themselves replaced by operators that are the primitive fields of quantum field theory. This approach to physical theory was developed by Dirac [11] and others in the 1920s and 30s. However, there is in fact a strong analogy between identical particles in many-body quantum field theory and macroscopic systems of many individuals, where a detailed description of the individuals is unimportant, but where the number of individuals within defined categories is all the information that is needed to define and model such systems. One reason for this strong connection is that the set of natural numbers that represent discrete populations corresponds to the spectrum of the eigenvalues of an operator. Then operator valued calculus becomes the appropriate way of dealing mathematically with population dynamics. We refer to this as *quantum counting* [9], because of the connection between operator valued variables and quantum physics.¹

The paper is set out as follows. In section 2, we review both the basic quantum operator formalism needed to represent discrete populations and also the Heisenberg representation of time dependence. Here we largely adopt Bagarello's [7] approach of importing the relevant algebra from quantum many-body physics. In section 3, we illustrate how operator formalism may be used to model the dynamics of interacting populations, using some simple examples. A comparison with a classical representation of two-category interaction in the form of the Lotka-Volterra predator-prey system is also presented in section 3. In section 4 we introduce a novel application of the general method to cell division and cell population dynamics. The results are summarised in section 5.

¹The term *quantum counting* is also used in the context of quantum search algorithms in quantum computing.[10]

2 Operator methods for discrete population dynamics

2.1 Operators and states of a system

The basic representation of a system using operators may be summarised by the equation

$$\hat{\Gamma}|\gamma\rangle = \gamma|\gamma\rangle,$$

where $\hat{\Gamma}$ is an operator, operating on a state, $|\gamma\rangle$ ² that has an eigenvalue γ . In any representation of operators, γ is invariably simply a number that constitutes some information about the state $|\gamma\rangle$ of a system. The system in question does not need to be anything physical, just something that can be represented mathematically. For example, the system could be an electronic bank account with γ the amount of money it contains. Typically, one specifies the operator first and then one solves the eigenvalue equation for both γ and $|\gamma\rangle$, simultaneously. There are usually several solutions, implying that the system can be in several states, each with its own value (i.e., eigenvalue). These correspond to some information about the system that we can, in principle at least, obtain from some measurements on the system.

There are two common representations of operators in use in quantum mechanics. One involves differential operators, in which case the eigenstates are represented by functions of the variable with respect to which they are differentiated. The other uses square matrices to represent the operator, then the eigenstates are represented by column vectors. However, these may well be of infinite dimensions and great care needs to be exercised in their use.

For the systems we will be dealing with in the rest of this paper, the only information we need to describe them is the number of items they contain, so the eigenvalues we need are simply the set of natural numbers.³ The only kind of measurement we need to carry out on such a system, in order to obtain the required information, is counting the number of items it contains. In the next section we summarize the basic properties of creation, annihilation and number operators for a system comprising a single category of countable individual items. These operators are then generalized for more elaborate multi-category systems in the subsequent sections.

²Here we use Dirac notation for states[12].

³In what follows, we always include zero in the set of natural numbers.

2.2 Creation and annihilation operators and the number operator

We begin by defining a non-commuting pair of operators, \hat{a} and \hat{a}^\dagger , where \hat{a}^\dagger is the adjoint of \hat{a} .⁴ Their non-commuting properties are defined by the commutation relation⁵

$$[\hat{a}, \hat{a}^\dagger] = \hat{I}, \quad (1)$$

where \hat{I} is the identity operator.⁶ From Eq.(1) it can be deduced that the eigenvalues of the product $\hat{a}^\dagger\hat{a}$ are natural numbers [14]. So we can write

$$\hat{a}^\dagger\hat{a}|n\rangle = n|n\rangle, \quad (2)$$

where $n = 0, 1, 2, 3, \dots$, and $|n\rangle$ represents a state containing n items. Eq.(2) invites the definition of a *number* operator, \hat{n} , as $\hat{n} = \hat{a}^\dagger\hat{a}$. From this definition we can infer that \hat{n} is self-adjoint, since $(\hat{a}^\dagger\hat{a})^\dagger = \hat{a}^\dagger\hat{a}$.⁷

In addition to the result in Eq.(2), the commutation relation, Eq.(1), allows us to deduce that[14]

$$\begin{aligned} \hat{a}|n\rangle &= \sqrt{n}|n-1\rangle, \\ \hat{a}^\dagger|n\rangle &= \sqrt{n+1}|n+1\rangle. \end{aligned} \quad (3)$$

Thus, the operation of \hat{a} has the effect of reducing by 1 the number of items in a state and the operation of \hat{a}^\dagger has the effect of increasing the number of items by 1. These properties have led to \hat{a} being called an *annihilation* operator and \hat{a}^\dagger a *creation* operator, when they are used in a particle physics context. However, as we shall see, they can be regarded in a less dramatic light when used as mechanisms for interchanging items between different subpopulations of a system. Notice that the pair of relations, Eq.(3) is consistent with Eq.(2). Also, notice that the definitions, Eq.(3) show that $|n\rangle$ is not an eigenstate of \hat{a} , nor of \hat{a}^\dagger .

We can construct the state containing n items from the empty state, $|0\rangle$, using the creation operator, by noting that applying \hat{a}^\dagger n times to the empty state gives a state containing n items, i.e., $\hat{a}^{\dagger n}|0\rangle = \sqrt{n!}|n\rangle$. Thus

$$|n\rangle = \frac{\hat{a}^{\dagger n}}{\sqrt{n!}}|0\rangle. \quad (4)$$

⁴See Weinberg[13] and also Bagarello[7] for mathematical details on adjoints.

⁵For any pair of operators, \hat{A} and \hat{B} , the difference, $\hat{A}\hat{B} - \hat{B}\hat{A}$ is written as $[\hat{A}, \hat{B}]$. \hat{A} and \hat{B} are said to commute if $[\hat{A}, \hat{B}] = 0$, which implies that the order in which the operators are applied makes no difference to the result.

⁶The identity operator, \hat{I} has the property that $\hat{I}|\Psi\rangle = |\Psi\rangle$ for any state $|\Psi\rangle$.

⁷Since, by definition $(\hat{A}\hat{B})^\dagger = \hat{B}^\dagger\hat{A}^\dagger$ and $\hat{A}^{\dagger\dagger} = \hat{A}$.

The empty, or unpopulated state, plays a key role in quantum physics, where it is referred to as the *vacuum* state.

Finally in this section we note that the set states, $|n\rangle$, with $n = 0, 1, 2, 3, \dots$ constitutes a set of basis states with the property

$$\langle m|n\rangle = \delta_{mn}, \quad (5)$$

where δ_{mn} is the Kronecker delta symbol and $\langle m|$ is the conjugate of $|m\rangle$, i.e. $\langle m| = (|m\rangle)^*$. In practice $|m\rangle$ is represented by a unit column vector and its conjugate by a unit row vector in which each element in $\langle m|$ is the complex conjugate of the corresponding element in $|m\rangle$. The product in Eq.(5) is a scalar product, which is zero unless $m = n$. So the set $|n\rangle$ may be viewed as a set of mutually orthogonal unit vectors from which one can construct any general vector within the space defined by the set, although here we are not restricted to the usual three dimensions of conventional configuration space. These vectors can in principle be of infinite dimensions, but in actual calculations it is possible to use finite dimensions because of the existence of certain constraints on the size of n [7].

The results above provide a natural mathematical framework for modelling a system that contains n items. It allows us to increase or decrease the population of such a system with the aid of creation and annihilation operators. This leads to the possibility of modelling the discrete population dynamics of such systems, as will be demonstrated shortly. However, before we look at dynamics we can generalise the results of this section to multi-category systems.

2.3 Populating a multi-category system: Occupation number formalism

In this section we describe briefly how the algebra of creation and annihilation operators may be generalised to deal with a system of individuals (or items) that can be placed in different and distinguishable categories. To do this, we ascribe to the i^{th} category a pair of operators, \hat{a}_i and \hat{a}_i^\dagger , whose properties are defined by

$$[\hat{a}_i, \hat{a}_j] = [\hat{a}_i^\dagger, \hat{a}_j^\dagger] = 0.$$

and

$$[\hat{a}_i, \hat{a}_j^\dagger] = \hat{I}\delta_{ij}. \quad (6)$$

Eqs.(6) are a generalisation of Eq.(3). They indicate that all of the operators involved commute with one another when the subscripts differ. If the subscripts are identical then only the creation-annihilation pair with the same

subscripts do not commute. We can generalise Eq.(4) by applying the set of creation operators, \hat{a}_i^\dagger , to the empty state, $|0\rangle$. Then we can generate a state of the system in which the i^{th} category contains n_i individuals by

$$|\{n_i\}\rangle = \prod_i \frac{\hat{a}_i^{\dagger n_i}}{\sqrt{n_i!}} |0\rangle, \quad (7)$$

where $\{n_i\}$ is a shorthand way of representing a system that can be subdivided into a set of categories with n_i individuals in the i^{th} category. The simplest and in many ways the most natural way to represent such a system is by using the occupation number notation for the states. This notation is taken from the quantum field theory of many-body systems that is widely used in condensed matter physics and quantum optics. Then the state, $|\{n_i\}\rangle$, of a system is represented by

$$|\{n_i\}\rangle = |n_1, n_2, n_3, \dots, n_i, \dots\rangle. \quad (8)$$

In this case, the value of i runs from 1, through adjacent counting numbers, up to the number of categories, which is always finite. By analogy with Eq.(5) we can define an orthogonality condition for the state $|\{n_i\}\rangle$

$$\langle\{m_i\}|\{n_i\}\rangle = \prod_i \delta_{m_i n_i}. \quad (9)$$

Operating with the annihilation operator, \hat{a}_i on the state $|\{n_i\}\rangle$, and with its adjoint, \hat{a}_i^\dagger on $|\{n_i\}\rangle$, results in

$$\begin{aligned} \hat{a}_i |\{n_i\}\rangle &= \sqrt{n_i} |n_1, n_2, n_3, \dots, n_i - 1, \dots\rangle, \\ \hat{a}_i^\dagger |\{n_i\}\rangle &= \sqrt{n_i + 1} |n_1, n_2, n_3, \dots, n_i + 1, \dots\rangle. \end{aligned} \quad (10)$$

Thus, \hat{a}_i reduces the number of items in the i^{th} category by 1, and correspondingly, \hat{a}_i^\dagger increases it by 1. It is straightforward to check that

$$\hat{a}_i^\dagger \hat{a}_i |\{n_i\}\rangle = n_i |n_1, n_2, n_3, \dots, n_i, \dots\rangle \quad (11)$$

and hence that $\hat{a}_i^\dagger \hat{a}_i = \hat{n}_i$ is the number operator for the i^{th} category. The states and operators of multi-category systems can be represented in matrix form. These are rather complicated to specify in general. However, the methods of calculation we adopt below do not depend on this representation so we leave the interested reader to consult Bagarello [7] for details.

An important use of the creation and annihilation operators, in multi-category systems, is to move items from one category to another. For example

$$\hat{a}_i^\dagger \hat{a}_j |n_1, \dots, n_i, \dots, n_j, \dots\rangle = \sqrt{(n_i + 1)n_j} |n_1, \dots, n_i + 1, \dots, n_j - 1, \dots\rangle, \quad (12)$$

so the operator combination $\hat{a}_i^\dagger \hat{a}_j$ takes an item from the j^{th} category and puts it in the i^{th} category. In physics this operator combination is a scattering operator that can be associated with a scattering potential that takes a particle from one energy state to another[15]. The use of this interchange property will be applied to some simple cases in section 3. First we need to outline how time dependence is treated.

2.4 Representing time dependence and dynamics

In physical systems, time dependence is associated with a Hamiltonian. In classical systems this is a scalar function of certain systems parameters, such as position and momentum. In quantum systems the Hamiltonian is an operator. In physics the Hamiltonian has the dimensions of energy, however, as Planck showed, energy is just the Planck constant times a frequency. Consequently, the Hamiltonian operator divided by the Planck constant is a frequency that we can associate with the derivative with respect to time. In macroscopic systems of populations that we will treat later we will not be interested in energy but only in the frequency and a rate of change with respect to time, so we can do without the Planck constant. In the Heisenberg representation which is used in many-body physics and quantum optics, and which will be used in what follows, operators are time dependent and the states are considered as time independent. In terms of angular frequency operator $\hat{\Omega}$, a time dependent operator, $\hat{Q}(t)$ in Heisenberg form is defined by[13]

$$\hat{Q}(t) = \exp(it\hat{\Omega})\hat{Q}(0)\exp(-it\hat{\Omega}), \quad (13)$$

where t is time and $\hat{Q}(0)$ represents the operator at some arbitrary initial time, and is assumed not to be explicitly time dependent. Explicit differentiation of $\hat{Q}(t)$ then yields

$$i\frac{d\hat{Q}}{dt} = [\hat{Q}, \hat{\Omega}]. \quad (14)$$

The Heisenberg construction relies on $\hat{\Omega}$ being self-adjoint, i.e. $\hat{\Omega}^\dagger = \hat{\Omega}$. For physicists, multiplying $\hat{\Omega}$ by the reduced Planck constant, \hbar , gives the Hamiltonian of the system and the requirement for the Hamiltonian to be self-adjoint ensures that energy eigenvalues are always real. However, even though we do not need \hbar when dealing with populations in macroscopic systems like those involving predators and prey, we can still regard $\hat{\Omega}$ as a Hamiltonian and then \hbar simply plays the role of a conversion factor between energy and frequency units. So, we will refer to $\hat{\Omega}$ as the Hamiltonian of a system in what follows. Also, Eq.(14) will be referred to as the Heisenberg

equation. It is assumed in what follows that any time dependent operator will have the Heisenberg form and thus its time derivative may be obtained with the aid of the Heisenberg equation.

The key point here is that the dynamics of a system is controlled by its Hamiltonian. Once the Hamiltonian of a system is known, then its dynamics can be investigated by calculating the time derivatives of any operators that are relevant to that system, by using Eq.(14). It is a matter of choosing an appropriate Hamiltonian to suit the situation under investigation. This is as much true of physical quantum systems as it is of populations one meets in ecology, social science and economics.

Often considerations of symmetry play a key role in selecting an appropriate Hamiltonian. For example, for an isolated population that is not subject to any external influences, then one might expect a population not to change with time. Such a situation is the case for a simple system with just one category that is well described by the number operator, \hat{n} , and the state, $|n\rangle$. Eq.(14) tells us that if an operator commutes with $\hat{\Omega}$, then its time derivative is zero and it is a constant of the motion. Such constants play a key role in deciding what parameters of a system are the important ones. In the case of our simple isolated single category population we should expect its population to be invariant and so the number operator for such a system would be expected to commute with the system Hamiltonian. Then, as we have seen, its time derivative would be zero. In this case, the simplest Hamiltonian that commutes with \hat{n} is \hat{n} itself, or at least one that is proportional to it. So, following Bagarello[7], we can choose $\hat{\Omega} = \omega\hat{n}$, where ω is a scalar constant angular frequency. These are appropriate units for the constant since the population number is dimensionless and our Hamiltonian also has the dimensions of an angular frequency. Then, we clearly have $[\hat{n}, \hat{\Omega}] = \omega[\hat{n}, \hat{n}] = 0$.⁸ This result, together with the Heisenberg equation, confirms that the time derivative of \hat{n} is zero.

It is also interesting to look at the time derivative of the creation and annihilation operators in this simple case. Thus,

$$i\frac{d\hat{a}}{dt} = \omega[\hat{a}, \hat{a}^\dagger\hat{a}] = \omega\hat{a}, \quad (15)$$

where the RHS of Eq.(15) is obtained with the aid of the expansion, $[\hat{A}, \hat{B}\hat{C}] = \hat{B}[\hat{A}, \hat{C}] + [\hat{A}, \hat{B}]\hat{C}$. The solution to the differential equation, Eq.(15) is just $\hat{a}(t) = \hat{a}(0)\exp(-i\omega t)$. Actually this result is no surprise. It represents a harmonic oscillator and indeed the Hamiltonian $\hat{\Omega} = \omega\hat{n}$ is the Hamiltonian of a quantum harmonic oscillator, within an additive constant that

⁸Notice that scalars commute with operators so ω can be factorized out of the commutator bracket.

does not affect the result[12]. Applying the Heisenberg equation to \hat{a}^\dagger yields $\hat{a}^\dagger(t) = \hat{a}^\dagger(0) \exp(i\omega t)$. Then it is clear that $\hat{a}^\dagger(t)\hat{a}(t) = \hat{a}^\dagger(0)\hat{a}(0)$, which again shows the invariance of \hat{n} in this case.

3 How interaction is modelled: The example of a two-category system

3.1 Interaction between a pair of categories

Consider a system with a pair of categories with number operators

$$\hat{N} = \hat{n} + \hat{m}, \quad (16)$$

where, $\hat{a}^\dagger\hat{a} = \hat{n}$ and $\hat{b}^\dagger\hat{b} = \hat{m}$, and \hat{N} represents the population of the whole system of the two categories. We will initially, at least, regard these two categories as being isolated from one another. Then, by analogy with the single isolated category treated in section 2.4, it is reasonable to assume that \hat{n} and \hat{m} will individually remain constant since they undergo no interactions, and that the Hamiltonian for the whole system will take the form[7]

$$\hat{\Omega} = \omega_a \hat{a}^\dagger \hat{a} + \omega_b \hat{b}^\dagger \hat{b}, \quad (17)$$

where ω_a and ω_b are constant scalar frequencies. The appropriate commutation relations are $[\hat{a}, \hat{a}^\dagger] = 1$ and $[\hat{b}, \hat{b}^\dagger] = 1$, with all other operator pair combinations in commutation brackets being zero. Then both \hat{n} and \hat{m} individually commute with $\hat{\Omega}$, so using the above Hamiltonian in the Heisenberg equation will confirm that the individual populations will be constant in time. We can also use the Heisenberg equation to show that $\hat{a}(t) = \hat{a}(0) \exp(-i\omega_a t)$ and $\hat{b}(t) = \hat{b}(0) \exp(-i\omega_b t)$. The state of the system may be specified in the occupation number notation, already mentioned in section 2.3, by $|\Psi_N\rangle = |n, m\rangle$.

However, the representation of the system in terms of \hat{a} and \hat{b} is not unique. We can linearly transform these two operators into a new pair, \hat{c} and \hat{d} , by

$$\begin{pmatrix} \hat{c} \\ \hat{d} \end{pmatrix} = \begin{pmatrix} \epsilon & \eta \\ \lambda & \mu \end{pmatrix} \begin{pmatrix} \hat{a} \\ \hat{b} \end{pmatrix}, \quad (18)$$

where ϵ , η , λ and μ are constant coefficients. Then it is straightforward to show that, $[\hat{c}, \hat{c}^\dagger] = \epsilon^2 + \eta^2$, $[\hat{d}, \hat{d}^\dagger] = \lambda^2 + \mu^2$ and $[\hat{c}, \hat{d}^\dagger] = \epsilon\lambda + \eta\mu$. At this stage the constants are arbitrary. With an appropriate choice of the constants, we can make, $[\hat{c}, \hat{c}^\dagger] = 1$, $[\hat{d}, \hat{d}^\dagger] = 1$ and $[\hat{c}, \hat{d}^\dagger] = 0$, so that \hat{c} and \hat{d} act as annihilation operators and their respective adjoints as creation operators,

obeying rules like those in Eq.(6). This requires⁹

$$\begin{pmatrix} \epsilon & \eta \\ \lambda & \mu \end{pmatrix} = \begin{pmatrix} \cos \alpha & \sin \alpha \\ -\sin \alpha & \cos \alpha \end{pmatrix}. \quad (19)$$

It also follows that, $\hat{c}^\dagger \hat{c} = \hat{a}^\dagger \hat{a} \cos^2 \alpha + \hat{b}^\dagger \hat{b} \sin^2 \alpha + (\hat{a}^\dagger \hat{b} + \hat{b}^\dagger \hat{a}) \cos \alpha \sin \alpha$ and $\hat{d}^\dagger \hat{d} = \hat{a}^\dagger \hat{a} \sin^2 \alpha + \hat{b}^\dagger \hat{b} \cos^2 \alpha - (\hat{a}^\dagger \hat{b} + \hat{b}^\dagger \hat{a}) \cos \alpha \sin \alpha$. Then¹⁰

$$\hat{N} = \hat{a}^\dagger \hat{a} + \hat{b}^\dagger \hat{b} = \hat{c}^\dagger \hat{c} + \hat{d}^\dagger \hat{d} \quad (20)$$

and we can represent the system by two new categories with population numbers, $\hat{c}^\dagger \hat{c} = \hat{p}$ and $\hat{d}^\dagger \hat{d} = \hat{q}$. However, the Hamiltonian now has the form

$$\hat{\Omega} = \omega_c \hat{c}^\dagger \hat{c} + \omega_d \hat{d}^\dagger \hat{d} + v_{cd}(\hat{c}^\dagger \hat{d} + \hat{d}^\dagger \hat{c}), \quad (21)$$

where, $\omega_c = \omega_a \cos^2 \alpha + \omega_b \sin^2 \alpha$, $\omega_d = \omega_b \cos^2 \alpha + \omega_a \sin^2 \alpha$, and $v_{cd} = (\omega_b - \omega_a) \cos \alpha \sin \alpha$. Now $\hat{\Omega}$ represents the interaction between two populations that are represented by the number operators, \hat{p} and \hat{q} , with an interaction term, $v_{cd}(\hat{c}^\dagger \hat{d} + \hat{d}^\dagger \hat{c})$. Notice that $\hat{\Omega}$ in the form it has in Eq.(21) is still self-adjoint, as it needs to be, since $(\hat{c}^\dagger \hat{d})^\dagger = \hat{d}^\dagger \hat{c}$, ensuring that $\hat{\Omega}^\dagger = \hat{\Omega}$. Eq.(21) is well-known in quantum many-body theory as the simplest type of system in which scattering of particles is included[15]. It has been used extensively by Bagarello and co-workers in a number of social science contexts [7, 16, 17].

Next we want to show that Eq.(21) represents interaction between categories. To understand how this comes about, we first note that neither of the category number operators, \hat{p} and \hat{q} , commutes with $\hat{\Omega}$ and so have non-zero time derivatives. Now consider the first two terms in the Hamiltonian in Eq.(21) together as $\hat{\Omega}_0 = \omega_c \hat{c}^\dagger \hat{c} + \omega_d \hat{d}^\dagger \hat{d}$, and note that both \hat{p} and \hat{q} commute with $\hat{\Omega}_0$. Thus if v_{cd} were zero, then both category populations would individually remain zero. It is the presence of what we shall call the interaction Hamiltonian, $\hat{\Omega}_I = v_{cd}(\hat{c}^\dagger \hat{d} + \hat{d}^\dagger \hat{c})$, that causes the time variations in the category populations. Indeed, using the Heisenberg equation we find

$$i \frac{d\hat{p}}{dt} = [\hat{p}, \hat{\Omega}] = v_{cd}(\hat{c}^\dagger \hat{d} - \hat{d}^\dagger \hat{c}) \quad (22)$$

and

$$i \frac{d\hat{q}}{dt} = [\hat{q}, \hat{\Omega}] = -v_{cd}(\hat{c}^\dagger \hat{d} - \hat{d}^\dagger \hat{c}), \quad (23)$$

from which we find $\frac{d(\hat{p}+\hat{q})}{dt} = 0$. So, although \hat{p} and \hat{q} vary individually, the total population does not change with time, as indicated by Eq.(20).

⁹We can recognise the matrix on the RHS of Eq.(19) as a rotation through an angle α .

¹⁰This result, though quite remarkable, is not surprising since it is a form of the well known Bogoliubov transformation that is widely used in many-body quantum physics [15].

It is instructive at this point to note that the eigenstates of $\hat{\Omega}_0$ are simply

$$|\Phi_N\rangle = |p, q\rangle. \quad (24)$$

where $\hat{p}|p, q\rangle = p|p, q\rangle$ and $\hat{c}|p, q\rangle = \sqrt{p}|p-1, q\rangle$, etc. and where the p and q are eigenvalues of \hat{p} and \hat{q} , respectively. Both p and q are natural numbers. Indeed the system, $\hat{\Omega}_0$, \hat{p} , \hat{q} , \hat{c} , \hat{d} and $|p, q\rangle$ behaves in exactly the same way as $\hat{\Omega}$ in Eq.(17) with \hat{n} , \hat{m} , \hat{a} , \hat{b} and $|n, m\rangle$. However, as we have seen, $\hat{\Omega}_I$ introduces a new element into the $|p, q\rangle$, namely the time dependence of \hat{p} and \hat{q} in Eqs. (22) and (23). We can now see in detail what $\hat{\Omega}_I$ does to $|p, q\rangle$ by noting that

$$\hat{c}^\dagger \hat{d}|p, q\rangle = \sqrt{(p+1)q}|p+1, q-1\rangle. \quad (25)$$

This is an example of the interchange property noted in Eq.(12). So, the operator combination $\hat{c}^\dagger \hat{d}$ increases by one the population of the category associated with \hat{p} and decreases by one that associated with \hat{q} . $\hat{d}^\dagger \hat{c}$ does the opposite. Since $\hat{\Omega}$ governs the time dependence of the system, a time dependent rise and fall in the populations results. We take this variation in the two populations as indicative of interaction between them, brought about by the non-zero $\hat{\Omega}_I$. We can calculate these population dynamics in the following way.

If we substitute the result from Eq.(22) back into the Heisenberg equation we get, after some manipulation

$$\frac{d^2 \hat{p}}{dt^2} + \omega^2 \hat{p} = \hat{\Omega}(\omega_c - \omega_d) + \hat{N}(2v_{cd}^2 - \omega_d(\omega_c - \omega_d)), \quad (26)$$

where $\omega^2 = (\omega_c - \omega_d)^2 + 4v_{cd}^2$, and where we have used $v_{cd}(\hat{c}^\dagger \hat{d} + \hat{d}^\dagger \hat{c}) = \hat{\Omega} - (\omega_c \hat{p} + \omega_d \hat{q})$ and $\hat{q} = \hat{N} - \hat{p}$. Eq.(26) is in closed form since both $\hat{\Omega}$ and \hat{N} commute with $\hat{\Omega}$ and are thus independent of time. Even so, we need to bear in mind that Eq. (26) involves operators. What we want is actual population values. To calculate these, in this case, the expectation value, $\langle \hat{p} \rangle$, of the operator \hat{p} , i.e., $\langle p, q | \hat{p} | p, q \rangle$, needs to be evaluated. However, recall that \hat{p} is in Heisenberg form and is time dependent, while, in Heisenberg form, the state $|p, q\rangle$ is time independent and so the values of p and q need to be chosen at some instant and fixed. It is convenient to pick $t = 0$, so let us write the state as $|p(0), q(0)\rangle$. Notice also that since $|p(0), q(0)\rangle$ is independent of time, then

$$\frac{d\langle \hat{p} \rangle}{dt} = \frac{d\langle p(0), q(0) | \hat{p} | p(0), q(0) \rangle}{dt} = \langle p(0), q(0) | \frac{d\hat{p}}{dt} | p(0), q(0) \rangle, \quad (27)$$

which means that the expectation value of a derivative is the same as the derivative of the expectation value. This result clearly then applies to higher

order derivatives. So, following Bagarello [7], we define the scalar function representing the time dependent expectation value of a category population, $p(t) = \langle p(0), q(0) | \hat{p} | p(0), q(0) \rangle$, and obtain

$$\frac{d^2 p(t)}{dt^2} + \omega^2 p(t) = (\omega_c - \omega_d)^2 p(0) + 2v_{cd}^2 (p(0) + q(0)). \quad (28)$$

Notice that this is a linear equation for $p(t)$, just as Eq.(26) is a linear equation for $\hat{p}(t)$. Also, Eqs.(26) and (28) are identical in form. We should stress that the development of the analysis from Eq.(26) to Eq.(28) is only possible because of the linear nature of the operators involved.

In solving the simple linear second order differential equation, Eq.(28), there are two initial values to consider. The first is obvious, $p(t) = p(0)$ at $t = 0$. The second, involving the value of $\frac{dp(t)}{dt}$ at $t = 0$ is obtained from Eq.(22) which shows that this derivative is zero at the origin, since $\langle p(0), q(0) | (\hat{c}^\dagger(0)\hat{d}(0) - \hat{d}^\dagger(0)\hat{c}(0)) | p(0), q(0) \rangle = 0$. Then the solution to Eq.(28) is

$$p(t) = \frac{\omega^2 p(0) - 2v_{cd}^2 (p(0) - q(0)) (1 - \cos(\omega t))}{\omega^2} \quad (29)$$

and $q(t) = p(0) + q(0) - p(t)$. An example of the type of solution one obtains in this case is illustrated in Fig. 1. It is interesting to note that the population variations of the two categories in this closed system, where the sum of the two populations is invariant, take the form of a mean plus a sinusoidal variation about the mean. In the case of Eq.(29) the mean is

$$p(0) - \frac{2v_{cd}^2 (p(0) - q(0))}{(\omega_c - \omega_d)^2 + 4v_{cd}^2}$$

and the amplitude of the oscillation is

$$\frac{2v_{cd}^2 (p(0) - q(0))}{(\omega_c - \omega_d)^2 + 4v_{cd}^2},$$

from which we can see that the ratio of v_{cd}^2 to $(\omega_c - \omega_d)^2$ determines how big the fluctuation amplitude is. Thus, the bigger ω_c and ω_d are the smaller is the fluctuation response, so that these two frequencies in the Hamiltonian act like inertia, i.e., reluctance to change, whereas, v_{cd} drives change. However, we can also see that the fluctuations disappear if $p(0) = q(0)$, but the maximum amplitude for a given set of initial conditions occurs when $\omega_c = \omega_d$.

Other features of this simple operator model will be discussed in the next section when we compare it with a purely classical model. However, it is important to ask at this point, why should we want to turn the Hamiltonian in

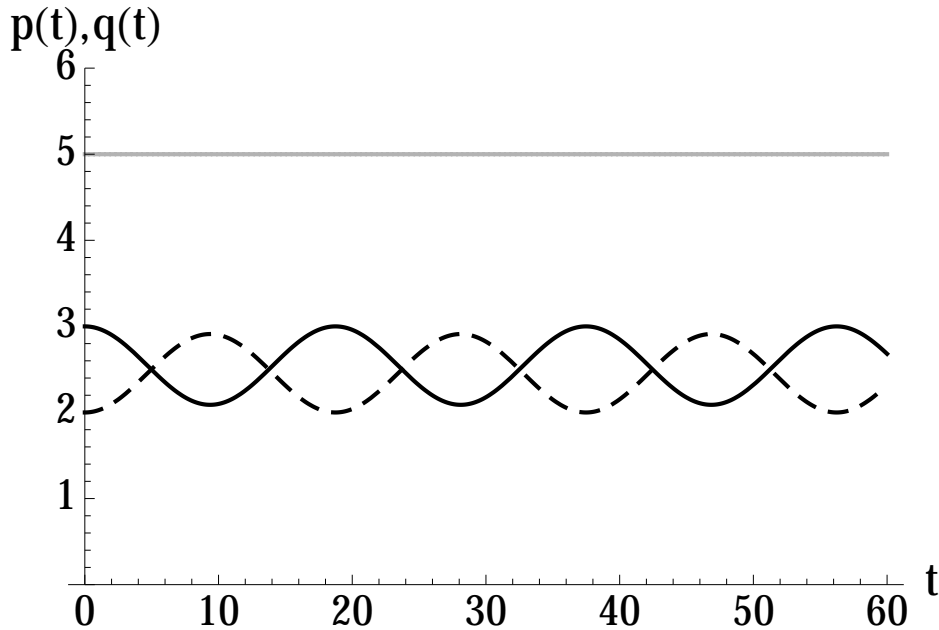


Figure 1: An example of the variation with time of the population values from Eq.(29), with $p(0) = 3$, $q(0) = 2$, $\omega_c = 0.2$, $\omega_d = 0.1$, and $v_{cd} = 0.16$.

its simple form, Eq.(17) into the obviously more complicated form in Eq.(21). It is simply that we could have started with Eq.(21) as a model of interacting categories, since we now know that is its role. That it is also equivalent to Eq.(17) then gives us the eigenfrequencies of the system, by effectively diagonalizing the matrix in Eq.(19). This is simply achieved by reversing the rotation brought about by the matrix in Eq.(19). The question then arises of how to interpret the two equivalent populations described by the states $|n, m\rangle$ and $|p, q\rangle$. In quantum physics this is no problem as compound combinations of particles arise in many situations, as for example in the BCS theory of superconductors, where Cooper pairs [18] of electrons play a key role. However, in a macroscopic world outside physics there are also instances of the simultaneous existence of both the interacting and non-interacting forms. Suppose, for example, $|n, m\rangle$ represents a group of two categories, n called male and m called female, that make up a total of $N = n + m$ people. We could divide that same group into p coffee drinkers and q tea drinkers, with $N = p + q$. The first description might then correspond to the Hamiltonian in Eq.(17), which would indicate the number of males and also the number of females does not change. On the other hand, the beverage preferences of the population could be modelled by the Hamiltonian

in Eq.(21). Then the preference for tea or coffee could be seen to fluctuate in a way that could depend on external factors like price or fashion.

The type of response we have found in the simple interaction model above, in which a fluctuation about a mean is observed is typical of even more complicated closed systems, as we shall see later. Indeed, the Hamiltonian, Eq.(21) and the time dependent population variations that it leads to serve as a blueprint for modelling interacting populations in a variety of situations, and it will be the basis for exploring interacting population models in what follows. In so doing, it is important to note that we must construct Hamiltonians that are self-adjoint, so that we can use the forgoing theory. In particular, the Heisenberg equation relies on the self-adjoint property of the Hamiltonian. This should really be seen as a mathematical rather than a physical requirement [19]. However, this necessity does raise some important issues that are relevant to more complicated applications that we will meet with later. In this regard, there is no problem with the simple examples we have treated so far. The $\hat{\Omega}_0$ part of the Hamiltonian in Eq.(21) is clearly self-adjoint, since the number operators are always self-adjoint. We can also see that the interaction part, $\hat{\Omega}_I$, in Eq.(21) is also self-adjoint, since $(\hat{c}^\dagger \hat{d})^\dagger = \hat{d}^\dagger \hat{c}$ and $(\hat{d}^\dagger \hat{c})^\dagger = \hat{c}^\dagger \hat{d}$, and both terms have the same coefficient v_{cd} , which can be taken as a real constant. This is the case because of the way we obtained Eq.(21) from Eq.(17), using the rotation in Eq.(19). We note that the value of v_{cd} is an indication of the rate of interchange between the populations. Had we started with Eq.(21) we would have had no *a priori* reason for assuming that the rate of interchange from one population to another was the same in both directions. It is not obvious that we could always assume this to be the case in *real* situations. So clearly we are dealing with an idealized case, where the interchange goes at the same rate in both directions. Bagarello [7] refers to this situation as the action and reaction of the interacting populations having the same strength. If we had say, $\hat{\Omega}_I = v_1 \hat{c}^\dagger \hat{d} + v_2 \hat{d}^\dagger \hat{c}$ and $v_1 \neq v_2$, then $\hat{\Omega}_I^\dagger \neq \hat{\Omega}_I$ and the problem is intractable with the mathematical formulation above. We could either leave it at that, in which case we are accepting that we can only deal with a very narrowly defined real problem in which $v_1 = v_2$, or we force our Hamiltonian to be self-adjoint by adding an adjoint term, $(v_1 \hat{c}^\dagger \hat{d} + v_2 \hat{d}^\dagger \hat{c})^\dagger$. Then we would get back to the $\hat{\Omega}_I$ in Eq.(21) if we set $v_1 + v_2 = v_{cd}$.

One way of viewing this is to note that $(v_1 \hat{c}^\dagger \hat{d} + v_2 \hat{d}^\dagger \hat{c})^\dagger$ is the time reversed version of $v_1 \hat{c}^\dagger \hat{d} + v_2 \hat{d}^\dagger \hat{c}$ [20]. So from a mechanistic point of view this means that we must always look for a reverse process that ensures forward rates match reverse rates. This does not mean that the nature of the forward and reverse mechanism need be the same, as long as they are mathematically equivalent. These considerations are involved in the applications we will be

dealing with later, in section 4.

3.2 Comparison with the classical approach

Here we briefly compare the operator calculation from the previous section with a classical model of population interaction in the form of the Lotka-Volterra predator-prey model. At their simplest, the Lotka-Volterra differential equations for the time dependence of a prey population, $x(t)$ and a predator population, $y(t)$, take the form

$$\begin{aligned}\frac{dx(t)}{dt} &= x(t)(f - gy(t)), \\ \frac{dy(t)}{dt} &= y(t)(-h + kx(t)),\end{aligned}\tag{30}$$

where f , g , h and k are constant parameters. The simple argument for this form of the equations is based on exponential growth and decay. It is assumed that the linear growth rate, f , of the prey population, which is the birth rate less a smaller death rate, is modified in the presence of the predator population, which increases the death rate in direct proportion to the predator population. On the other hand the birth rate of the predator population is increased in direct proportion to the prey population. It is well known that in a certain part of that parameter space, the populations are bound and cyclic. An example of this kind of solution, obtained numerically with the aid of Mathematica software, is shown in Fig. 2.

However, the oscillating nature of the solution is rather hidden within the nonlinear equations and in order to more easily compare this classical model with the quantum one, it is useful to look at a linearized perturbation solution to Eqs.(30) which exhibit this oscillatory nature more explicitly. To do this we expand each population to first order of smallness, with a small time-dependent part, plus a larger mean. Thus we assume that $x(t) = \bar{x} + \delta x(t)$ and $y(t) = \bar{y} + \delta y(t)$, where $\delta x(t)$ is assumed to always be smaller than \bar{x} etc. We now substitute these back into the original equations and separate them into the time dependent parts and also the time independent parts that contain only mean values. In the time dependent parts we also neglect any terms which contain products of small values like $\delta x(t)\delta y(t)$. Now the mean values from the time independent parts satisfy $\bar{x} = h/k$ and $\bar{y} = f/g$. Then the time dependent parts simplify to $\frac{d\delta x(t)}{dt} = -\frac{gh}{k}\delta y(t)$ and $\frac{d\delta y(t)}{dt} = \frac{fk}{g}\delta x(t)$, which lead to

$$\frac{d^2\delta x(t)}{dt^2} + fh\delta x(t) = \frac{d^2\delta y(t)}{dt^2} + fh\delta y(t) = 0.\tag{31}$$

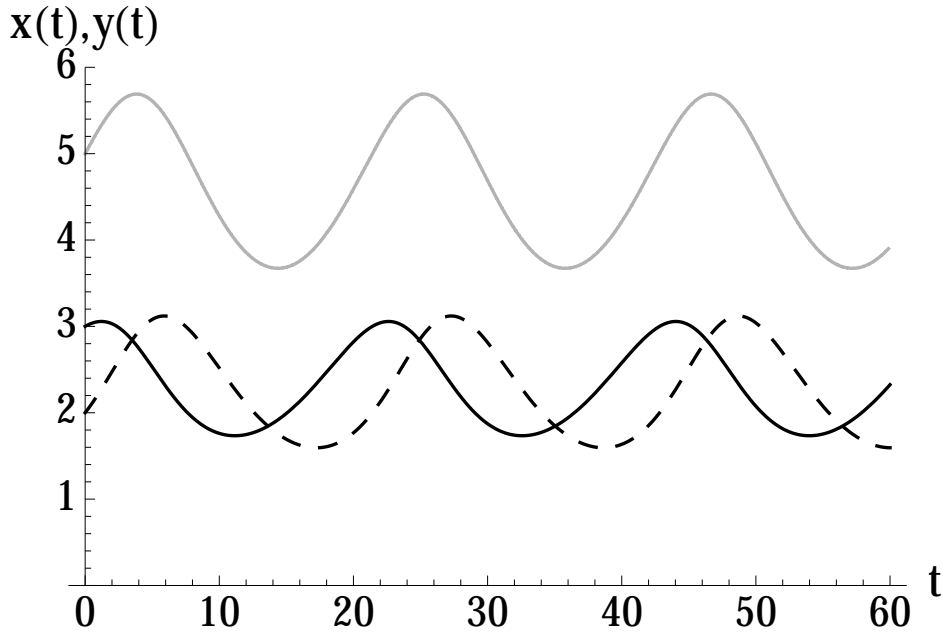


Figure 2: Variation of the prey (solid curve) and predator (dashed curve) populations. The sum of the two populations is indicated by the grey curve.

These two equations are those of sinusoidal oscillations of the same frequency, $\omega = \sqrt{fh}$. We can take the solutions of the form

$$\begin{aligned}
 x(t) &= \bar{x} + (x(0) - \bar{x}) \cos(\omega t) - (y(0) - \bar{y}) \frac{gh}{k\omega} \sin(\omega t), \\
 y(t) &= \bar{y} + (y(0) - \bar{y}) \cos(\omega t) + (x(0) - \bar{x}) \frac{fk}{g\omega} \sin(\omega t),
 \end{aligned} \tag{32}$$

where we have used the boundary conditions, $x(0) = \bar{x} + \delta x(0)$ and $\frac{d\delta x}{dt}|_{t=0} = \omega \delta x(0) = -\frac{gh}{k} \delta y(0)$, etc. The approximate perturbation solution for the example in Fig. 2 is shown in Fig. 3. The two results look quite similar, though the effect of the nonlinearity can be seen in the slight sharpening of the peaks and flattening of the troughs compared with the purely sinusoidal linear results. However, the amplitudes and the periodicity are well captured in the linear solution. As already observed, the error in the linear result is of order $\delta x(t)\delta y(t)$. In the case treated this is about 25 times smaller than $\bar{x}\bar{y}$, making the percentage error in each variable about 20%. However, we are not really interested here in the accuracy of this approximation, rather we are interested in revealing the periodic nature of the results.

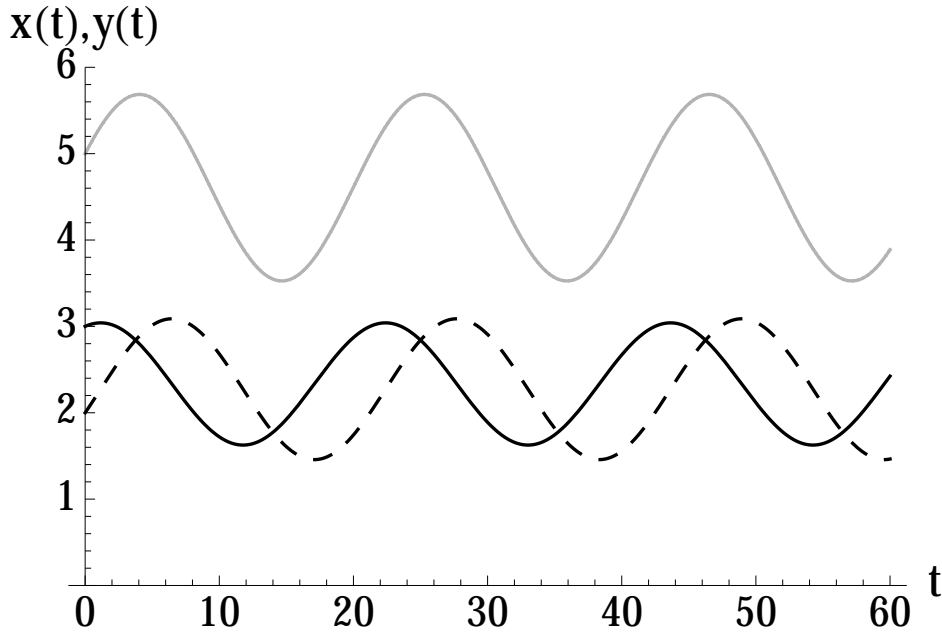


Figure 3: The perturbation solution for the example in Fig. 2.

We can compare the linearized solution of the Lotka-Volterra equations which take the form of sinusoidal oscillations about a mean more easily with the operator model of interaction from the previous section. That model can be applied to a variety of scenarios involving a pair of categories. Here the two categories are obviously a predator species and a prey species. In simple terms, the interaction part of the Hamiltonian in Eq.(21) is interpreted as meaning that an increase in the predator population (by one) is correlated with a decrease in the prey population (by one), and vice-versa. Clearly there are similarities in the predicted population statistics from the quantum and classical models. This is mainly due the fact that both yield exactly sinusoidal variations superimposed on a mean level. It is clearly possible to adjust the free parameters of the two approaches to get the frequencies to agree. However, it is not possible to adjust the parameters so that the amplitudes and mean levels also in general agree, nor should we expect them to do so. A more important issue is that of phase, which to a certain degree is associated with the conservation of total population that is such a clear and important feature of the quantum result. There, the fact that the two populations must add to a constant means that any variation in the population levels of individual species have to be in anti-phase. The fact that the classical results are not in anti-phase explains why these populations are not conserved in the

same way. Maybe a more critical point is that the quantum results indicate that, at $t = 0$ the phase of an individual population must produce a crest or a trough. This feature can be traced back to the fact that Eq.(29) only has a time-dependent cosine term and no sine term, unlike Eq.(32) which has both and hence at $t = 0$ the classical result can have any phase, depending on the parameters. In the quantum case this is due to the fact that the rates of change of the individual populations are zero at $t = 0$ for the situation treated. However, this does not have to be the case.

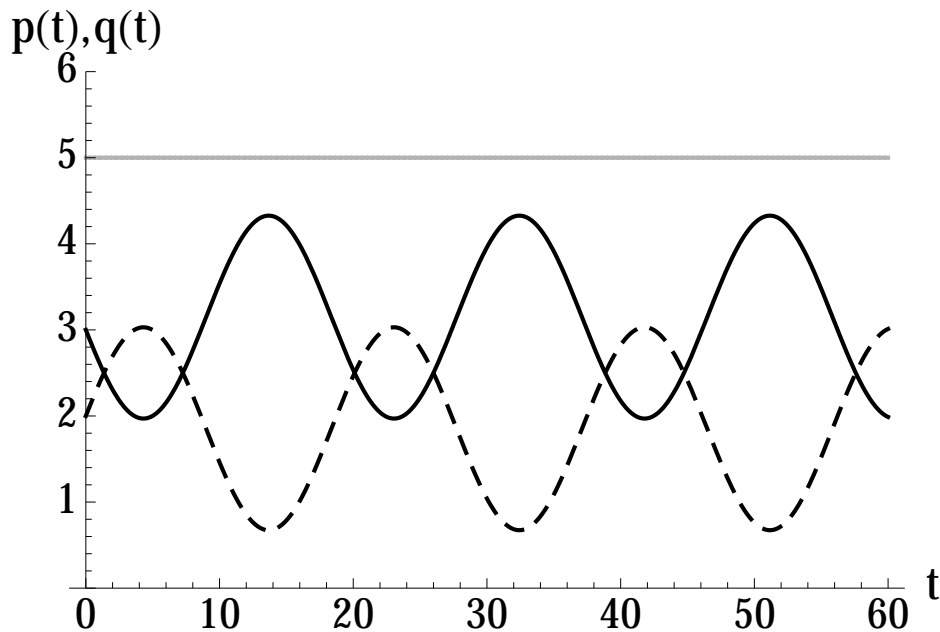


Figure 4: As Fig.1, but with coherent states at $t = 0$, with a phase separation of $\Delta = \pi/6$, between them.

This apparent limitation on the phase for the quantum case is entirely a consequence of assuming that the system is initially in an eigenstate of the number operators. In quantum mechanics this is not a necessary condition. Quantum systems can exist in so called *mixed states*, i.e., a system can be assigned a state that corresponds to a linear superposition of eigenstates [12, 13]. A particularly interesting state of this kind is the quantum *coherent state* [21, 22]. The coherent state acts rather like a classical system from a statistical point of view. It is a state in which there is a Poisson distribution of probabilities of the population having a particular natural number. From a quantum mechanical point of view its most important property is that it is an eigenstate of an annihilation operator, not a number operator (and hence

not of a creation operator either). In fact the expectation value of the number operator is the mean occupation number. These properties also mean that $\frac{dp(t)}{dt}$ and $\frac{dq(t)}{dt}$ are not zero at $t = 0$. Indeed, if the initial states of the two populations are coherent states, then the populations vary as

$$p(t) = \bar{p} + (p_0 - \bar{p}) \cos \omega t + \frac{2v_{cd}\sqrt{p_0q_0} \sin \Delta \sin \omega t}{\omega}, \quad (33)$$

where

$$\bar{p} = \frac{(\omega_c - \omega_d)^2 p_0 + 2v_{cd}((p_0 + q_0)v_{cd} + (\omega_c - \omega_d)\sqrt{p_0q_0} \cos \Delta)}{\omega^2} \quad (34)$$

and where p_0 and q_0 are the mean population values of the initial coherent states and Δ is the phase angle between the coherent states at $t = 0$. Notice that Eq.(33) contains both sine and cosine terms that are time dependent. An example of the quantum result for initial coherent states is shown in Fig. 4, where it is clear that the initial phases no longer need to correspond to peaks or troughs, nor are the oscillation amplitudes as restricted as those in Eq.(29).

3.3 Multiple category interactions

It is a straightforward matter to generalize the Hamiltonian for a pair of non-interacting categories in Eq.(17) to a system comprising multiple categories by using $\hat{\Omega} = \sum_i \omega_i \hat{a}_i^\dagger \hat{a}_i$. This can then be transformed into one describing interactions, by generalizing the transformation matrix in Eq.(19) to higher dimensions. Letting $\hat{a}_i = \sum_j \beta_{ij} \hat{b}_j$, then $\hat{\Omega}$ has the form

$$\hat{\Omega} = \sum_i \omega_i \hat{b}_i^\dagger \hat{b}_i + \sum_{jk} v_{jk} \hat{b}_j^\dagger \hat{b}_k, \quad (35)$$

where the sums are over the number of categories. This type of Hamiltonian has been used extensively by Bagarello [7, 16] to model stock market trading. As long as the matrix, β_{jk} , is unitary [13], as is the 2×2 matrix in Eq.(19), then \hat{b}_i and \hat{b}_i^\dagger take the form of annihilation and creation operators, respectively and obey commutation rules analogous to those of \hat{a}_i and \hat{a}_i^\dagger in Eq.(6). Then one also finds $\sum_i \hat{a}_i^\dagger \hat{a}_i = \sum_j \hat{b}_j^\dagger \hat{b}_j$, ensuring that in spite of exchange of population numbers between categories, the total population is fixed.

Models involving multiple category systems of this type have a variety of applications. For example, the categories may be several competing species in ecological environments [8] or in the case of the migration of a single species, then the different categories are spatially distributed cells [7] and

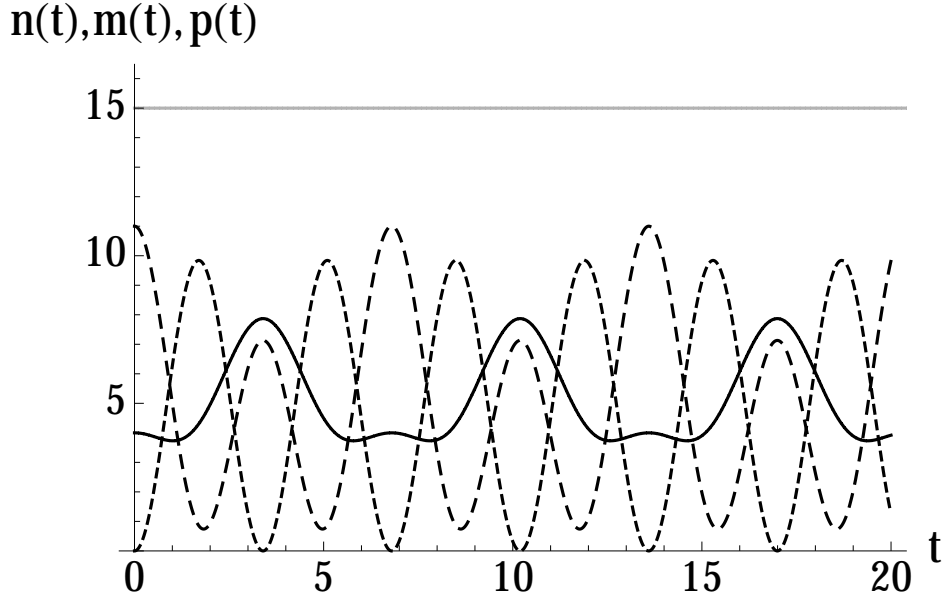


Figure 5: An example of interaction between three categories.

the number operators, $\hat{m}_i = \hat{b}_i^\dagger \hat{b}_i$, represent the population of a cell labelled, i . In this latter case, then the interaction coefficients v_{jk} represent the rate of population transport between cells and are only non-zero for neighbouring cells. This method is particularly apt for closed ecological systems since the total population remains fixed irrespective of how individual category populations might vary.

The method used to determine the time dependence of the population expectation values that was used in the case of two interacting species in the previous section, becomes unwieldy for more than three categories, as it requires a differential equation of order $N_c(N_c - 1)$, where N_c is the number of categories. So for two categories we need a second order equation, for three categories we need a sixth order and so on. A more efficient approach at higher category numbers involves using the Heisenberg equation to solve for the annihilation operators rather than the number operators. This produces a set of N_c linear coupled equations that are readily solved by matrix methods [7]. Fig. 5 illustrates the solution to a three category interaction, where, even at this modest level of complication, the increasing complexity of the response can be discerned, particularly in the solid curve which is no longer a pure sinusoid. With growing category numbers, the responses become increasingly like noisy fluctuations (see Bagarello [7] and references therein for numerous

examples of this type).

3.4 Higher order interactions

As pointed out by Bagarello and co-workers [7, 17] the interaction term in the Hamiltonian can be generalized to involve higher order contributions than the second order ones in the creation and annihilation operators, and this does not alter the basic dynamical framework. This means that the commutation relations in Eq.(6) still apply and the dynamical equations that result from the Heisenberg equation remain valid (also see [9]). An example of this higher order generalization may be found in the case of an interaction between a pair of categories, where the interaction Hamiltonian is given by

$$\hat{\Omega}_I = v_{ab}(\hat{a}^\dagger{}^P \hat{b}^\dagger{}^Q \hat{a}^R \hat{b}^S + \hat{b}^\dagger{}^S \hat{a}^\dagger{}^R \hat{b}^Q \hat{a}^P), \quad (36)$$

where P , Q , R and S are positive integers. The first thing to note about $\hat{\Omega}_I$ in Eq.(36) is that it is self-adjoint, as it needs to be if it is to be used in the Heisenberg equation. It represents asymmetrical competition between categories, since, if we operate on $|n, m\rangle$ with $\hat{a}^\dagger{}^P \hat{b}^\dagger{}^Q \hat{a}^R \hat{b}^S$, we get the state $|n + P - R, m + Q - S\rangle$, as long as $n - R \geq 0$ and $m - S \geq 0$. However, the total population, $N = n + m$ is no longer generally conserved. Instead, there is a new conservation rule,

$$\frac{d}{dt} \left(\frac{\hat{n}}{P - R} + \frac{\hat{m}}{S - Q} \right) = 0, \quad (37)$$

as long as both of the denominators in Eq.(37) are non-zero. Then, the total population is only constant if $P - R = S - Q$. This is a generalization of the interaction Hamiltonian that Bagarello and co-workers have used (there $Q = R = 0$) in a variety of social science contexts (see [7, 17]). We will also use a version of it in section 4.

Although the generalization to higher order interactions like those above adds versatility in terms of applications, there is quite a big price to pay in terms of the difficulty in solving the equations of motion, which are often highly nonlinear. The difficulty is moderated somewhat by the conserved quantities like those in Eq.(37). However, we can sometimes avoid these difficulties and use approximate methods that can give us enough information about the key characteristics of the system under investigation, as is the case with the novel approach to cell division dynamics which is outlined in the next section.

4 Cell division and cell population dynamics

4.1 A simplified picture of cell division

Our aim in this section is to show how, in an elementary way, the basic features of cell division can be captured using the creation and annihilation operator formalism as outlined above. The basic picture of cell division is simply that a single cell splits into two cells [23]. In splitting the cell first grows, but this is not an explicit part of the following schematic picture. In the operator picture we can describe this process as the disappearance of a single cell and the appearance of a pair of cells. We can associate the dividing cells with an annihilation operator \hat{c} , then the cell division can be represented by a factor in an interaction Hamiltonian of the form, $\hat{c}^\dagger \hat{c}^\dagger \hat{c}$.

This operator, operating on a state, $|n\rangle$, which is an eigenstate of $\hat{n} = \hat{c}^\dagger \hat{c}$, and which contains n cells, will subtract one and add two to the total of cells, thus having a net effect of adding one to the total. It may be thought the same result could be obtained simply by operating with \hat{c}^\dagger . This is not the case, for several reasons. One is that the coefficient multiplying the final state is different in the two cases and results in entirely different dynamics from the Hamiltonian. Further, using \hat{c}^\dagger does not mimic the cell division process accurately, since it implies a single cell appears where none existed (see Fig. 6 below). Below we extend this picture to include the presence of a population of m stimuli that trigger the cell division process. We will look at two different scenarios. In the first (Model A) the stimulus is exhausted in some way in the division process and in the second (Model B) we will assume that the stimulating agent acts as a true catalyst and although its presence is essential for triggering the cell division, it remains after cell division has taken place.

In many respects, these models reflect the differences between division of a normal cell population (Model A) and a cancer cell population (Model B). Stimulation of normal cell division depends on the presence of an extrinsic factor, such as a growth factor, which can be quickly diluted out or degraded thereby removing the stimulus. In contrast, stimulation of cancer cell division is driven by an intrinsic factor, such as an activated oncogene, which is regenerated upon DNA replication and passes from one generation to the next; hence it acts as a catalyst and is never lost [24, 25]. However, we should emphasize that the two models below are not intended to be exact, faithful replicas of all of the biochemical detail of cell division processes. Rather, they are an attempt to translate these processes, in schematic terms, into a form that is amenable to treatment by population operator methods, from which we can hope to reproduce the characteristics of the population dynamics that

result from the cell division process.

4.2 Model A: Expended stimuli

In this first model, Model A, we envisage that the stimulus whose presence is necessary to trigger cell division is exhausted in some way by its participation in the process. If the stimulating agent is associated with an annihilation

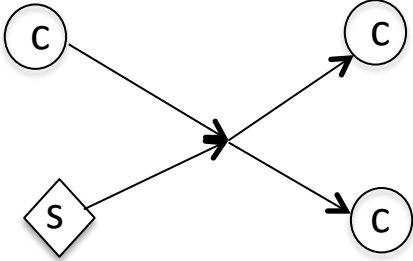


Figure 6: Schematic of cell division (Model A) in which a cell (c) and a stimulating agent (s) enter the process and two cells result.

operator, \hat{s} , then the combined contribution to the interaction Hamiltonian of the cell division and stimulus is $\hat{c}^\dagger \hat{c}^\dagger \hat{c} \hat{s}$. The cell division process described by this set of operators is shown schematically in Fig. 6. Note that the direction of the arrows in Fig. 6 give an indication of time evolution. Adding the time reversed form of this, to preserve the self-adjoint property, the interaction Hamiltonian is then

$$\hat{\Omega}_I = V(\hat{c}^\dagger \hat{c}^\dagger \hat{c} \hat{s} + \hat{s}^\dagger \hat{c}^\dagger \hat{c} \hat{c}), \quad (38)$$

where V is the cell division rate in the presence of the stimulus, and where $[\hat{c}, \hat{s}] = [\hat{c}^\dagger, \hat{s}] = 0$ and $[\hat{c}, \hat{c}^\dagger] = [\hat{s}, \hat{s}^\dagger] = 1$ apply. Notice that this is an example of the general form of interaction Hamiltonian in Eq.(36), with $P=2$, $Q=0$, $R=1$ and $S=1$. The resulting Hamiltonian for the whole process is then

$$\hat{\Omega} = U\hat{n} + W\hat{m} + V(\hat{c}^\dagger \hat{n} \hat{s} + \hat{s}^\dagger \hat{n} \hat{c}), \quad (39)$$

where $\hat{m} = \hat{s}^\dagger \hat{s}$, and U and W are the intrinsic rates associated with \hat{c} and \hat{s} , respectively, when there is no interaction. By intrinsic we mean that in the absence of any interaction, then we would find $\hat{c}(t) = \hat{c}(0) \exp(-iUt)$, and $\hat{s}(t) = \hat{s}(0) \exp(-iWt)$. The Hamiltonian in Eq. (39) is very similar to that used in quantum optics for modelling parametric amplifiers, where photon doubling is stimulated by a laser pump [26].

Before proceeding with the analysis of this system, we should give some explanation of the second, time-reversed, term in Eq.(38), in the light of the

comments on this issue made in section (3.1). It can be visualized as the situation in Fig. 6, but with the arrows reversed. So an initial state with two cells becomes a state with one cell and a stimulating agent. As pointed out in section (3.1), the reverse process does not have to involve the same mechanism as the forward process, as long as the rates involved are the same. Cell fusion, which may be regarded as a reverse mechanism to cell division does actually take place in certain circumstances, but it is not commonly observed. However, cell death does occur and is a balancing mechanism to population increases due to cell division.[23] So here we interpret the change from two cells to one as a simple proxy for the death of one cell. The appearance of one stimulating agent we interpret as a source term, which balances the sink of stimuli in the forward process. There is, of course, no substantial reason to suppose that cell death and the source for the stimulating agents are causally connected. Rather we should view the reverse process, here highly idealized, as a crude but convenient packaging of the two effects into a single hypothetical process that serves the overriding mathematical purpose.

Applying the Heisenberg equation to the population operators, we get

$$i \frac{d\hat{n}}{dt} = [\hat{n}, \hat{\Omega}] = V(\hat{c}^\dagger \hat{n} \hat{s} - \hat{s}^\dagger \hat{n} \hat{c}) \quad (40)$$

and

$$i \frac{d\hat{m}}{dt} = [\hat{m}, \hat{\Omega}] = -V(\hat{c}^\dagger \hat{n} \hat{s} - \hat{s}^\dagger \hat{n} \hat{c}) \quad (41)$$

from which it is clear that $\frac{d(\hat{n}+\hat{m})}{dt} = 0$, in agreement with Eq.(37). So, despite the more complicated form of the interaction, the combined populations of the dividing cells and the stimuli is fixed, and we can conclude that the cell population is bound. The state of the system is then one of quasi-equilibrium where the individual population numbers of the participating categories may fluctuate, but only in such a way as to maintain the total population. This is enough for us to know that no unbounded growth in the cell population can occur in this model. However, it is worth looking a little further into the character of the equilibrium. A further application of the Heisenberg equation to Eq.(40), together with the population conservation rule yields

$$\frac{d^2\hat{n}}{dt^2} + \omega^2\hat{n} - 6V^2(1 + N_0)\hat{n}^2 + 8V^2\hat{n}^3 = (U - W)(\hat{\Omega} + WN_0), \quad (42)$$

where $N_0 = n(0) + m(0)$ and $\omega^2 = (U - W)^2 + 2V^2(1 + N_0)$. The non-linear terms in the operator equation present considerable difficulties. The reason for the difficulty is that in general the expectation value of the operator squared (cubed) is not the same as the square (cube) of the expectation

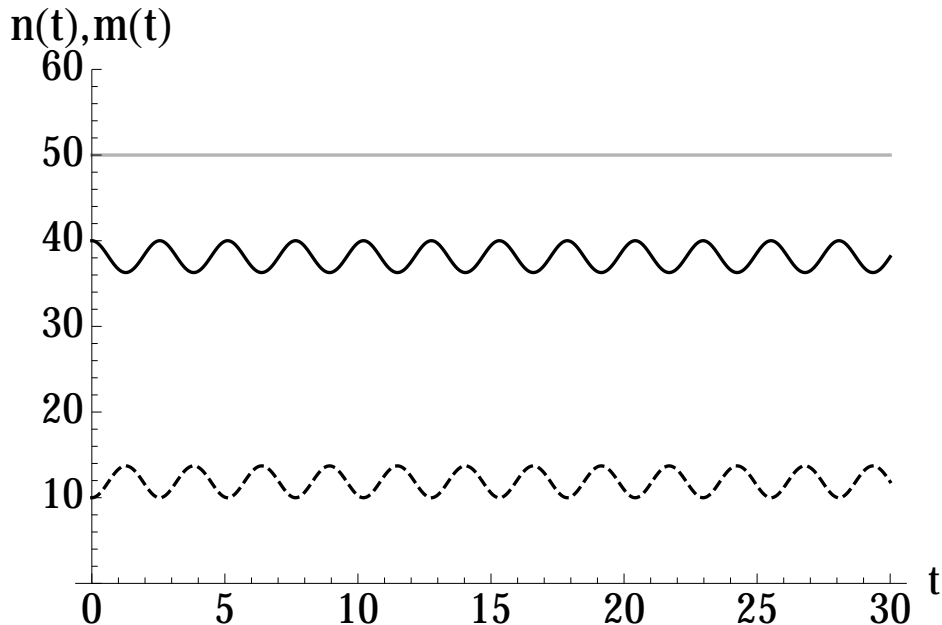


Figure 7: Approximate solution for Model A of cell and stimuli populations as functions of (scaled) time, by numerical integration of Eq.(43).

of the operator¹¹. This means that we cannot immediately obtain an equation in terms of the expectation values of the population number operators. However, we are not looking for detailed solutions to Eq.(42), rather we want to understand the type of solution we can get. We already know that the populations are bound by the initial conditions. We can obtain a useful and instructive solution by utilizing a semi-classical approximation [27, 28] widely used in quantum optics, where photon populations are under investigation. Then, employing what is referred to as a first level of approximation [27], operators are replaced by their time dependent expectation values. Thus Eq.(42) is transformed into

$$\frac{d^2 n(t)}{dt^2} + \omega^2 n(t) - 6V^2(1 + N_0)n(t)^2 + 8V^2 n(t)^3 = (U - W)^2 n(0), \quad (43)$$

where, $n(t) = \langle \hat{n} \rangle$. The first level of approximation here means we use $\langle \hat{n}^2 \rangle = \langle \hat{n} \rangle^2$. This means that we are neglecting the variance, $\langle \hat{n}^2 \rangle - \langle \hat{n} \rangle^2 = \Delta n^2$,

¹¹This is rather like the inequality between squares of means and means of squares in ordinary statistics.

which is a measure of quantum noise¹²[29]. This arises from non-diagonal terms that come from unpaired creation or annihilation operators in $\hat{\Omega}_I$. We will briefly look at the size of this effect later after we have explored Model B.

The great advantage of this approximation is obvious. It means we can use ordinary scalar methods to solve the nonlinear equation. An example of the numerical integration of Eq.(43) is shown in Fig. 7. The result shows a fluctuating pair of populations, with something very close to sinusoidal form on constant means, rather like the linear cases in section 3. However, it is interesting to note, that, unlike in the linear cases, the fluctuation amplitudes here are not very sensitive to the interaction rate, V . There is actually greater sensitivity to the ratio of $n(0)$ to N_0 .

The semi-classical approximation can further be refined by adopting a technique involving numerical stochastic integration via the Fokker-Planck equation [27]. However, the first level approximation has proven to be in reasonable qualitative agreement with the more refined approach. There has also been work in support of the semi-classical method that is based on the use of complex coordinates [30, 31] to replace the creation and annihilation operators in Hamiltonians, like that in Eq.(39). Then Poisson brackets can be used instead of the Heisenberg equation. In this bound population case, the matrix methods used by Bagarello and co-workers [7] can also be utilized.

4.3 Model B: Catalytic stimuli

In the second model, Model B, the division process is as before, but here the stimulus is a catalyst and so needs to be involved in such a way that it survives division process. This is achieved by using the form $\hat{c}^\dagger \hat{c}^\dagger \hat{s}^\dagger \hat{c} \hat{s}$ in the interaction term in the Hamiltonian, which then has the self-adjoint form

$$\hat{\Omega}_I = V(\hat{c}^\dagger \hat{c}^\dagger \hat{s}^\dagger \hat{c} \hat{s} + \hat{s}^\dagger \hat{c}^\dagger \hat{s} \hat{c} \hat{c}). \quad (44)$$

This is again of the form in Eq.(36), but here, $P = 2, Q = 1, R = 1$ and $S = 1$. Since $R = S$ here, then there is no conserved quantity involving just population numbers¹³. The cell division process corresponding to the interaction Hamiltonian is shown in Fig. 8. The total Hamiltonian of the system is then

$$\hat{\Omega} = U\hat{n} + W\hat{m} + V\hat{m}(\hat{c}^\dagger \hat{n} + \hat{n} \hat{c}). \quad (45)$$

We can interpret the time reversed term in Eq.(45) in a similar manner to that for Model A, i.e., the change from two cells to one is a representation

¹² Δn^2 must be non-negative, since $\langle \hat{n}^2 \rangle \geq \langle \hat{n} \rangle^2$, by the Schwarz inequality.

¹³The Hamiltonian itself is still, of course, a system constant

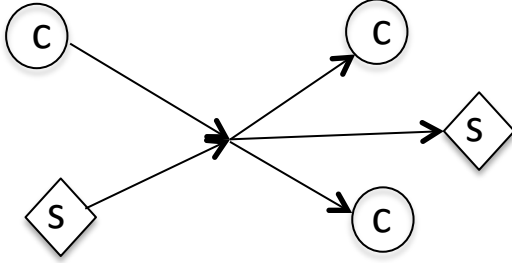


Figure 8: Schematic of cell division (Model B) in which a cell (c) and a stimulating agent (s) enter the process and two cells result, but now the stimulating agent survives the process.

of cell death. Since, in Model B there is no loss of the stimulus, the reverse process needs no further explanation.

Since \hat{m} now commutes with $\hat{\Omega}$, we can conclude that the population of stimuli is conserved in the cell division process in Model B. From now on it can be taken as a fixed number, m , since $|n, m\rangle$ will remain in the same eigenstate of \hat{m} for all time. However, \hat{n} will be time dependent, since

$$i \frac{d\hat{n}}{dt} = [\hat{n}, \hat{\Omega}] = Vm(\hat{c}^\dagger \hat{n} - \hat{n} \hat{c}) \quad (46)$$

and then

$$\frac{d^2\hat{n}}{dt^2} + \omega^2 \hat{n} - 6V^2 m^2 \hat{n}^2 = U\hat{\Omega}, \quad (47)$$

where $\omega^2 = U^2 + 2V^2 m^2$. As with Model A, here again we end up with a nonlinear equation for \hat{n} , with its corresponding difficulties, but again we can make good progress by using the semi-classical approach and get

$$\frac{d^2 n(t)}{dt^2} + \omega^2 n(t) - 6V^2 m^2 n(t)^2 = U^2 n(0). \quad (48)$$

The solutions to Eq.(48) are very different from those for Model A, as we shall see. The key features of $n(t)$ in Model B depend, essentially, on the parameter combination $\frac{m^2 V^2 n(0)}{U^2}$. The importance of this factor can be seen by scaling $t \rightarrow Ut$ and $n \rightarrow \frac{n}{n(0)}$. Then the nonlinear term in Eq.(48), becomes $6V^2 m^2 n(t)^2 \rightarrow \frac{m^2 V^2 n(0)}{U^2} \left(\frac{n}{n(0)}\right)^2$. Thus the scaling factor is a measure of the strength of the nonlinearity of the system. It is also a measure of

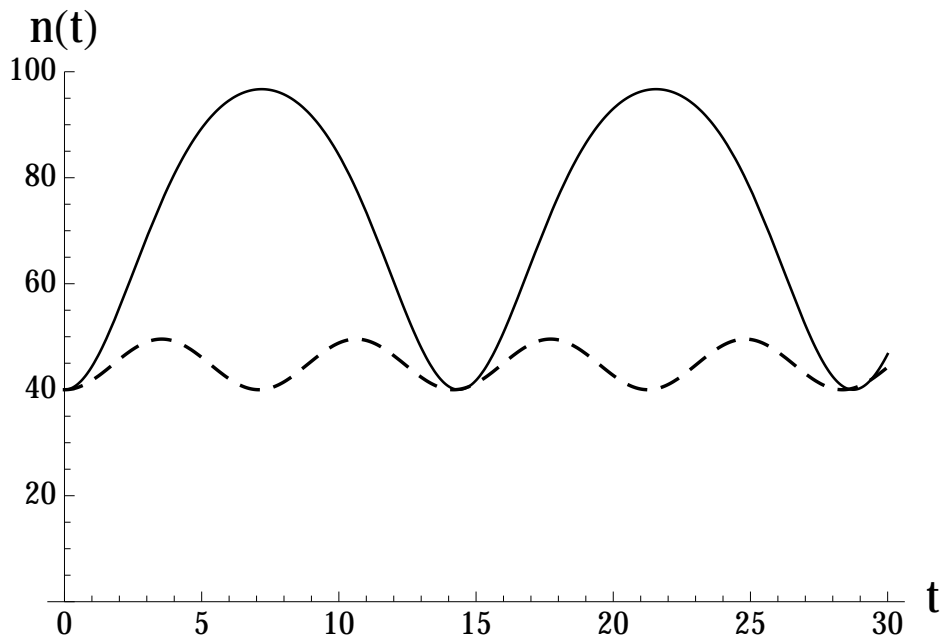


Figure 9: Semi-classical solutions for dividing cell population as a function of (scaled) time for Model B. For the solid curve, $\frac{mV}{U} = 0.31$ and for the dashed curve, $\frac{mV}{U} = 0.2$.

the quantum noise, as we shall see later. When $\frac{m^2V^2n(0)}{U^2}$ is small, $n(t)$ is an almost sinusoidal fluctuation superimposed on a mean value a little above $n(0)$, as in the dashed curve in Fig. 9. As $\frac{m^2V^2n(0)}{U^2}$ increases the amplitude increases and becomes less sinusoidal. Also the frequency decreases with increasing values of $\frac{m^2V^2n(0)}{U^2}$. All this is clear from a comparison between the two curves in Fig. 9. Eventually, with further increases in the value of $\frac{m^2V^2n(0)}{U^2}$, the frequency goes to zero and the dividing cell population becomes unstable. This process is best illustrated by a population number phase space diagram. This is obtained by integrating Eq.(48) to give

$$\frac{dn}{dt} = \pm \sqrt{2U^2n(0)n - \omega^2n^2 + 4V^2m^2n^3 + K}, \quad (49)$$

where K is a constant of integration.

Fig. 10 shows population phase space curves of $\frac{dn}{dt}$ against $n(t)$, from Eq.(49), plotted for different values of $\frac{mV}{U}$, with K chosen to make $\frac{dn}{dt} = 0$ at $n(t) = n(0)$, which in this case is chosen to be 40, to be consistent with Fig. 9. These results in Fig. 10 are very revealing. The closed part of the dashed curves correspond to a quasi-stable states where the cell population

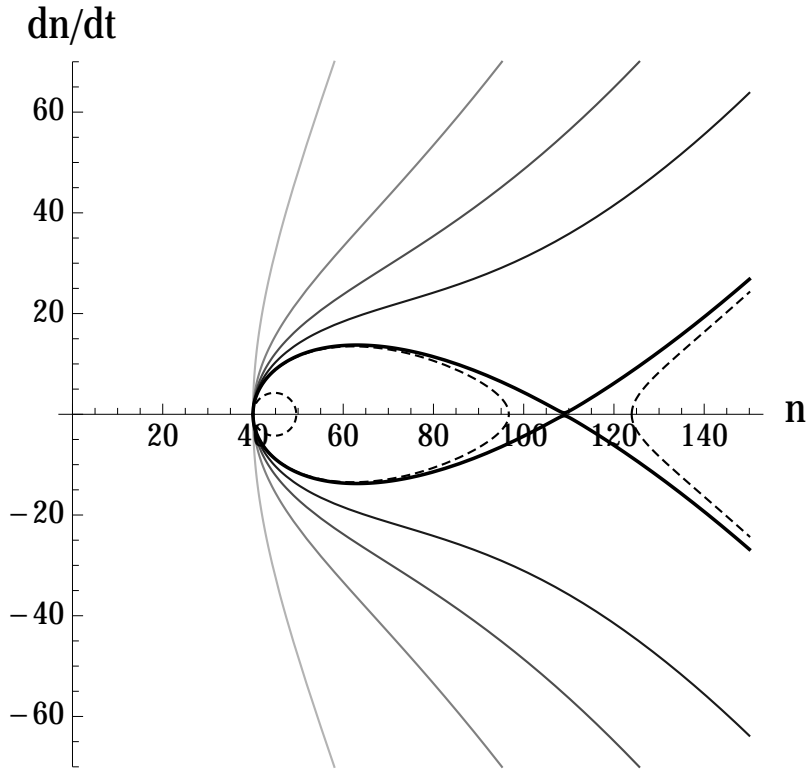


Figure 10: Population phase space curves for different values of $\frac{mV}{U}$ for Model B, with $n(0) = 40$. The smaller the value of $\frac{mV}{U}$, the darker the curve (the range used is $0.02 < \frac{mV}{U} < 0.1$). The black curve is the boundary between the regions where bound states exist and where they do not. It occurs at a value of $\frac{mV}{U} = 0.03116$. The closed dashed curves correspond to bound states, with $\frac{mV}{U} = 0.02$ for the small circle and $\frac{mV}{U} = 0.031$ for the other dashed curve.

gyrates around between an upper and lower bound (where the closed curves cross the n axis). The lower bound is $n(0)$. The closed (dashed) curves correspond to the two lowest values of $\frac{mV}{U}$ in the plot. The smaller the value of $\frac{mV}{U}$ the more circular the closed curve becomes, and the smaller and more exactly sinusoidal becomes the amplitude of its oscillations. The bold curve corresponds to the threshold value of $\frac{mV}{U} = 0.03116$. As the value of $\frac{mV}{U}$ is increased beyond threshold, there are no longer closed curves and the phase space curves show that the population values are capable of reaching

levels well above their threshold values¹⁴. This result is consistent with the existence of an instability that is triggered in the above threshold conditions.

Here we will briefly assess the possible impact of neglecting the quantum noise, Δn^2 , mentioned above. It essentially comes from the inclusion, on the RHS of Eq.(47), of the interaction Hamiltonian, Eq.(44), which contains unpaired creation and annihilation operators. We can gauge the significance of this by defining $\hat{N} = \frac{\hat{Q}}{U} = \hat{n}(0) + \frac{mV}{U}(\hat{a}^\dagger(0)\hat{n}(0) + \hat{n}(0)\hat{a}(0))$, then $\langle \hat{N} \rangle = n(0)$, but $\Delta N^2 = \langle \hat{N}^2 \rangle - \langle \hat{N} \rangle^2 = 2(\frac{mV}{U})^2 n(0)^3$. So the ratio of ΔN^2 to $\langle \hat{N}^2 \rangle$ is $2(\frac{mV}{U})^2 n(0)$, which involves the same factor that was associated with the level of nonlinearity in the system, which we noted earlier. For the instability threshold values from Fig. 10, this ratio is approximately 0.08. This suggests that neglecting quantum noise at levels of this order does not make a huge impact on the qualitative features of the outcome. Actually, including it should increase the nonlinear effect slightly and thus increase slightly the level of instability. We should point out that the nonlinearity is not the cause of the quantum noise. Even in the linear case treated earlier, the population variance is non-zero. However, there it does not directly affect the expectation value of the time dependent number operator.

The instability is ultimately due to the fact that the \hat{n}^2 term in Eq.(48), which is always positive, is subtracted from the linear terms on the LHS of the equation. This provides positive feedback which leads to a nonlinear frequency shift that reduces ω^2 and eventually turns it negative. As $n(t)$ increases there is a shift to lower frequencies. The nonlinear nature of the frequency dependence is clear from the flattening of the peaks compared to the troughs in the solid curve in Fig. 9. We know that this nonlinear quantity always leads to positive feedback because $\langle \hat{N}^2 \rangle = \langle n(0) | \hat{N}^2 | n(0) \rangle = ||\hat{N}|n(0)\rangle||^2 \geq 0$. Contrast this with the highest order nonlinear term in Eq.(42) for Model A. This adds to the linear terms in Eq.(42) and provides negative feedback that increases ω^2 , which has the effect of stabilizing the system and keeping the populations bounded.

What the model predicts then, is that a given initial cell population will maintain a quasi-stationary state with time, i.e., cell division will be going on, stimulated by the presence of a population of stimuli, as long as that population remains below a certain threshold. However, if the stimulating population numbers exceed that threshold, then the dividing cell population will undergo unstable growth. Thus Model B has appropriate characteris-

¹⁴It may appear that with this mathematical framework the values that $n(t)$ could reach infinite levels. They can certainly reach levels that are much larger than $n(0)$, but, in practice, in instabilities of this kind there is always a limit imposed by external factors, such as, the system occupying a finite volume and having a finite energy source.

tics that make it suitable for modelling cancer cells, in spite of its obvious simplicity.

5 Comments and conclusions

In this paper, we have outlined the mathematical formalism involved in representing natural numbers as the eigenvalues of an operator, in the context of discrete populations of items. This approach involves the representation of the dynamical interaction between different sets of populations of countable items via Hamiltonian operators and the Heisenberg equation. The mathematical formalism largely derives from that used in many-body quantum field theory that deals with the scattering of interacting particle populations between different energy states. Such a process is quite analogous to the way in which a macroscopic system of individuals that is divided into different interacting categories may be modelled using operator methods. We have examined the predictions of this formalism for a pair of simple interacting populations and compared the results with those from the classic (and classical) Lotka-Volterra equations for predator-prey competition, and pointed out certain broad similarities and some particular differences between the two approaches.

As an example of an application of the method, we have examined a novel approach to modelling cell division and the resulting cell population dynamics. This highly simplified model is presented in two forms, each of which utilizes the idea that cell division is stimulated by a population of stimulating agents. In Model A, we assume that the participating member of the stimulating population does not emerge from the division process, while in Model B, we assume that the stimulus acts as a catalyst and survives the cell division process. The two models have quite different dynamical characteristics. In Model A, the total population of dividing cells plus the stimuli remains fixed so that the two individual populations fluctuate about their individual means. Model B exhibits two types of response. When the initial population numbers are below certain threshold values, the model behaves in a manner similar to Model A, the only difference being that the stimuli population does not change, while the dividing cell population fluctuates about a mean. However, if the threshold levels are exceeded, then the dividing cell population is subject to an instability, in which the cell population grows monotonically to levels that may be many orders of magnitude greater than the initial ones. It is feasible that the instability in the cell population dynamics that leads to uncontrolled population growth could be identified with the cancerous growth phase of cell populations that is known to occur

as part of the process [23]. Thus, Model A does appear to exhibit the key characteristics of normal cell division in which the population of dividing cells is stable, whereas Model B exhibits behaviour that may be associated with cancer cells. It is also worth pointing out that Model B has an interesting and possibly important characteristic with regard to the role of the catalyst. This is that we could replace $\hat{m}V$ with a modified scalar, V_m , say and get exactly the same results as we obtained in section 4.3. We could interpret this as implying that the catalyst is truly intrinsic to the process. This picture may be a better match to the biological description of the cancer cell than one in which the stimulus appears as an external agent. So, in principle we could just remove the stimuli from Fig. 8 and use V_m as the cell doubling rate in a modified Hamiltonian. This is made more credible by the fact that W in the the Hamiltonian in Eq.(46), does not appear in Eq.(48) and could in fact be set to zero.

Admittedly, the present models of cell division are very simplistic and would need further development before they could be regarded as realistic models of both cell division and cancer-like processes, that might eventually be useful in a clinical context. However, there is sufficient evidence here to suggest that the present model could constitute a basis for such developments. These could take the form of the inclusion of other processes, such as the interaction of the stimuli and the dividing cells with other populations of active agents in the system and also using a combination of Models A and B. One might also envisage including the effects of radiation or of chemical suppressors that act to cause the population of stimuli to decay. It has been suggested that population decay could be treated by the use of non-self-adjoint Hamiltonians, but this is somewhat controversial, since it requires an *ad hoc* modification to the usual Heisenberg equation [8, 30]. It would also be interesting to explore further the overlap between nonlinear quantum optics and population dynamics outside physics. The inclusion of results from quantum optics in relation to the cell dynamics that we have looked at above offers sufficient encouragement that such an approach could prove fruitful, especially in the large population limit [32] where matrix methods are computationally expensive. Quantum optics is a very mature subject and the physical insights that it brings are as important as the purely mathematical elements. These and other developments are beyond the scope of the present paper, but will be considered in future publications.

Finally, we should like to point out that the use of quantum methods outside physics is an exciting and growing field of interdisciplinary research that has many areas of application including social science and finance [33], psychology [34] and decision-making [35].

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