Quantum-like interference effect in gene expression: glucose-lactose destructive interference

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Abstract In this note we illustrate on a few examples of cells and proteins behavior that microscopic biological systems can exhibit a complex probabilistic behavior which cannot be described by classical probabilistic dynamics. These examples support authors conjecture that behavior of microscopic biological systems can be described by quantum-like models, i.e., models inspired by quantum-mechanics. At the same time we do not couple quantum-like behavior with quantum physical processes in bio-systems. We present arguments that such a behavior can be induced by information complexity of even smallest bio-systems, their adaptivity to context changes. Although our examples of the quantum-like behavior are rather simple (lactose-glucose interference in *E. coli* growth, interference effect for differentiation of tooth stem cell induced by the presence of mesenchymal cell, interference in behavior of PrP^C and PrP^{Sc} prions), these examples may stimulate the interest in systems biology to quantum-like models of adaptive

dynamics and lead to more complex examples of nonclassical probabilistic behavior in molecular biology.

Keywords Quantum-like interference · Nonclassical probabilistic behavior · Lactose-glucose interference · *E. coli* growth · Differentiation of tooth stem cell · Mesenchymal cell · Interference of PrP^C and PrP^{Sc} prions

Introduction

Behavior of each cell is characterized by huge complexity. It can be compared with an actor who is playing simultaneously at a few different scenes participating in different (sometimes mutually incompatible) performances (e.g., Wanke and Kilian 2009). Even smaller biological systems, such as viruses and even proteins, also exhibit complex behavior which is characterized by nontrivial context-dependence and adaptivity to context variations. During the last ten years *adaptive dynamics* was successfully used to model information processing by quantum systems (Ohya 2008; Asano et al. 2007). Behavior of such systems is extremely complex as well. It cannot be described by classical evolution, neither by classical stochastic dynamics, e.g., classical Markov chains. More tricky evolutionary processes are in usage, so called quantum stochastic processes, in particular, quantum Markov chains. The authors come with the conjecture that similar mathematical models can be applied to describe activity of biological microsystems (Accardi et al. 2009). At the same time we do not couple quantum-like behavior with quantum physical processes in bio-systems. We present arguments that such behavior can be induced by information complexity of even smallest bio-systems, their adaptivity to context changes. Although our examples of the quantum-like behavior are

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rather simple (lactose-glucose interference in *E. coli* growth, interference effect for differentiation of tooth stem cell induced by the presence of mesenchymal cell, interference in behavior of PrP^C and PrP^{Sc} prions), these examples may stimulate the interest in systems biology to quantum-like models of adaptive dynamics and lead to more complex examples of nonclassical probabilistic behavior in molecular biology.

Recently a few authors started to explore quantum-like statistical models in psychology and cognitive science (Khrennikov 2003, 2004, 2006, 2009, 2010; Busemeyer et al. 2006, 2008; Acacio de Barros and Suppes 2009; Accardi et al. 2008, 2009; Conte et al. 2008, 2009; Fichtner et al. 2008; Khrennikov and Haven 2009; Cheon and Takahashi 2010). The notion of a *quantum-like model* was invented (Khrennikov 2003) to distinguish models in which information processing can be formally described by the mathematical formalism of quantum mechanics (QM) from really quantum physical models—models which are based on physical carriers of information (Penrose 1989, 1994; Homeroff 1994). The usage of quantum-like models extends essentially the domain of applications. There is no need to worry about conditions of applicability of quantum physics.¹ A crucial point is that the mathematical formalism of quantum mechanics presents a version of probability theory which differs from classical probability theory. The difference between laws of classical and quantum probabilities is so large and quantum laws are so counter-intuitive that some people speak about mysteries and paradoxes.

It was shown (Accardi et al. 2008) that such “quantum-like” probabilistic models can be applied in situations characterized by context dependence of behavior.² The contextual viewpoint to quantum and more general quantum-like probabilistic models demystified their laws (at least partially). This stimulates applications of the mathematical formalism of QM outside of physics, especially in biology.

One of the most important nonclassical features of quantum-like models is *interference of probabilities*. Interference can be either constructive or destructive. In the latter case (which will be considered in this paper) the reaction of a system to one factor, say B_+ , can destroy its reaction to another factor, say B_- . Thus the presence of both factors, $B = B_+ \cup B_-$, can, in principle, minimize practically to

zero the activity induced by B_+ . Such destructive interference is well known in quantum physics.

In the famous two slit experiment a quantum particle passes a screen with two slits (numerated as $s = 1, 2$), before to approach another screen covered by photo-emulsion. The latter is used for registration of system's position. Experiment is done under three contexts. In the first two cases only one slit of two is open and in the last case both slits are open. Denote the first two contexts by B_s , $s = 1, 2$. It is possible to find regions on the registration screen covered by photo-emulsion such that they attract a large number of systems under the context B_+ (i.e., only $s = 1$ slit is open), but they attract a small number of systems when the second slit is also open. Typically this behavior is coupled to wave-particle duality. However, we interpret it in a more general framework, namely, as a consequence of *contextuality*. A change of context changes behavior. In this way we can proceed to contextual non-physical models.

It was shown that interference effects can be demonstrated by cognitive systems. We can mention experiments with recognition of ambiguous figures (Conte et al. 2009). Moreover, recently such effects had been found in known statistical data from cognitive psychology (Hofstadter 1983, 1985; Shafir and Tversky 1992; Tversky and Shafir 1992; Croson 1999)—in experiments on so called disjunction effect. For the latter it was shown (Busemeyer et al. 2006, 2008; Accardi et al. 2009) that it is impossible to construct a classical Markovian model reproducing the experimental data from experiments in cognitive psychology (Shafir and Tversky 1992; Tversky and Shafir 1992). At the same time a *quantum Markov chain* reproducing statistical data from cognitive psychology was constructed (Accardi et al. 2009).

The aim of this paper is to show that quantum-like interference (at least destructive) can be found in microbiology; in particular, as effects of activity of genetic systems. A possibility that not only humans, but even animals can “behave in quantum-like way” had been already discussed (Khrennikov 2006). However, it was always emphasized that quantum-like behavior is a feature of advanced cognitive systems having the nervous system of high complexity. In this note we consider the simplest biological system, a cell, and we shall see that it can exhibit (under some special contexts) quantum-like behavior. Of course, we understood well that gene expression regulation is behind this behavior. And the genome is an advanced information system. From this viewpoint, it is not surprising that genome's activity can induce quantum-like behavior of a cell.

Although, from the biological viewpoint, we discuss a rather simple phenomenon (the glucose effect on *E. coli* growth), our example of destructive interference in cell's

¹ For example, in applications to cognitive modelling, one need not worry whether the brain is too hot to perform real quantum physical computations.

² For instance, context dependence plays an important role in cognitive science and psychology. Therefore the quantum-like probability can be applicable here.

activity, interference of two factors: the presence of lactose and glucose in a *E. coli* cell (Inada et al. 1996)³, is very important from foundational viewpoint. It demonstrates that laws of classical probability can be violated not only by advanced cognitive systems (human beings in mentioned cognitive experiments), but even by cells.

The interference test is one of the basic tests in quantum physics to confirm that a system behaves in a quantum way (“nonclassically”). It played an important role in cognitive science to motivate applications of quantum-like models (Khrennikov 2004; Busemeyer 2006; Conte 2009). In this paper we apply this test to statistical data on the glucose effect on *E. coli* growth (Inada et al. 1996). It is demonstrated that these data is nonclassical, i.e., quantum-like interference of probabilities is found.

Moreover, we show that quantum-like probabilistic behavior can be exhibited by even simpler molecular structures, namely, by *proteins*: interference of prions (PrP^C) and mutant prions PrP^{Sc} .

As was shown (Khrennikov 2004), in statistical tests the interference effect can be found through violation of the formula of total probability. And we shall demonstrate that the formula of total probability is really violated by real experimental statistical data (Inada et al. 1996). The formula of total probability is the base of *the Bayesian approach*. Thus, the story about quantum-like behavior is, in fact, about impossibility to use the Bayesian methods in some contexts (and these methods are very popular in genetics and bioinformatics). The main source of violation of the formula of total probability is contextuality—existence of incompatible contexts (in the same way as in QM). Incompatible contexts cannot be described by a single probability space (as it is done in classical theory). As a consequence, the basic formula of Bayesian approach is violated. Hence, in general (i.e., without the direct connection with quantum-like modelling) the result of this paper supports usage of non-Bayesian methods in genetics and cell’s biology.

We hope that this paper will motivate researches towards quantum-like models in genetics and cell-biology. It is a good place to state once again that we are not looking for really quantum effects in gene and cell activities, i.e., effects generated by quantum physical processes going on quantum scales of space and time. We are in search of quantum-like models of information processing by genes and more generally cells.

One of complications in the application of quantum-like probabilistic models outside of physics is that the standard calculus of quantum probabilities which is applicable to

e.g. photons and electrons is too restrictive to describe probabilistic behavior of biological systems. Biological systems are not only nonclassical (from the probabilistic viewpoint), but they are even “worse” than quantum systems. They react to combinations of incompatible contexts by exhibiting stronger interference than quantum physical systems. Instead of standard trigonometric interference of the $\cos \theta$ -type which is well known in quantum physics, *hyperbolic interference* of the $\cosh \theta$ -type can be exhibited in experiments with cognitive systems. Experiments of the latter type cannot be described by the standard mathematical formalism of QM. A generalization of the QM-formalism based on so called hyperbolic amplitudes should be applied (Khrennikov 2010). Formally, the hyperbolic quantum-like formalism is constructed by using an imaginary element j such that $j^2 = +1$, instead of the usual imaginary element i such that $i^2 = -1$, see [Appendix](#).

In the experiment discussed in this paper gene expression generates hyperbolic interference, i.e., interference which is essentially stronger than the standard quantum-like interference. In any event the data collected in the mentioned experiment (Inada et al. 1996) violates basic laws of classical probability theory.

We really hope that this paper will explain researchers working in genetics, molecular biology and in general biology the basic ideas of quantum probability, i.e., representation of probabilities by amplitudes (complex or more general). It will stimulate the usage of quantum and more general quantum-like probabilistic methods. Basic ideas are presented in a simple form. We hope that this paper will be readable for biologists.

Classical law of total probability and its quantum-like modification

Consider two disjoint events, say B_+ and B_- , such that $P(B_+ \cup B_-) = 1$ (the probability of realization of either B_+ or B_- equals to 1) and consider any event A . Then one of basic laws of classical probability can be expressed in the form of the formula of total probability

$$P(A|B_+ \cup B_-) = P(B_+)P(A|B_+) + P(B_-)P(A|B_-), \quad (1)$$

where the conditional probability of one event with respect to another is given by the Bayes formula:

$$P(A|H) = P(A \cap H)/P(H), \quad (2)$$

for H with $P(H) > 0$. We do not discuss here applications of these rules in Bayesian analysis of statistical data; they are well known.

For statistical data obtained in experiments with quantum systems, this formula is violated (Khrennikov 2010). Instead of the classical formula of total probability (1, QM

³ Since the operon theory was proposed in 1956–1961 (Jacob and Monod 1961), the regulatory system of gene expression of lactose operon has been extensively studied and the molecular mechanism of it has been mostly elucidated including the catabolite repression phenomenon.

uses its perturbed version—“the formula of total probability with an interference term”:

$$P(A|B_+ \cup B_-) = P(B_+)P(A|B_+) + P(B_-)P(A|B_-) + 2 \cos \theta \sqrt{P(B_+)P(A|B_+)P(B_-)P(A|B_-)}, \quad (3)$$

where θ is a phase vector. In physics this angle has a natural geometric interpretation. However, already in cognitive science the geometric interpretation of phase is impossible (or at least unknown). The phase can be interpreted as a measure of incompatibility of events (Khrennikov 2004). Mathematically incompatibility is described as impossibility to use Boolean algebra (set-theoretic representation).

Already in quantum physics the event interpretation of $B_{\pm}$ in the equality (3) is misleading. In real experiments, e.g., the two slit experiment, $B_{\pm}$ are not events, but experimental contexts. In applications to biology we proceed in the same way, especially in experimental situations which are characterized by violation of Bayes formula (2). Therefore we prefer to call probabilities $P(A|B_{\pm})$ not conditional, but contextual.

The constructive wave function approach (Khrennikov 2010) provides a possibility to reconstruct the wave function (in experiments with quantum systems), the complex probabilistic amplitude. We have

$$\psi_A = \alpha + e^{i\theta} \beta, \quad (4)$$

where

$$\alpha = \sqrt{P(B_+)P(A|B_+)}, \quad \beta = \sqrt{P(B_-)P(A|B_-)} \quad (5)$$

and the phase θ can be found from the “coefficient of interference”

$$\lambda_A = \frac{P(A|B_+ \cup B_-) - (P(B_+)P(A|B_+) + P(B_-)P(A|B_-))}{2\sqrt{P(B_+)P(A|B_+)P(B_-)P(A|B_-)}}. \quad (6)$$

We remark that, for quantum physical systems, the magnitudes of coefficients of interference are always bounded by 1,

$$|\lambda_A| \leq 1. \quad (7)$$

For statistical data, collected in quantum physical experiments, the phase is given by

$$\theta = \arccos \lambda_A. \quad (8)$$

We state again that the coefficient of interference λ_A can be found on the basis of experimental data (this is the essence of the constructive wave function approach (Khrennikov 2010)). The nominator of (6) gives a measure of nonclassicality of data: this is the magnitude of violation of the law of total probability; the denominator is simply a normalization coefficient.

In the absence of the experimental data the ψ -function can be obtained e.g. from the evolution equation, Schrödinger’s equation. If the complex probabilistic amplitude is known then probability can be calculated with the aid of the basic formula of quantum probability, Born’s rule:

$$P(A|B_+ \cup B_-) = |\psi_A|^2 = |\alpha + e^{i\theta} \beta|^2. \quad (9)$$

If $\theta \neq \pi/2$, then $P(A|B_+ \cup B_-) \neq |\alpha|^2 + |\beta|^2$. The presence of the phase θ induces interference

$$P(A|B_+ \cup B_-) = |\alpha|^2 + |\beta|^2 + 2 \cos \theta |\alpha| |\beta|.$$

The same approach can be used not only for quantum physical systems, but for biological systems demonstrating nonclassical probabilistic behavior (Khrennikov 2010). Instead of probabilities, one operates with wave functions, probabilistic amplitudes.

As was mentioned in introduction, biological systems can demonstrate even stronger violation of the formula of total probability than quantum physical systems, i.e., the coefficient of interference λ_A , see (6), can be larger than 1. In such situations the modified formula of total probability has the form

$$P(A|B_+ \cup B_-) = P(B_+)P(A|B_+) + P(B_-)P(A|B_-) \pm 2 \cosh \theta \sqrt{P(B_+)P(A|B_+)P(B_-)P(A|B_-)}, \quad (10)$$

i.e., the hyperbolic cosine has to be used. This type of interference was found for cognitive systems (Khrennikov 2010).

The constructive wave function approach can be generalized to the hyperbolic case. Let us consider the algebra of hyperbolic numbers: $z = x + jy$, where x, y are real numbers and the imaginary element j is such that $j^2 = 1$. Then the formula of total probability with the hyperbolic interference term, see (10), induces the representation of the probability by the hyperbolic amplitude:

$$\psi_A = \alpha \pm e^{j\theta} \beta, \quad (11)$$

where the coefficients are again given by (5), θ is a “hyperbolic phase”. The latter can be found (similar to the usual “trigonometric phase”), see (8), as

$$\theta = \operatorname{arccos} |\lambda_A|. \quad (12)$$

The sign in (11) is determined by the sign of the coefficient of interference λ_A .

Generalization of Born’s rule (9) gives the representation of the probability as the squared amplitude:

$$P(A|B_+ \cup B_-) = |\psi_A|^2 = |\alpha \pm e^{j\theta} \beta|^2 = |\alpha|^2 + |\beta|^2 \pm 2 \cosh \theta |\alpha| |\beta|. \quad (13)$$

The application of this general framework to molecular biology is not totally straightforward. Sometimes it is difficult to determine probabilities $P(B_{\pm})$ in experiments with cells. Therefore the direct test of the formula of total

probability (1) is not possible (or it requires additional experiments). However, this is not a problem, because the formula (1) is a consequence of a more fundamental law of classical theory of probability, namely, the law of additivity of probabilities. We recall the derivation of (1). It can be found on the first pages of any textbook on probability theory:

$$P(A|B_+ \cup B_-) = P(A \cap (B_+ \cup B_-)) \\ = P(A \cap B_+) + P(A \cap B_-), \quad (14)$$

which is a consequence of additivity of probability. This is the basic law. Then, to obtain (1), one does the formal algebraic transformation to conditional probabilities:

$$P(A|B_+ \cup B_-) = P(B_+) \frac{P(A \cap B_+)}{P(B_+)} + P(B_-) \frac{P(A \cap B_-)}{P(B_-)}.$$

Therefore it is reasonable to test the basic law of additivity of classical probability (14) whose violation implies violation of the formula of total probability. We easily rewrite all above formulas on complex and more general probabilistic amplitudes by placing

$$P(B_{\pm})P(A|B_{\pm}) \mapsto P(A \cap B_{\pm}). \quad (15)$$

We point out that in experimental studies typically A is determined by values of a random variable, say ξ , which are measured in the experiment. In the simplest case ξ is dichotomous, e.g., $\xi = \pm 1$, and A can be chosen either as $A_+ = \{ \xi = +1 \}$ or as $A_- = \{ \xi = -1 \}$.

Violation of the law of total probability in molecular biology

Glucose effect on *E. coli* growth

Our considerations are based on an article reporting the glucose effect on *E. coli* (*Escherichia coli*) growth (Inada et al. 1996). There was measured the β -galactosidase activity at certain growth phase: grown in the presence of 0.4% lactose, 0.4% glucose, or 0.4% lactose + 0.1% glucose. The activity is represented in Miller units (enzyme activity measurement condition). There was obtained the probabilistic data: 0.4% glucose, 33 units; 0.4% lactose, 2,920 units; 0.4% lactose + 0.1% glucose, 43 units.

We recall that by full induction, the activity reaches to 3,000 units. We want to represent these data in the form of contextual probabilities and put them into the formula of total probability.

We introduce a random variable, say ξ , which describes the level of activation. We also consider two contexts: L —the presence of molecules of lactose and G —the presence of molecules of glucose. The experimental data provide the contextual (conditional) probabilities

$$P(\xi = +1|L) = \frac{2,920}{3,000} \approx 0.973, \quad P(\xi = +1|G) = \frac{33}{3,000} \\ \approx 0.011.$$

Consider now the context $L \cup G$ of the presence of molecules of lactose and glucose. In classical probability theory the set-theoretical description is in usage. We can represent L as the set of lactose molecule and G as the set of glucose molecule and, finally, C as (disjoint) union of these sets. (Of course, there are other types of molecules. However, we ignore them, since the random variable ξ depends only of the presence of lactose and glucose.)

We have

$$P(\xi = +1|L \cup G) = \frac{43}{3000} \approx 0.014$$

In the classical probabilistic framework we should obtain the equality (14), a consequence of the law of additivity of probabilities:

$$P(\xi = +1|L \cup G) = P(\xi = +1 \cap L) + P(\xi = +1 \cap G). \quad (16)$$

By putting the data into (16) we obtain

$$0.014 = 0.984, \quad (17)$$

Thus the basic law of classical probability theory, additivity of probability, and, hence, the formula of total probability, is violated. This violation is a sign that, to describe cell's behavior, a more complex version of probability theory has to be used. This is the quantum-like probabilistic model corresponding to contextual behavior. We state again that we are not looking for physical quantum sources of violation of classical probabilistic rules. We couple nonclassical probability with nontrivial contextuality of cell's reactions.

We now can find the coefficient of interference corresponding to the value $\xi = +1$:

$$\lambda_+ = (0.014 - 0.984) / 2\sqrt{0.973 \times 0.011} \approx -4.3$$

We see that interference (destructive) is very strong, essentially stronger than typical interference for quantum physical systems. This situation can be described by the hyperbolic probability amplitude:

$$\psi_+ = \sqrt{0.973} - e^{2.138j} \sqrt{0.011} \approx 0.986 - e^{2.138j} 0.105,$$

where $\theta_+ = 2.138 = \operatorname{arccosh} |\lambda_+| = \operatorname{arccosh} 4.3$. Then the hyperbolic version of Born's rule, see (9), gives

$$P(\xi = +1|L \cup G) = |\psi_+|^2.$$

We operated with contexts L , the presence of lactose, and G , the presence of glucose, without pointing to concrete levels of concentrations of corresponding molecules. This description is justified by the following remark:

Remark We recall that lactose induces the enzyme, but without induction certain percentage would be expressed by fluctuation of gene expression. The concentration of glucose is not important, but the following should be taken into account:

If we add 0.2% glucose in the medium, cells can grow to its stationary phase on glucose only and they do not try to utilize lactose. So, if we want to see the enzyme induction during the growth, we have to limit the glucose concentration, usually 0.02%. That amount is insufficient for support of cell growth and cells try to utilize lactose after consumption of glucose. If we add only 0.02% glucose in the medium without any other carbon (energy) source, then the enzyme level would be similar as in the presence of 0.2% glucose and cells stop growing. If there is any other carbon source than 0.02% glucose, then cells continue to grow and the enzyme level changes depending on the kind of carbon source (for lactose, the level is quite high; for maltose, the level would be low, but significant; for pepton (amino acid mixture), the level would be a little bit more).

Mesenchymal cells context

It is well known that a dental epithelial cell grows in a medium as it is (no differentiation). A dental mesenchymal cell grows similarly. However, if they are grown together (mix), then a dental epithelial cell differentiates to a tooth cell (Nakao et al. 2007). Growth condition is the same. Hence, if independently grown, they grow as they are (no differentiation). If mixed and grown, dental epithelial cells differentiate.

We introduce a random variable $\xi = +1$, in the case of differentiation of a cell, and $\xi = -1$, in the opposite case. We also introduce two contexts B_+ —represented by an ensemble of mesenchymal cells and B_- —by an ensemble of tooth stem cells (In the classical probability model these contexts are represented by sets; in principle, ensembles can be chosen as sets used in the model. However, in general these are abstract sets.). Although we do not have the complete statistical data, we can assume that $P(\xi = +1|B_+) \approx 0$ (the probability of differentiation in the ensemble consisting of only mesenchymal cells) and $P(\xi = +1|B_-) \approx 0$ (the probability of differentiation in the ensemble consisting of only tooth stem cells) and also that $P(\xi = +1|B_+ \cup B_-) \approx 1$ (the probability of differentiation in a mixture of mesenchymal cells and tooth stem cells). If the basic law of classical probability theory, additivity of probability were applicable, we should get $1 \approx P(\xi = +1|B_+ \cup B_-) = P(\xi = +1|B_+) + P(\xi = +1|B_-) = 0 + 0 = 0$. The basic law of classical probability theory, additivity of probability, and, hence, the formula of total probability, is violated.

We can also mention an experiment (Clement et al. 2010) on differentiation of $PL1^+$ cells. This experiment was performed in the process of study on new methods of identification of cancer cells. A population of $PL1^+$ cells was identified by exposing it under two complementary contexts: a) differentiation context (serum rich media) and b) stem cells culture context. We can use this experiment as an additional example of (destructive) quantum-like interference.

Interference induced by the presence of PrP^{Sc} prion proteins

In spite of its small size, a cell is still an extremely complex biological system. Now we are looking for interference effects and violation of laws of classical probability theory for essentially simpler systems, namely, proteins.

Let us consider prion protein (cause of CJD, mad cow disease (Yam 2003)). Usually it stays as globular soluble form in mono-dispersed state; this is safe conformation. By heating it may denature and aggregate taking random conformations. If there exists a seed for β -form conformation (a mutant prion protein, or wild type prion protein but after long time incubation), they tend to make filamentous aggregate (this is the cause of CJD) as a whole, which is resistant to solubilization with detergent and to denaturation by heat. So, wild type prion from normal animal can be incubated for a long time as a clear solution. But by adding mutant prion or rather β -form wild type prion obtained by incubating for very long time of the wild type prion solution, most of the prion proteins become insoluble as filamentous aggregates. After this, the prion proteins can no more resume the initial soluble conformation.

We introduce a random variable $\xi = +1$, if protein can be incubated for a long time as a clear solution, and $\xi = -1$, in the opposite case. We also introduce two contexts: B_+ —represented by an ensemble of mutant prion proteins PrP^{Sc} (in the classical set-theoretical probability model by a set B_+) and B_- —by an ensemble of prion proteins PrP^C .⁴ (In the classical set-theoretical probability model this context is represented by a set B_- . We remark that the intersection of the sets B_+ and B_- is empty, since the intersection of the corresponding ensembles of protein molecule is empty. We also remark that $P(B_+ \cup B_-) = 1$, since we ignore a possibility of influence of other molecules, proteins, or DNAs, or viruses; the latter is an important assumption reflecting the present state of art in microbiology of prions.) Although we do not have statistical data, we can assume that $P(\xi = +1|B_-) \approx 1$ and

⁴ The same effect, destructive interference, can be approached, by using, instead of mutant proteins, wild type prion protein, but after long time incubation.

$P(\xi = +1|B_+) \approx 0$ and also that $P(\xi = +1|B_+ \cup B_-) \approx 0$. (in the classical probability model the context $B_+ \cup B_-$ is represented by the union of sets B_+ and B_- ; in our biological model this is an ensemble obtained by mixing the ensembles of cells representing B_+ and B_- .) If the basic law of classical probability theory, additivity of probability were applicable, we should get $0 \approx P(\xi = +1|B_+ \cup B_-) = P(\xi = +1|B_+) + P(\xi = +1|B_-) \approx 1 + 0 = 1$. The basic law of classical probability theory, additivity of probability, and, hence, the formula of total probability, is violated.

To reconstruct the probability amplitude, we need the real data. Nevertheless, even in their absence we can proceed a little bit further. In real experiments, one can never speak about such probabilities as one and zero. Therefore let us assume that $P(\xi = +1|B_-) \approx 1 - \delta_-$ and $P(\xi = +1|B_+) \approx \delta_+$ and also that $P(\xi = +1|B_+ \cup B_-) = \delta_{+-}$, where all δ s are very small. Then we have

$$\begin{aligned} \lambda_+ &= \frac{P(\xi = +1|B_+ \cup B_-) - P(\xi = +1|B_+) - P(\xi = +1|B_-)}{2\sqrt{P(\xi = +1|B_+)P(\xi = +1|B_-)}} \\ &= \frac{\delta_{+-} - (1 - \delta_- + \delta_+)}{2\sqrt{\delta_+(1 - \delta_-)}} > 1. \end{aligned}$$

Thus this is very strong destructive interference, of the hyperbolic type.

On double stochasticity of contextual probabilities

We turn to the formula of total probability with the interference term (3). Consider the QM formalism in the two dimensional space. There are given two quantum observables, symmetric matrices $(2 \times 2)\hat{a}$ and $\hat{b}$ with eigenvalues ± 1 (these are values which can be obtained in measurements of these observables). Let $B_{\pm} = \{b = \pm 1\}$ and let $A_{\pm} = \{a = \pm 1\}$. Consider contextual probabilities $P(A|B_+)$ and $P(A|B_-)$, where $A = A_+$ or $A = A_-$. Then the QM-formalism implies that

$$P(A|B_+) + P(A|B_-) = 1.$$

This property is called double stochasticity (DS) and this is an essentially quantum property of contextual probabilities. But cognitive systems can produce contextual probabilities which violate the DS-condition (Khrennikov 2010). Hence, sometimes the conventional quantum observables given by symmetric matrices cannot be used. More general quantum observables given by so called positively defined operator valued measures (Ingarden 1997) have to be used. What is a situation in molecular biology? Take the example of the glucose effect on *E. coli* growth. Here $P(\xi = +1|L) + P(\xi = +1|G) =$

$0.984 + 0.011 = 0.984 \neq 1$. Hence, DS is violated (as in cognitive science).

Quantum or classical interference?

Some authors claim that interference effects can also be described with non-quantum oscillators as wave sources (Khrennikov 2006, 2008, 2010; Acacio de Barros and Suppes 2009). For example, in microbiology these might be chemical waves. It was emphasized that quantum and more general quantum-like interference can be exhibited by any system (including biological and social) which is sensitive to changes of context (Khrennikov 2010). Ohya developed a general theory of adaptive dynamical systems (Ohya 2008; Asano et al. 2007). Such systems produce interference effects – induced by adaptivity to new contexts.

One of referees of this paper asked the following question:

“In describing the interference effects with quantum-like formalism, what is the advantage of the QM-like model over chemical oscillators model?”

This question is in the very heart of quantum foundations. It is well known that interference is one of the basic features of classical waves. In particular, interference of light had been first observed for classical sources of light and only then for quantum ones. Can quantum interference, interference of photons, be considered as a purely classical wave phenomenon? This is a complicated question. The majority of the quantum community believes that quantum interference cannot be reduced to classical one. At the same time a part of the quantum community considers interference as a purely classical wave phenomenon. They claim that quantum and classical phenomena can be distinguished only on the basis of a more complex statistical test, violation of Bell’s inequality (Khrennikov 1999, 2010).

As was mentioned, the authors of this paper do not claim that interference is a solely quantum phenomenon. Our approach is *quantum-like*. We tell: contextuality can induce interference and nonclassical probabilistic behavior. We do not claim that contextuality could not be induced by classical adaptive dynamics; in particular, by adaptive oscillating processes. Nevertheless, we would like to point to essentially quantum features of interference in cell’s biology. In some sense microbiological interference is closer to quantum interference, i.e., interference for photons or electrons, than interference discussed in cognitive science and psychology. We shall stress the role of the *wave-particle duality* in distinguishing purely classical wave interference from quantum interference. The standard argument about the role of the wave-particle duality in the

two slit experiment is the following, see (Khrennikov 1999, 2010):

Consider the two slit experiment, see introduction. It is clear that classical light can produce destructive or constructive interference. For two open slits, the intensity of light can be different from the sum of intensities for contexts B_+ (only the upper slit is open) and B_- (only the lower slit is open).

Now we modify the experiment. Consider classical light in context – both slits are open. But now two detectors are placed directly after slits ($s = 1, 2$). And they click simultaneously, since a classical wave goes through both slits. Thus each pulse from a source produces a wave which passes through both slits.

Consider now quantum light, the same context, and the same location of detectors. In this case only one of two detectors clicks. Thus a photon passes only one slit (demonstrating a corpuscular feature). Thus even in the context $B_+ \cup B_-$ (both slits are open) we can distinguish photons: those passed $s = 1$ and those passed $s = 2$. (We remark that by distinguishing photons we destroy their wave feature—interference).

Our example of the glucose effect on *E. coli* growth mimics the quantum situation. We can distinguish chemical molecules not only for the contexts L and G , but even for the context $L \cup G$. (Even for an ensemble consisting of a mixture of molecules of lactose and glucose we can distinguish molecules by their type.) This is a corpuscular feature of “chemical waves” which produce interference. It is a consequence of the corpuscular structure of carriers of information in molecular biology. Thus the quantum-like model is more adequate to this situation than the classical wave model.⁵

Finally, we stress the role of the Bell-type tests for cells (or proteins). Such tests will essentially clarify the situation, cf. with Bell’s test in cognitive science (Conte et al 2008).

Discussion

We demonstrated that statistical data from molecular biology can violate the basic law of classical probability theory; the formula of total probability. This can stimulate applications of quantum probability or its quantum-like generalizations, i.e., operating with amplitudes, instead of classical probabilities. In particular, quantum decision theory may be used, instead of classical Bayesian decision making.

⁵ As was mentioned, in quantum physics by determining a slit which was passed by a photon we destroy the interference effect. It is not clear whether the same would happen in molecular biology.

As was emphasized, we do not connect the quantum-like probabilistic behavior in molecular biology with quantum physical processes in cells or protein molecules. We pointed to a possibility to couple quantum-like probabilistic models with *contextuality* of biological processes – well developed ability of even microscopic biological systems to adapt their behavior to context variations. Contexts under consideration can vary due to variations in the chemical environment (as in the example with interference of lactose and glucose) or due to arrival of new microbiological systems, e.g., cells (as in the example with appearance of mesenchymal cells in a population of tooth stem cells) or even smaller systems such as proteins (as in the example with interference of two types of prions). Dynamics of one bio-system is adapted to new context. Therefore the quantum-like probabilistic behavior can be considered as an exhibition of adaptive dynamics of microsystems. The general theory of adaptive dynamical systems was developed by one of the coauthors of this paper (Ohya 2008). The main message of this note to the community of molecular biology is that the theory of adaptive dynamical systems can be used to describe behavior of cells, viruses, genes, and proteins.

One of referees of this paper formulated a number of important questions on expected impact of quantum-like modelling in molecular biology:

Why computing the coefficient of interference (lambda parameter) important in molecular biology? How to use it to predict phenomena of molecular biological interest? Can it predict the existence or nature of unknown biological elements (e.g., new proteins, microorganisms in the cell) or structures of biological machineries? Does QM-like model lead us to a better mechanistic understanding of the molecular biological phenomena?

The coefficient of interference provides a measure of incompatibility of contexts. Thus, e.g., in the example of the glucose effect on *E. coli* growth, we found that the lactose-context exhibits a very strong destructive interference with the glucose context. Starting with the coefficient of interference we can reconstruct the wave function (complex or more general) probabilistic amplitude, see “[Classical law of total probability and its quantum-like modification](#)” (Khrennikov 2010). However, further application of this “wave function” confronts with the following complicated problem. This wave function can be used as the initial condition for the Schrödinger equation for the probability amplitude. This equation will provide a probabilistic description of microbiological processes. However, at the moment it is not clear at all how to construct quantum-like Hamiltonians in microbiology. (We remark that we discuss not really quantum physical processes in cells, but quantum-like dynamics of some observables used in molecular biology.) Hence, at the moment the main value of calculation of

the coefficient of interference is to show that processes are really quantum-like and, hence, stimulate future research in creation of quantum-like dynamical models, cf. cognitive science (Asano et al. 2010). Regarding the last question on a better mechanistic understanding of the molecular biological phenomena we can say that the ordinary QM provides only a probabilistic description. The orthodox Copenhagen viewpoint is that it cannot say anything about dynamics of individual quantum particles. Nevertheless, some nonorthodox approaches provide a possibility to present a detailed mechanistic description matching QM. We can mention Bohmian mechanics. Unfortunately, majority of such mechanistic “prequantum models” are *nonlocal*. Although many people speculate about nonlocality in quantum mechanics and cognitive science and even psychology, we prefer to stop here and not proceed towards a discussion on nonlocal effects in molecular biology.

We also hope that this publication will stimulate experimental activity to provide quantitative statistical data on quantum-like interference in molecular biology. Finally, we state once again that from our viewpoint quantum-like probabilistic effect is a consequence of context-dependent behavior of cells, viruses, proteins.

Appendix: hyperbolic numbers

The algebra of hyperbolic numbers $\mathbf{G}$ is a two dimensional real algebra with basis $e_0 = 1$ and $e_1 = j$, where $j^2 = 1$ (a two dimensional Clifford algebra). Elements of $\mathbf{G}$ have the form $z = x + jy$, $x, y \in \mathbf{R}$. We have $z_1 + z_2 = (x_1 + x_2) + j(y_1 + y_2)$ and $z_1 z_2 = (x_1 x_2 + y_1 y_2) + j(x_1 y_2 + x_2 y_1)$. This algebra is commutative. It is not a field - not every element has the inverse one. We introduce an involution in $\mathbf{G}$ by setting $\bar{z} = x - jy$. We set

$$e^{j\theta} = \cosh \theta + j \sinh \theta, \theta \in \mathbf{R}.$$

We remark that $e^{j\theta_1} e^{j\theta_2} = e^{j(\theta_1 + \theta_2)}$, $\overline{e^{j\theta}} = e^{-j\theta}$. By operating with hyperbolic exponents we can proceed in the same way as in ordinary complex quantum mechanics (Khrennikov 2010).

References

- Acacio de Barros J, Suppes P (2009) Quantum mechanics, interference, and the brain. *J Math Psychol* 53:306–313
- Accardi L, Khrennikov A, Ohya M (2008) The problem of quantum-like representation in economy, cognitive science, and genetics. In: Accardi L, Freudenberg W, Ohya M (eds) *Quantum bio-informatics II: from quantum information to bio-informatics*. WSP, Singapore, pp 1–8
- Accardi L, Khrennikov A, Ohya M (2009) Quantum Markov model for data from Shafir-Tversky experiments in cognitive psychology. *Open Syst Inform Dyna* 16:371–385
- Asano M, Ohya M, Togawa Y (2007) Entropic chaos degree of rotations and log-linear dynamics. In: Accardi L, Freudenberg W, Ohya M (eds) *Quantum bio-informatics: from quantum information to bio-informatics*. WSP, Singapore, pp 36–52
- Asano M, Ohya M, Togawa Y, Khrennikov A, Basieva I (2010) On application of Gorini-Kossakowski-Sudarshan-Lindblad equation in cognitive psychology. *Open Syst Inform Dyna* 17:1–15
- Bussemeyer JR, Wang Z, Townsend JT (2006) Quantum dynamics of human decision making. *J Math Psychol* 50:220–241
- Bussemeyer JR, Matthews M, Wang Z (2006) A quantum information processing explanation of disjunction effects. In: Sun R, Myake N (eds) *The 29th annual conference of the cognitive science society and the 5th international conference of cognitive science*, Erlbaum, Mahwah, pp 131–135
- Bussemeyer JR, Santuy E, Lambert-Mogiliansky A (2008) Comparison of Markov and quantum models of decision making. In: Bruza P, Lawless W, Rijsbergen K, Sofge DA, Coeke B, Clark S (eds) *Quantum interaction-2*. College Publications, London, pp 68–74
- Cheon T, Takahashi T (2010) Interference and inequality in quantum decision theory. *Phys Lett A* 375:100–104
- Clement V, Marino D, Cudalbu C, Hamou MF, Mlynarik V, de Tribolet N, Dietrich PY, Gruetter R, Hegi ME, Radovanovic I (2010) Marker-independent identification of glioma-initiating cells. *Nat Methods* 7:224–229
- Conte E, Khrennikov A, Todarello O, Federici A, Zbilut JP (2008) A preliminary experimental verification on the possibility of Bell inequality violation in mental states. *Neuroquantology* 6:214–221
- Conte E, Khrennikov A, Todarello O, Federici A, Zbilut JP (2009) Mental states follow quantum mechanics during perception and cognition of ambiguous figures. *Open Syst Inform Dyna* 16:1–17
- Croson R (1999) The disjunction effect and reasoning-based choice in games. *Organ Behav Hum Decis Process* 80:118–133
- Fichtner KH, Fichtner L, Freudenberg W, Ohya M (2008) On a quantum model of the recognition process. *QP-PQ:Quantum Prob. White Noise Anal* 21:64–84
- Hameroff S (1994) Quantum coherence in microtubules. A neural basis for emergent consciousness?. *J Conscious Studies* 1:91–118
- Hameroff S (1994) Quantum computing in brain microtubules? The Penrose-Hameroff orch or model of consciousness. *Phil Trans R Sci Lond A* 1(28):1–28
- Hofstadter DR (1983) Dilemmas for superrational thinkers, leading up to a luring lottery. *Sci Am* 6:121–134
- Hofstadter DR (1985) *Metamagical themes: questing for the essence of mind and pattern*. Basic Books, New York
- Inada T, Kimata K, Aiba H (1996) Mechanism responsible for glucose-lactose diauxie in *Escherichia coli* challenge to the cAMP model. *Genes Cells* 1:293–301
- Ingarden RS, Kossakowski A, Ohya M (1997) *Information dynamics and open systems: classical and quantum approach*. Kluwer, Dordrecht
- Jacob F, Monod J (1961) Genetic regulatory mechanism in the synthesis of proteins. *J Mol Biol* 3:318–356
- Khrennikov A (2010) *Ubiquitous quantum structure: from psychology to finance*. Springer, Heidelberg
- Khrennikov A (1999) *Interpretations of probability*. VSP Int. Sc. Publishers, Utrecht/Tokyo; (2009) De Gruyter, Berlin, second edition (completed)
- Khrennikov A (2003) Quantum-like formalism for cognitive measurements. *Biosystems* 70:211–233
- Khrennikov A (2004) On quantum-like probabilistic structure of mental information. *Open Syst Inform Dyna* 11(3):267–275

- Khrennikov A (2006) Quantum-like brain: interference of minds. *BioSystems* 84:225–241
- Khrennikov A (2008) The quantum-like brain on the cognitive and subcognitive time scales. *J. Consciousness Studies* 15:39–77
- Khrennikov A (2009) Quantum-like model of cognitive decision making and information processing. *Biosystems* 95:179–187
- Khrennikov A, Haven E (2009) Quantum mechanics and violations of the sure-thing principle: the use of probability interference and other concepts. *J Math Psychol* 53:378–388
- Nakao K, Morita R, Saji Y, Ishida K, Tomita Y, Ogawa M, Saitoh M, Tomooka Y, Tsuji T (2007) The development of a bioengineered organ germ method. *Nat Methods* 4:227–230
- Ohya M (2008) Adaptive dynamics and its applications to chaos and NPC problem. *QP-PQ:Quantum Prob. White Noise Anal* 21: 186–216
- Penrose R (1989) *The emperor's new mind*. Oxford University Press, Oxford
- Penrose R (1994) *Shadows of the mind*. Oxford University Press, Oxford
- Shafir E, Tversky A (1992) Thinking through uncertainty: nonconsequential reasoning and choice. *Cogn Psychol* 24:449–474
- Tversky A, Shafir E (1992) The disjunction effect in choice under uncertainty. *Psychol Sci* 3:305–309
- Wanke D, Kilian J (2009) A basic introduction to gene expression studies using microarray expression data analysis. In: Accardi L, Freudenberg W, Ohya M (eds) *Quantum bio-informatics II: from quantum information to bio-informatics*. WSP, Singapore, pp 314–326
- Yam P (2003) *The pathological protein: mad cow, chronic wasting, and other deadly prion diseases*. Springer, Heidelberg