Quantum noise influencing human behaviour could fake effectiveness of drugs in clinical trials

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Abstract

To test the effectiveness of a drug one can advice two randomly selected groups of patients to take or not to take it, respectively. It is well-known that the causal effect cannot be identified if not all patients comply. This holds even when the non-compliers can be identified afterwards since latent factors like patient’s personality can influence both his decision and his physical response. However, one can still give bounds on the effectiveness of the drug depending on the rate of compliance. Remarkably, the proofs of these bounds given in the literature rely on models that represent all relevant latent factors (including noise) by hidden classical variables. In strong analogy to the violation of Bell’s inequality, some of these bounds fail if patient’s behavior is influenced by latent quantum processes (e.g. in his nervous system). Quantum effects could fake an increase of the recovery rate by about 13% although the drug would hurt as many patients as it would help if everyone took it. The other bounds are true even in the quantum case.

We do not present any realistic model showing this effect, we only point out that the physics of decision making could be relevant for the causal interpretation of every-day life statistical data.

1 The problem of noncompliance in randomized clinical trials

Evaluating statistical data from clinical trials is one of the most applied methods to investigate the effect of drugs or certain therapies on the patient’s health. To compare the recovery rate of the patients that have taken the drug to the recovery rate of the others is among the most popular methods of research in medicine. Despite the simplicity of this method, it can produce an abundance of misconclusions if it is not applied carefully. One of the most popular errors in too naive applications of this kind of statistical reasoning is not to distinguish clearly between so-called experimental and

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**non-experimental** data. Experimental data is produced if some (randomly selected) patients are advised to take the drug and some are advised not to take it. In the second case the patients may decide for their own whether they want to take it or not. Although one may prefer the second method for ethical reasons, the worth of the produced data for drawing causal statements is considerably reduced. There is even no way to *prove* any causal effects of the drug by those data sets. The reason is that the possibly observed correlation between recovery rate and taking the drug may stem from a hidden common cause: There may be an (unobserved) feature of certain patients that makes them decide to take the drug and at the same time makes them recover. In the simplest case, this common feature may be a variable that could be observable in principle. Assume for instance, the elderly people tend less to take the drug than the younger ones. On the other hand, they recover less likely. This would produce a correlation that fakes a causal effect of the drug. But this misconception could be avoided by taking into account the patient’s age and evaluating the recovering rates separately for each age. However, in the generic case, the common cause is less simple and may even be something that is not accessible at all. Imagine, for instance, there is something like a strong wish to recover without drugs that is highly correlated with a high recovery rate. Then the variable describing the common cause is a feature like personality (including mental and physiological constitution) and we are no able to quantify it in order to compare only persons with “equal personality”. Randomized experiments seem to avoid this problem completely. However, there is still a problem that is directly related to the problem above. In typical tests we cannot expect that all patients act like they are advised to do: Some may not take it although they should and some may even acquire it although they were not advised to take it. Assume that it is even possible to prove (by blood-tests, for instance) that some patients did not comply. Unfortunately, even this does not solve the problem completely since we cannot identify which part of the correlations are caused by the common personal feature influencing the patient’s decision and his recovery behavior and which part of the correlation is a causal effect of the drug. However, it is clear that the causal effect of the drug can *almost* be identified if *almost all* patients comply since this case approximates the perfectly randomized experiment. This intuition shows that quantitative lower and upper bounds on the causal effect of the drug can be given depending on the compliance rate. This has been investigated thoroughly in the literature (see [1] and references therein). First we rephrase their most intuitive conclusion. Imagine a naive researcher, not aware of the non-compliance, observes the two binary variables $Z$ and $Y$ where $Z = z_1$ or $Z = z_0$ means that the patient had or had not been selected to take the drug and $Y = y_1$ or $Y = y_0$ means that the patient recovered or not, respectively. Then he takes the difference between the probability to recover if one was advised to take the drug minus the probability to recover if one was not advised, i.e.,

$$P(y_1|z_1) - P(y_1|z_0)$$

as the (positive) causal effect of the drug. Now imagine that a less naive statistician asks for the maximal error that this naive conclusion can cause. He observes the

\[\text{Here we use the large sampling assumption, i.e., the sample size is large enough to estimate the joint distribution } P \text{ on all observed random variables. Issues of significance of correlations can therefore be neglected here.}\]
variable $X$ where $X = x_1$ or $X = x_0$ means that the patient has or has not taken the drug, respectively. He concludes that in the worst case of overestimating the effect, all those that have been advised to take the drug but complied and have recovered, would have stayed ill if they had complied. On the other hand, all those that had been advised not to take it and took it nevertheless and did not recover may have recovered if they would have complied. By this intuition he concludes that the causal effect of the drug is to increase the probability to recover at least by

$$P(y_1|z_1) - P(y_1|z_0) - P(y_0,x_0|z_1) - P(y_0,x_1|z_0),$$

where $P(y_0,x_0|z_1)$ denotes the conditional probability of the event ‘no drug taken and recovered’, given that the advice was to take it. The other definitions are similarly.

By the same kind of arguments one can give bounds on the underestimation of the causal effect. One obtains that the recovery rate is increased by at most

$$P(y_1|z_1) - P(y_1|z_0) - P(y_0,x_0|z_1) - P(y_0,x_1|z_0).$$

Note that the increase of recovery rate we are talking about is the increase that would happen if all patients took the drug, also those that have decided not to take it. Therefore the definition of the causal effect relies on the hypothetical result of an experiment where all patients are forced to comply.

For a formal proof of statements of this kind one needs a precise model in which terms as “the recovery rate if all patients take the drug” make sense.

Here we follow the approach of Pearl [1] to formalize causal claims of this kind within graphical models. Random variables $X_1, \ldots, X_n$ are the nodes of directed acyclic graphs and an arrow from variable $X$ to $Y$ indicates that there is a causal effect from $X$ to $Y$. Furthermore, one has to specify the transition probabilities for each node, i.e. for each variable $X_j$ one has the conditional probabilities

$$P(x_j|x_{j_1}, \ldots, x_{j_k})$$

where $X_{j_1}, \ldots, X_{j_k}$ are the parents of $X_j$. The joint distribution on all the random variables decomposes into

$$P(x_1, \ldots, x_n) = \prod_j P(x_j|x_{j_1}, \ldots, x_{j_k}).$$

An essential part of Pearl’s theory is that it distinguishes carefully between the probability measure that is obtained once one has observed that the variable $X_j$ takes the value $x_j$ and the measure that is obtained if $X_j$ is set to $x_j$ by external control. The first one is the usual conditional probability

$$P(x_1, \ldots, x_n|x_j),$$

whereas he denotes the latter one by

$$P(x_1, \ldots, x_n| \text{do } x_j).$$

He formalizes this probability by

$$P(x_1, \ldots, x_n| \text{do } \hat{x}_j) := \prod_{i \neq j} P(x_i|x_{i_1}, \ldots, x_{i_k}) \delta(x_j, \hat{x}_j).$$
The intuition behind this definition is that the values of \( X_j \) do no longer depend on the values of those variables that influence \( X_j \) directly (“the parents of \( X_j \)”) or indirectly (“the ancestors of \( X_j \)”). Hence the transition probabilities “probability that \( X_j \) takes the value \( x_j \), given the value of the parents of \( X_j \)” have to be substituted by the Kronecker symbol. This manipulation, for instance, does not change the probability distribution of the ancestors of \( X_j \). It changes only the distribution of the descendants of \( X_j \). Whereas conditional probabilities reflect correlations among variables, the probabilities obtained by the do-operator reflect causal effects and distinguish between causal directions.

Following [1] the relevant variables in our drug testing problem are \( X, Y, Z \) as already introduced and a latent variable \( U \) that includes unobservable features as personality and physical constitution. The graphical model of the causal structure is shown in Fig. 1.

Whether there is an arrow from \( X \) to \( Y \) should be clarified by the clinical trial. A priori, we assume that there is an arrow. Then the model is specified by the following parameters

\[
P(z), \ P(x|z,u), \ P(y|x,u), \ P(u).
\]

Whether or not and how \( P(y|x,u) \) dependends really on \( x \) is not clear yet. The calculation of \( P(y|\text{do}\ x) \) would require to know these parameters, whereas only the joint distribution on \( X, Y, Z \) is observable. But one can find bounds on the so-called average causal effect [1]

\[
ACE(X \rightarrow Y) := P(y_1|\text{do}\ x_1) - P(y_1|\text{do}\ x_0) = \sum_u \left( P(y_1|x_1,u) - P(y_1|x_0,u) \right) P(u)
\]

in terms of observable quantities. Above, we have already mentioned one upper and one lower bound rather informally, namely inequalities (1) and (2). Following [1] we will call them “natural bounds”. They can formally be proven by the following considerations. As argued in [2] one can chose \( U \) w.l.o.g. such that it can attain 16 = 4 × 4 possible values and such that \( U \) determines \( X \) and \( Y \) deterministically if the actual value \( z \) of \( Z \) is given (compare also [3, 4]). The values of \( U \) can be considered
as a cartesian product of a variable $B$ that determines the patient’s decision $X$ and a component $R$ that determines $Y$, i.e., the physical response to the drug, i.e., to recover or not. The values of the first component are “never take”, “always take”, “comply” and “non-comply” [3]. Following [3] the response behavior to the drug is given by “never recover”, “always recover”, “helped”, and “hurt”. We denote these 4 values by $R = r_1, R = r_2, R = r_3, R = r_4$. In this deterministic model, the only free parameters remaining are $P(z)$ and $P(u)$. Then the average causal effect is given by the difference [1],

$$P(r_3) - P(r_4),$$

i.e., the probability to recover because of the drug minus the probability not to recover because of the drug. Counterfactual statements like “the patient would have recovered without using the drug” are subject of philosophical debates with a long history (see [1]). Therefore it may cause unease to some readers to find causal implications of data based on such terms. However, Pearl has come up with convincing arguments (to our opinion) that counterfactual statements do make sense if appropriate models are available. Provided that one accepts that all variables describing mental and physiological processes are classical random variables the conclusion that it can be represented w.l.o.g. by a 16-state variable seems indubitable. However, the assumption that all mental and physiological states (influencing human decision and health) are described by classical variables, is not self-evident at all. Here we do not participate in the (sometimes speculative) debate on the relevance of quantum superposition and incompatibility of quantum observables for mental processes [4, 5]. We just want to find out which rules in classical statistics can be violated in case quantum uncertainty is relevant for mental and physiological processes.

2 The instrumental inequalities

Within the hidden variable model where $U$ can attain 16 different values one can prove the natural bounds (1) and (2) and even tighter bounds [1]. These so-called instrumental inequalities read [1]:

$$ACE \geq \begin{cases} 
    P(y_1, x_1|z_1) + P(y_0, x_0|z_0) - 1 \\
    P(y_1, x_1|z_0) + P(y_0, x_0|z_1) - 1 \\
    P(y_1, x_1|z_0) - P(y_1, x_1|z_1) - P(y_1, x_0|z_1) - P(y_0, x_1|z_0) - P(y_1, x_0|z_0) \\
    P(y_1, x_1|z_0) - P(y_1, x_1|z_0) - P(y_1, x_0|z_0) - P(y_0, x_1|z_1) - P(y_1, x_0|z_1) \\
    -P(y_0, x_1|z_1) - P(y_1, x_0|z_1) \\
    -P(y_0, x_1|z_0) - P(y_1, x_0|z_0) \\
    P(y_0, x_0|z_1) - P(y_0, x_1|z_1) - P(y_0, x_0|z_1) - P(y_0, x_1|z_0) - P(y_0, x_0|z_0) \\
    P(y_0, x_0|z_0) - P(y_0, x_1|z_0) - P(y_1, x_0|z_0) - P(y_0, x_1|z_1) - P(y_0, x_0|z_1) \end{cases}$$

Note that the problem to identify the causal effect

$$P(y_1 | do \ x_1) - P(y_1 | do \ x_0) = P(y_0 | do \ x_0) - P(y_0 | do \ x_1)$$

is symmetric with respect to the joint substitution $x_1 \leftrightarrow x_0$ and $y_1 \leftrightarrow y_0$. Furthermore it is symmetric with respect to the substitution $z_1 \leftrightarrow z_0$ since, abstractly considered,
Z is only an arbitrary binary variable that influences the patient’s decision. Note that perfect non-compliance would also make it possible to identify the effect of the drug. The 8 inequalities form two groups, namely 1, 2, 5, 6 and 3, 4, 7, 8 such that members of the same group can be converted into each other by those symmetries.

The upper bounds on the causal effect are given similarly by the substitution $y_1 \leftrightarrow y_0$ and reversing the signs of all probabilities:

$$
ACE \leq \left\{ \begin{array}{l}
1 - P(y_0, x_1|z_1) - P(y_1, x_0|z_0) \\
1 - P(y_0, x_1|z_0) - P(y_1, x_0|z_1) \\
-P(y_0, x_0|z_0) + P(y_0, x_1|z_1) + P(y_0, x_0|z_1) + P(y_1, x_1|z_0) - P(y_0, x_0|z_0) - P(y_0, x_1|z_0) - P(y_0, x_0|z_1) + P(y_0, x_0|z_1) - P(y_0, x_1|z_0) - P(y_0, x_0|z_0) \\
-P(y_0, x_0|z_1) + P(y_0, x_1|z_1) + P(y_0, x_0|z_1) + P(y_0, x_1|z_0) + P(y_0, x_1|z_0) + P(y_0, x_0|z_0) - P(y_0, x_1|z_0) \\
-0 \end{array} \right. 
$$

These bounds imply the natural bounds (1) and (2) (for details see (1) and references therein).

### 3 Quantum model of latent factors

Here we do not want to discuss the difficult question to what extent quantum mechanical effects play a crucial role for mental and physiological processes. However, we do not want to base causal conclusions from statistical data on the assumption, that quantum effects are irrelevant in our brain and our body. For doing so, we have to propose a model that generalizes the model above from classical to quantum probabilities. We chose the formal setting of algebraic quantum theory which is general enough to include quantum and classical physical processes.

In this setting, the observable algebra of an arbitrary physical system is described by a $C^*$-algebra $\mathcal{A}$ (see (1), (1)) containing the unity 1. The algebra $\mathcal{A}$ is called the “algebra of observables”. In a pure quantum system with unrestricted superposition principle (“without super-selection rules”) $\mathcal{A}$ may for instance be the algebra of bounded linear operators on an arbitrary Hilbert space. An element $a \in \mathcal{A}$ is positive, written $a \geq 0$ if it can be written as $a = \rho \rho^*$.

A functional

$$
\rho : \mathcal{A} \rightarrow \mathbb{C}
$$

is called positive if it maps positive elements on non-negative numbers. The states are positive functionals $\rho$ of norm 1, where the norm is described by

$$
\|\rho\| := \sup_{a \in \mathcal{A}} |\rho(a)|/\|a\| = |\rho(1)|,
$$

and $\|a\|$ denotes the operator norm of $a$. Every yes-no experiment, i.e. an experiment with two possible outcomes, is described by a positive operator $a$ with $a \leq 1$, i.e., $1 - a \geq 0$ and $\rho(a)$ is the probability for the outcome “yes” if the system is in the state $\rho$. 

6
A physical process changing the system’s state can either be described by a completely-positive map $G^*$ (“CP-map”) on the set of positive functionals with $\|G^*(\rho)\| = \|\rho\|$ or, by duality, as CP-map $G: \mathcal{A} \to \mathcal{A}$ with $G(1) = 1$. In this formulation, the process acts on the state by transforming $\rho$ to $G^*(\rho)\rho \circ G$. Measurements with any finite number $k$ of outcomes are described by so-called positive operator valued measures (“POVMs”), i.e., a family $m_1, m_1, \ldots, m_k$ of positive operators with $\sum_i m_i = 1$. Then $\rho(m_i)$ denotes the probability to obtain the result “$i$”. Note that the POVM does not describe the effect of the measurement instrument on the state. If the state after the measurement is relevant, we have to describe the instrument by a family of $k$ CP-maps $G_1, \ldots, G_k$ with $\sum_i G_i(1) = 1$. If the measurement outcome is “$i$” the state $\rho$ is transformed to $\tilde{\rho}$ with $\tilde{\rho}(a) := \rho(G_i(a))/\rho(G_i(1))$, where $\rho(G_i(1))$ is the probability to obtain the result “$i$”. Hence $G_1(1), \ldots, G_k(1)$ is the POVM representing the measurement. Without observing the measurement outcome, the instrument transforms $\rho$ to $\rho \circ G$ with $G := \sum_i G_i$.

The formal setting for investigating the violation of the instrumental inequalities by quantum latent factors is based on the following assumptions.

1. The advice to take or not to take the drug is perfectly randomized and independent of all other factors.

2. All relevant latent factors influencing the patient’s decision and his response behavior to the drug are described by the state of a physical system in the sense of algebraic quantum theory. This state includes the patient’s mental and physical state as well as noise that influences the decision or response or both. The state is the state $\rho$ of a physical system (in the sense above) described by an observable algebra $\mathcal{A}$. The system is either purely quantum, purely classical, or a mixture of both. Although this may be a too materialistic view on mind and consciousness this approach is more general than any hidden variable model in the literature.

3. To take or not to take the drug is a classical event that either occurs or does not occur but there is no quantum superposition between both. The process of human decision is therefore like a measurement process in its broadest sense explained above. This instrument is described by CP-maps $D_1, D_0$ acting on $\mathcal{A}$. Hence the state $\rho$ is transformed to $\rho \circ D_1/\|\rho \circ D_1\|$ if the patient has decided to take the drug and $\rho \circ D_0/\|\rho \circ D_0\|$ otherwise. If the decision itself is ignored, the process of decision making is described by the process $\rho \mapsto \rho \circ D$ with $D := D_0 + D_1$.

4. The advice to take or not to take the drug is a classical signal that influences the patient’s internal state. The advice to take or not to take transforms the state to $\rho \circ G_1$ or $\rho \circ G_0$, respectively. Here $G_j$ are CP-maps on $\mathcal{A}$.

5. The effect of the drug is to transform the internal state $\rho$ to $\rho \circ E_1$, whereas the natural evolution without drug in the considered time interval changes the state according to the operation $E_0$. The operations $E_j$ are CP-maps on $\mathcal{A}$. 


6. Whether the patient recovers or not is a classical event and is therefore equivalent to a measurement process in the sense above. It corresponds to a yes-no-experiment described by a positive operator $m \in \mathcal{A}$.

7. The advice to take or not to take the drug has no direct causal influence on the health, it influences the probability of recovery only indirectly by influencing the decision. This corresponds to the fact that the graphical model Fig. 1 for the classical setting has no arrow from $Z$ to $Y$.

One may think that it would be more appropriate to assume that the operations $G_j$ and $E_j$ act on different systems: $G_j$ acts on the mind and $E_j$ on the body. But we do not want to restrict our proofs to this assumption. In particular, we emphasize that there may be a part of the body with the property that its quantum state influences the decision and the recovery. This may, for instance, be a cell that influences the production of some hormone that has a causal effect on both mood and health.

For the observable quantities we obtain:

$$P(y_1, x_k | z_j) = \rho(G_jD_kE_k(m))$$

(4)

is for $k = 1$ ($k = 0$) the probability to take (take not) the drug and recover, given that the advice was to take the drug, i.e. $j = 1$ (not to take, $j = 0$). Similarly we have

$$P(y_0, x_k | z_j) = \rho(G_jD_kE_k(1 - m)).$$

(5)

For causal statements the following unobservable counterfactual probabilities are important:

$$\rho(G_jD_kE_l(m))$$

with $k \neq l$. It expresses the hypothetical experiment that we observe the patients decision to take or not to take the drug and prevent him from taking it although he has decided to or force him to take it although he has refused to. In the following we use the abbreviation $m_l := E_l(m)$. Assumption 7 translates to the statement

$$\rho(G_1D(m_l)) = \rho(G_0D(m_l)),$$

(6)

for $l = 0, 1$.

The increase of the recovery probability that is caused by the drug (ACE) is given by

$$ACE = \rho(G_1D(m_1)) - \rho(G_1D(m_0)) = \rho(G_0D(m_1)) - \rho(G_0D(m_0)).$$

Note that $\rho(G_1D(m_1))$ is a sum of the observed probability $\rho(G_1D_1(m_1))$ and the counterfactual probability $\rho(G_1D_0(m_1))$. This reflects the fact that the causal effect of the drug could only be identified if the taking of the drug was decoupled from the patient’s decision to take it. In the next section we will present a model violating the third instrumental inequality. Due to the symmetry of the problem we can violate inequalities 4, 7, 8 similarly.
4 Violation of instrumental inequalities and Bell inequality

The violation of the so-called Bell inequality \[12\] is one of the most convincing arguments supporting the hypothesis that micro-physics cannot be described by classical probability theory. The idea behind Bell’s inequality is that it describes quantitatively the difference between those statistical correlations that appear in quantum theory and those that can be explained by a classical probability space where all uncertainty stems from our missing knowledge on the values of some hidden parameters. These parameters should decide deterministically which event will occur in future. Whereas Einstein, Podolsky, and Rosen (in the so-called EPR-paradox) gave intuitive arguments why quantum correlations may behave rather strange, Bell’s inequality formalized a testable difference between quantum and classical correlations.

As already noted in \[1\] the instrumental inequalities have some formal analogies to Bell’s inequality since they give bounds on the possible correlations between two random variables that are influenced by a common hidden parameter. We took this “formal analogy” seriously and show that the well-known setting that shows the violation of Bell’s inequality can be modified to violate the instrumental inequalities 3, 4, 7, and 8.

We consider a quantum system in $\mathbb{C}^4$ and decompose it into $\mathbb{C}^4 = \mathbb{C}^2 \otimes \mathbb{C}^2$. The two basis states of each subsystem can be for instance the horizontal and vertical polarization of a photon, denoted by $|h\rangle$ and $|v\rangle$, respectively. The superposition

$$\cos(\theta)|h\rangle + \sin(\theta)|v\rangle$$

describes a polarization in the direction of an axis with the angle $\theta$ with respect to the horizontal axis. The polarization can be measured by a polarization filter. All photons that pass the filter are polarized in the direction of the axis of the filter. A photon with polarization $\theta$ has the probability $1/2(1 + \cos(2\theta - 2\tilde{\theta}))$ to pass the filter if $\tilde{\theta}$ is the direction of the filter’s axis. We write the measurement result “1” if it passes and “0” if it doesn’t. Then we consider the so-called singlet state

$$|\psi\rangle := \frac{1}{\sqrt{2}}(|h\rangle|v\rangle - |v\rangle|h\rangle).$$

It has the following interesting property: For each filter both results appear with equal probability. If the polarization axis of filter 1 and filter 2 have the angles $\alpha$ and $\beta$, respectively, the probability that both measurement results coincide is

$$\frac{1}{2}(1 - \cos(2\alpha - 2\beta)).$$

For $\alpha = \beta$ this means that the results are always different and for $\alpha = \beta \pm 90^\circ$ they always coincide.

In the typical setting to show that those kind of quantum correlations are fundamentally different from classical correlations there is a source emitting a photon pair in a singlet state in two different directions and the polarization axis of the two filters are chosen randomly and independently. Bell has shown \[12\] that there exist angles $\alpha_0, \alpha_1$ for the first polarization analyzer and $\beta_0, \beta_1$ for the second such that the correlations
cannot be explained by any hidden variable theory that is local. Here locality means that causal effects between physical systems require physical signals traveling through the space not faster than the speed of light. Explicitly, Bell’s inequality is as follows. Assign the values \( e_j = \pm 1 \) to the result “photon has passed the filter \( j \)” or “photon has not passed”, respectively. Then define the covariance

\[
C(\alpha, \beta) := \sum_{e_1 = \pm 1, e_2 = \pm 1} e_1 e_1 P(e_1, e_2 | \alpha, \beta),
\]

where \( P(|\alpha, \beta) \) describes the joint distribution on the measurement outcomes given the position of the filters. Then Bell’s inequality states that

\[
|C(\alpha_0, \beta_0) + C(\alpha_0, \beta_1) + C(\alpha_1, \beta_0) - C(\alpha_1, \beta_1)| \leq 2
\]

is satisfied whenever any hidden variable determines both measurement results in advance, i.e., before one has chosen the filter angles. In contrast, with the singlet state one can achieve the values \( \pm 2\sqrt{2} \) if the angles are chosen appropriately. The factor \( \sqrt{2} \) describing the difference between quantum and classical correlations will also appear in the violation of instrumental inequalities below.

Meanwhile, experiments of this kind \cite{13, 14} have given strong evidence for the fact that micro-physical effects are really in good agreement with quantum theory and hence in contradiction to any local hidden variable theory. Since the experiment above is one of those that cannot be explained by any local hidden variable model it is straightforward to use this setting to construct a causal toy model for patient’s decision and his physical response that violates the instrumental inequalities. Let the left polarization filter initially have the angle \( \alpha_0 \). The advice to take the drug turns the filter to the angle \( \alpha_1 \). The result of the left polarization measurement is the patient’s decision. The right filter is initially in the position \( \beta_0 \). The drug turns the filter to the position \( \beta_1 \). The measurement of the right photon decides whether the patient recovers. This is shown in Fig. 2

In this setting the decisive conditional probabilities are given by

\[
P(y_j, x_k | z_l) = \frac{1}{4} \left( 1 - (-1)^{j+k} \cos(2\alpha_l - 2\beta_k) \right).
\]

This can be seen as follows: The indices \( l \) (advice to take/ not to take) and \( k \) (taken or not) determine the angles \( \alpha \) and \( \beta \) of the filters. The probability that the patient’s decision (0 or 1) coincides with his response to the drug (0 or 1) is given by \( (1 - \cos(2\alpha_l - 2\beta_k))/2 \). The probability that the results disagree is \( (1 + \cos(2\alpha_l - 2\beta_k))/2 \). The probabilities for the results 1 and 0 in the first measurement are 1/2 each, regardless of the measurement angle. This gives an additional factor 1/2. Here we will not really need the general setting using CP-maps as described in Section 3. In order to show, that the experiment described above fits in the general formalism we shortly give the definitions of the CP-maps \( G_j, D_k, E_l \) in an informal way. The maps \( G_0 \) and \( G_1 \) describe the turning of the first filter by the angle \( \alpha_0 \) or \( \alpha_1 \), respectively. \( D_0 \) and \( D_1 \) describe the operations on the system caused by a vertical polarization measurement if the result is negative or positive, respectively. \( E_0 \) and \( E_1 \) correspond to the filter rotations by the angles \( \beta_0 \) and \( \beta_1 \), respectively. The yes-no experiment that is given by polarization a measurement of the second photon (with respect to the vertical
Figure 2: Unrealistic toy model of human behavior. The process of decision making and the process determining the physical response to the drug are influenced by a common quantum state.
axis) is described by the operator $m$. Hence the operators $E_0(m)$ and $E_1(m)$ describe polarization measurements with angles $\beta_0$ and $\beta_1$, respectively. Let $P_1^\alpha$ and be the projector onto the subspace of $\mathbb{C}^2$ spanned by

$$\cos \alpha |h\rangle + \sin \alpha |v\rangle$$

and $P_0^\alpha$ be the projector onto the orthogonal subspace. Then $G_j \circ D_k$ is the CP-map

$$a \mapsto (P_k^{\alpha_j} \otimes 1) a (P_k^{\alpha_j} \otimes 1).$$

Here we have assumed for simplicity that the polarizator is not a filter that absorbs some photons and let the others pass but we assume that it splits the photon beam into those with vertical and those with horizontal polarization. Otherwise the operation $D_0$ would be more difficult to describe formally since it annihilates the photon completely.

The positive operators $m_j = E_j(m)$ are given by

$$E_l(m) = 1 \otimes P_1^{\beta_l}.$$ 

By applying the CP maps $G_j$ and $D_j$ to $m_l$ we obtain

$$G_j D_k(m_l) = P_k^{\alpha_j} \otimes P_1^{\beta_l}.$$ 

Due to

$$P_1^{\alpha_j} + P_0^{\alpha_j} = 1$$

we have

$$G_0 D(m_l) = G_1 D(m_l) = 1 \otimes P_1^{\beta_l}.$$ 

This shows that equation (9) is satisfied.

It is almost obvious, that the average effect of the drug is zero since in both filter positions the probability to pass is 1/2. If we would decouple the taking from the patient’s decision the recovery probability was in both cases 1/2 whether the drug was taken or not.

This does not mean that the drug does not have any causal effect on the patient’s health at all: The drug might help the patients that have decided to take it and could hurt the others if they had been forced to take it. Hence the effect is only zero in the average for a hypothetical experiment where all patients are forced to take the drug, even those that would have decided against it. Since we have already argued that the average causal effect is zero, the third instrumental inequality is violated if we find polarizator positions $\alpha, \beta, \gamma, \delta$ such that

$$P(y_1, x_1|z_0) - P(y_1, x_1|z_1) - P(y_1, x_0|z_1) + P(y_0, x_1|z_0) - P(y_1, x_0|z_0) > 0. \quad (9)$$

For doing so, we show that we can chose the angles such that

$$P(y_1, x_1|z_0) = \frac{1}{4} (1 + 1/\sqrt{2}) =: a^+$$

and all the other four terms should be

$$\frac{1}{4} (1 - 1/\sqrt{2}) =: a^-.$$
The equation $P(y_1, x_1|z_0) = a^+$ is satisfied if

$$\alpha_0 - \beta_1 = 90^\circ \pm 22.5^\circ.$$  

By setting

$$\alpha_1 - \beta_1 = \pm 22.5^\circ$$

we achieve that $P(y_1, x_1|z_1) = a^-$. With

$$\alpha_1 - \beta_0 = 90^\circ \pm 22.5^\circ$$

we have $P(y_1, x_0|z_1) = a^-$. By

$$\alpha_0 - \beta_1 = 90^\circ \pm 22.5^\circ$$

we obtain $P(y_0, x_1|z_0) = a^-$. By

$$\alpha_0 - \beta_0 = 90^\circ \pm 22.5^\circ$$

we achieve $P(y_1, x_0|z_0) = a^-$. All these equations can be satisfied if

$$\beta_1 = 0^\circ, \; \alpha_0 = 67.5^\circ, \; \beta_0 = -45^\circ, \; \alpha_1 = 22.5^\circ.$$  

Then the left hand side of inequality (1) is

$$a^+ - 4a^- = 1/4(-3 + 5/\sqrt{2}) \approx 0.134.$$  

Hence the third instrumental inequality claims the average causal effect to be about 13% although it is zero. Note that in this setting it was essential that there is indeed a causal effect of the drug on the recovery - sometimes negative and sometime positive depending on the patient’s decision. Hence the conclusion that the drug influences patient’s health is true nevertheless.

However, we present a modified version of the Gedankenexperiment where every classical statistician should come to the conclusion that there is a causal effect although the drug does not influence health at all. This version is even more analogue to the violation of Bell’s inequality, actually it is just a reinterpretation of it. Assume as above that some randomly selected patients are advised to take or not to take a drug, respectively. Not everyone complies but we can identify the non-compliers afterwards. After waiting for a while some of the patients (randomly selected) are given another drug. Since it is given in the presence of the doctor, we exclude the possibility of noncompliance here. Then we observe which patients have recovered. We describe the experiment by 4 observed binary random variables $X, Y, Z, W$, where $X, Y, Z$ are as in Section 3 and $W$ is the taking of the second drug. As in Section 3 the there is a latent variable $U$ that influences decision and recovery behavior. The complete causal structure is given by the graphical model in Fig. 3.

Whether or not there is an arrow from $X$ to $Y$ should be clarified by statistical data.

Now we consider once more the singlet states and assume that the advice to take the drug turns the filter position from $\alpha_0$ to $\alpha_1$. As above, the result of the measurement at the left filter is the patient’s decision. In contrast to the setting above, the taking
of the drug does not have any effect on the second filter. The second filter is turned from angle $\beta_0$ to $\beta_1$ by the second drug. With the definition of eq. (8) the singlet state can produce a joint measure on the outcomes such that

$$C(\alpha_0, \beta_0) + C(\alpha_1, \beta_0) + C(\alpha_0, \beta_1) - C(\alpha_1, \beta_0) = \pm 2\sqrt{2},$$

for appropriate polarizator angles $\alpha_j$ and $\beta_j$. In analogy to Bell’s original argument, this value for the sum of covariances cannot be explained by any classical variable $U$ in the graphical causal model of Fig. 3 if there is no causal effect from $X$ to $Y$. The classical statistician should therefore come to the erroneous conclusion that there must be a causal effect from the first drug on the recovery.

Admittedly, we do not know of any example, where classical statistics draw causal conclusions based on Bell’s inequality. However, we want to point out that causal conclusions based on classical probability theory may even fail if the physiological and mental processes that are decisive for human behavior are sensitive to quantum noise. It is not necessary that the mental and physiological processes themselves are non-classical.

5 Some instrumental inequalities are still valid

We will prove that the group 1, 2, 5, 6 of instrumental inequalities is still valid in the quantum setting of Section 3. Due to the symmetry of the problem it is sufficient to prove only the first one given by

$$ACE \geq P(y_1, x_1|z_1) + P(y_0, x_0|z_0) - 1.$$

It can be shown using simple operator inequalities. We have to show that

$$\rho(G_1D(m_1)) - \rho(G_1D(m_0)) \geq \rho(G_1D_1(m_1)) + \rho(G_0D_0(1 - m_0)) - 1. \quad (10)$$

We show this by simple calculations with operators. Note that

$$G_0D_1(1 - m_0) \geq 0, \quad (11)$$
since $1 - m_0$ is a positive operator. The reason is that $1 - m$ is positive and $1 - m_0 = 1 - E_0(m) = E_0(1 - m)$ is positive because it is obtained by the application of the CP-map $E_0$ on $1 - m$. Similarly, the application of the CP-maps $D_1$ and $G_0$ conserve positivity. By the same arguments, $G_1 D_0(m_1)$ is positive. Hence we obtain

$$G_0 D_1(1 - m_0) + G_1 D_0(m_1) \geq 0.$$  (12)

Inequality (12) is equivalent to

$$G_0 D_0(m_0) + G_0 D_0(1 - m_0) + G_0 D_1(1 - m_0) + G_1 D_0(m_1) \geq G_0 D_0(1)$$

Using $D_0 + D_1 = D$ we obtain

$$G_0 D_0(m_0) + G_0 D(1 - m_0) + G_1 D_0(m_1) \geq G_0 D_0(1).$$

This is equivalent to

$$G_0 D_0(m_0) + G_1 D(1) + G_1 D_0(m_1) \geq G_0 D_0(1) + G_1 D(m_0).$$

By $G_1 D(1) = 1$ we obtain

$$G_0 D_0(m_0) + 1 + G_1 D_0(m_1) + G_1 D_1(m_1) \geq G_0 D_0(1) + G_1 D(m_0) + G_1 D_1(m_1),$$

and

$$G_1 D(m_1) - G_1 D(m_0) \geq G_1 D_1(m_1) + G_0 D_0(1 - m_0) - 1.$$ (13)

Applying the state $\rho$ to both sides, we obtain inequality (10). The second, fifth, and sixth instrumental inequality follow similarly due to the two symmetries of the problem according to the substitution $z_1 \leftrightarrow z_0$ (corresponding to the substitution $G_1 \leftrightarrow G_0$) and a common substitution $x_1 \leftrightarrow x_0, y_1 \leftrightarrow y_0$. Note that the substitution $y_1 \leftrightarrow y_0$ corresponds to the substitution $m_j \leftrightarrow 1 - m$ and $x_0 \leftrightarrow x_1$ to the substitutions $D_0 \leftrightarrow D_1$ and $m_1 \leftrightarrow m_0$. Hence the second symmetry corresponds to the operator substitutions $D_1 \leftrightarrow D_0$ and $m_1 \leftrightarrow 1 - m_0$.

The same techniques can be used to prove the more intuitive natural bound (11)

$$ACE \geq P(y_1 | z_1) - P(y_1 | z_0) - P(y_1, x_0 | z_1) - P(y_0, x_1 | z_0).$$

Note that the probability $P(y_1 | z_1)$ is given by $\rho(G_1 D_1(m_1) + G_1 D_0(m_0))$ and $P(y_1 | z_0)$ is given by $\rho(G_0 D_1(m_1) + G_0 D_0(m_0))$. The probabilities that appear as the third and the fourth term in (13) can be obtained from eq. (4) and eq. (3).

We show that the operator inequality corresponding to inequality (11) is true which reads

$$G_1 D(m_1) - G_1 D(m_0) \geq G_1 D_1(m_1) + G_1 D_0(m_0) - G_0 D_0(m_0) - G_0 D_1(m_1) - G_1 D_0(m_0) - G_0 D_1(1 - m_1).$$

Due to $G_1 D(m_0) = G_0 D(m_0)$ this is equivalent (by some elementary calculations) to

$$G_1 D_0(m_1) + G_0 D_1(1 - m_0) \geq 0,$$

which is certainly true. Hence the most intuitive bound, which is probably the best known one, cannot be violated by quantum effects. This is another interesting result.
6 No large-scale entanglement required

The EPR-setting above suggested that the violation of the instrumental inequalities requires large-scale entanglement between the part of the brain where the decision is made and the part of the body where the disease is located. We emphasize that large-scale entanglement of this kind is not necessary. Consider two nervous cells, one sending a signal to any endocrine gland that produces a hormone that supports the recovery process and the other one that sends signals to the central nervous system and influence human decisions. We assume that the output of both cells is a classical signal but its internal state cannot completely described by classical variables. Hence the internal process that decides whether the cell sends a signal or not is a quantum measurement process. Then our setting requires that both cells share an entangled quantum state and that their input signals operate on the corresponding internal quantum system. Our considerations show that entanglement between two cells may even produce interesting effects. Such an entangled state may for instance be provided by quantum correlated noise influencing both cells. Note that the EPR-pair provided by the noise may even be “one-particle-entanglement”, i.e., a particle being in a superposition of arriving at one cell and arriving at the other.

Nevertheless we do not want to speculate whether such models may be realistic. It is not really plausible that quantum noise influencing a small number of cells would produce correlations like in our toy model. One may also object that there is a large period of time between the decision and the response to the drug. Hence the violation of the instrumental inequalities requires quantum coherence that is stable for a long time (compared to time scales of decoherence in technical quantum systems). Therefore the violation seems to be even less likely.

However, the main purpose of this paper was to show that some classical causal interpretations of every-day life statistical data could in principle fail if latent quantum effects influence our behavior.

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