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Objective and subjective probability in gene expression

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ABSTRACT

In this paper I address the question of whether the probabilities that appear in models of stochastic gene expression are objective or subjective. I argue that while our best models of the phenomena in question are stochastic models, this fact should not lead us to automatically assume that the processes are inherently stochastic. After distinguishing between models and reality, I give a brief introduction to the philosophical problem of the interpretation of probability statements. I argue that the objective vs. subjective distinction is a false dichotomy and is an unhelpful distinction in this case. Instead, the probabilities in our models of gene expression exhibit standard features of both objectivity and subjectivity.

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1. Introduction

Over the past few decades, advances in experimental techniques have led to surprising discoveries about numerous cellular processes. For example, genetically identical clones of *Escherichia coli* put in the same medium in the same conditions will exhibit differing patterns of phenotypic expression. This could be due to a number of factors, perhaps most obviously, fluctuating concentrations of molecules such as regulatory proteins that can vary from cell to cell. But even holding fixed the concentration patterns of various intracellular components still leads to non-identical outcomes (Elowitz et al., 2002). Similar studies show variability with respect to cell division, cell differentiation, cell death, and essentially every other cellular process that has been studied in detail. For simplicity, I will talk about all of these processes are being included under the broad heading of "stochastic gene expression". For recent reviews of the experimental literature, cf. Eldar and Elowitz, 2010; Huang, 2010; McCullagh et al., 2009; Niepel et al., 2009; Singh and Weinberger, 2009.

How should we interpret these results? According to Gandrillon et al. (introduction, this volume), it has been "demonstrated that gene expression is a stochastic process" and Kupiec (2010) says, "It is now widely recognized that gene expression and cellular processes include a probabilistic component". Many authors agree and often provide similar sorts of explanations for the fundamental reasons behind these results: "Many cellular processes are subject to substantial stochastic variation, because they depend on interactions among a small number of molecules" (Wang and Zhang, 2011), "Gene expression is an inherently stochastic process: Genes are activated and inactivated by random association and dissociation events, transcription is typically rare, and many proteins are present in low numbers per cell" (Paulsson, 2005), and "All cellular events directly or indirectly depend on probabilistic collisions between molecules" (Paulsson, 2005).

1.1. Models and reality

But is it really true that gene expression is an inherently stochastic process? How do we know this? To answer these questions, first, we have to ask what it would mean for gene expression to be an inherently stochastic process. To begin, let's distinguish between models and reality. A model represents the world as being a certain way. We use models to make predictions and to explain phenomena. A model is something we use. Reality is the way the world really is. There are good models that are useful to us since they help us to make accurate predictions or we think they represent some important truths about the world and then there are bad models that fail in some important respects. We think Ptolemy's model of the solar system is a bad model for all sorts of reasons – the primary reason being that we think it fundamentally misrepresents the sun and all the planets as traveling around the Earth when, in fact, the Earth and the other planets travel around the sun. But Ptolemy's model is a model nevertheless. In fact, Ptolemy's model is quite good at making certain kinds of predictions – at least as good as Copernicus's heliocentric model in this respect (I refer to the actual model of Copernicus – we could do far better by Kepler's time). What makes for a good model is an extremely difficult question, but it is clear, for example, that despite the example of Ptolemy, models need not represent everything in perfect detail and it can even represent the world falsely. For example, good models can contain idealizations of point-mass

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particles, infinitely deep water, or frictionless planes; these misrepresentations of reality do not guarantee that they are bad models.

It is usually fairly straightforward to say whether a model is stochastic. "Stochastic" is synonymous with "probabilistic" where some of the probabilities are non-trivial (between 0 and 1). What we do know is that molecular biologists regularly use stochastic models to predict and explain various biological phenomena. What happens in a cell depends, in part, upon the location of various molecules inside it. The births and deaths of molecules can be modeled probabilistically leading to "random" fluctuations in concentrations. A Langevin equation, which is a stochastic differential equation, is used to model their movements through the fluids in a cell. Poisson processes are used to model the length of time required for transcription and translation (Paulsson, 2005). We could go on, but there is no need. Stochastic models are everywhere in molecular biology.

We want to understand what these stochastic models are telling us about the world. It seems that in order to know this, we need to know what probabilistic statements mean. This is the goal of providing an "interpretation of probability" which is an answer to the question of what probability statements mean – what makes them true, if they are true. A natural question to ask is whether these probabilities should be understood as "objective" or "subjective". Roughly speaking, this is asking for whether the probabilities represent real facts about the world or the system in question or merely represent facts about our minds or our beliefs. Perhaps we only use probabilities because we are ignorant of some important variables and we want to estimate the results without being too far off. Then we might ascribe subjective probabilities representing how sure we are of the outcome. On the other hand, perhaps the movements of molecules in the cell are irreducibly or fundamentally chancy and indeterministic in the way that we might think that the radioactive decay of an isotope is indeterministic. Then it seems the probabilities would be objective features of the world. But these are not the only two possibilities.

While this is a natural question to ask, I will argue that the words "objective" and "subjective" are so loaded with semantic implications about what would follow from each that it turns out that the probabilities in question are not usefully described in either way. In this paper, I will not be offering any definitions of what it would take for a probability to be objective. I do think that the distinction can be helpful to make in some contexts since there are fairly clear cases of each. However, as a general classification tool for sorting probabilistic claims, it is rather unhelpful and even downright harmful and I will argue that gene expression is precisely the kind of example that shows this to be true.

2. Determinism and indeterminism

We began with quotations that suggest that the process of gene expression itself is stochastic. This is a kind of "ontological" as opposed to "epistemic" understanding of stochasticity and so the probabilities in question would surely be classified as objective. Here it seems that the implication is that the world is genuinely indeterministic. Clarifying the concept of determinism is an important and difficult philosophical project. Some things are clear – for example, that we should not equate determinism with predictability (Suppes, 1993; Franceschelli this volume). But other aspects are not so clear. For example, despite appearances to the contrary, it is not clear that classical physics is deterministic, nor that modern quantum theories are indeterministic. There are difficult conceptual and technical issues involved (cp. Earman, 1986; Butterfield, 2005; Hoefer, 2010). But I think the concept of determinism is clear enough for our purposes. The world is deterministic if the exact state of the world at a time guarantees what will happen in the future. It is indeterministic if the exact state of the world is consistent with multiple, possible futures. Gene expression would thus be indeterministic if the question of whether a gene will be expressed in a given cell in a given time frame is not determined even by the exact state of all of the cellular and environmental components at a given time.

What arguments could be given that gene expression is genuinely indeterministic? One possibility is starting from an indeterministic process and showing step by step how this leads to gene expression being indeterministic. For example, if we knew that quantum mechanics was indeterministic and we knew how indeterministic quantum processes were responsible for individual gene expression events, and we could calculate the probabilities of these events, then we could show that gene expression is genuinely indeterministic. But obviously, no such science exists. We do not have a detailed understanding of how quantum mechanics and molecular biology are connected. If we accept a certain kind of determination of the biological by the physical, then in theory, quantum probabilities could bubble up. But there is no reason to think that the probabilities that result will be anything other than numbers extremely close to 0 or 1 for any particular event. While this would mean that gene expression was indeterministic, the models in question often predict probability values such as .5 and so these values could not be explained in this way.

It is worth pointing out here that there is a philosophical literature on the question of whether evolutionary processes are genuinely indeterministic and more generally, the question of how to interpret the probabilities found in evolutionary theory, such as in models of genetic drift. Many of the arguments and positions in that literature will parallel obvious positions about gene expression. For example, Rosenberg (1994) argues the biological world is deterministic (or so close that it doesn't matter) and the probabilities are subjective, while Brandon and Carson (1996) and Sansom (2003) argue that they are objective and represent genuine indeterminacy. However, Millstein (2003), Sober (2011), and Werndl (2012) convincingly argue that we simply don't know if evolutionary processes are indeterministic and so the probabilities that appear in evolutionary theory must be consistent with either an underlying determinism or indeterminism.

In fact, our simple distinction between models and reality can help to make clear why we should not expect a good argument for indeterminism from these theories. I mentioned that molecular motions are often modeled with a Langevin equation. This model is based on the idea of the Brownian motion of particles. Strictly speaking, Brownian motion assumes that the particles move about and collide randomly with other particles. But we do not think that the particles *actually* move randomly. Instead, we think that they are governed by the dynamical laws of mechanics which themselves are in almost every circumstance, modeled quite well by Newton's laws of motion. In fact, we have a theory of why a stochastic model could work so well under the assumption of an underlying deterministic Newtonian dynamics. As the number of collisions of particles increases, various averages become better and better approximations to the actual movements. In the limit, the averages are perfectly modeled by random collisions and so when the actual number of collisions is very high but finite, say on the order of 10^{21} collisions per second, then we should think that while the movement of a particle as determined by collisions is actually deterministic, it is very closely approximated by a stochastic model which treats various kinds of collisions as "averaging out". Sober (2011) uses a coin tossing model of Diaconis (1998) based on work with Keller (1986) to argue that while initial conditions might deterministically lead to a particular coin toss outcome, they can "average out" in the right way such that it could be objectively correct to say that the probability of this coin landing heads = .5. This is similar to how statistical mechanics uses an underlying deterministic dynamics to make probabilistic predictions about the increase of entropy in a system (Le Bellac this volume).

The worry goes deeper. There are debates about whether quantum mechanics is itself indeterministic. Given that various quantum theories really are meant to ultimately govern all kinds of interactions, such as those that operate within the cell, if quantum processes are fundamentally deterministic, then biological processes must therefore also be deterministic. But are quantum processes deterministic? We don't know. There are indeterministic interpretations such as the Copenhagen interpretation and there are deterministic interpretations such as Bohmian mechanics. Both agree on the relevant macro-facts that lead to cellular interactions. If the mere fact that stochastic models are used in biology meant that biological processes were indeterministic, we could settle the debate about quantum mechanics. But it is pretty clear that looking at molecular biology is not the way to settle this particular debate.

Worse, there appear to be theorems that directly show that we couldn't possibly have observational evidence for indeterminism (or determinism). Bertin (this volume) shows the difficulties in separating the two concepts in practice and Suppes (1993) and Werndl (2009) argue that Ornstein's theorem (Ornstein, 1974) effectively shows that the choice between deterministic and indeterministic models is necessarily underdetermined by any currently possible empirical observations. Wüthrich (2011) disagrees with the general result for the case of quantum mechanics, but for reasons that will not apply in the molecular biology case.

Whether the world is fundamentally deterministic is a difficult question. But it is not answered by pointing out that we have good models in molecular biology that have stochastic elements. And even if molecular processes are fundamentally indeterministic, there is no reason to think that the probabilities that are generated in a model of gene expression represents these fundamental chances. If we did know the exact internal state of the cell, perhaps it would still be indeterminate if and when a gene product will be produced. But it is doubtful that the probabilities would remain unchanged from the models we currently have. Rather, they would all be very close to 0 or 1. The probabilities that arise from our models do not represent fundamental, irreducible chances. We must look elsewhere for their interpretation.

3. Interpreting probabilities

There are a number of "standard" interpretations of probability in the literature that have been proposed as the ultimate meaning of probability statements. For a good, brief survey, see Hájek (2011). If we knew what probability statements meant in general, we would know what they mean in this specific case. It is not clear what counts as a good interpretation, but as a first pass, it looks like there are at least two desiderata – first, the interpretation must make the axioms of the mathematical theory of probability true. If your interpretation says it is possible for the probability of an event to be 6.2 then it is a bad interpretation. A more complicated desideratum is that the interpretation should explain how and why frequencies seem to be related to probabilities and how probabilities can be a good guide to evidence and decision making.

Perhaps the oldest interpretation is called the "classical" interpretation such as described by (1814). Here, the probability of an event is simply the fraction of the total number of possibilities in which the event occurs. For example, the probability of rolling an even number on a six-sided die is 3/6. Obvious problems immediately arise such as when there is not a unique way to divide up all of the possibilities. What is the probability that Bob is in France given that he is in Europe? We could count each country as a possible location or each geographical region of equal area as equally likely, or we could find the total fraction of people in France relative to Europe and treat Bob as a random individual. Each of the three methods will almost certainly lead to a different answer. Another difficulty arises when considering the possibility of fundamental bias. For example, it looks like a coin has two possible outcomes – heads or tails. But how can we make sense of a biased coin that has a probability of heads of .75? There is no easy way according to this interpretation.

In the 19th century, various versions of frequency interpretations of probability first appeared. The actual frequencies of the outcomes of various trials satisfy the axioms and it is plausible that when we say the probability of a man in the United States having a heart attack between the ages of 60 and 65 is 1/2, that we do in fact simply refer to the actual frequency of heart attacks in this group. Various versions of frequency theories have been defended such as Venn (1876) who allowed only finite frequencies as well as those who consider hypothetical infinite sequences of trials such as von Mises (1957). Both versions of frequentism have well-known problems (Hájek, 2011). A coin tossed only 3 times and then destroyed might have a probability of heads of 1/3, which seems wrong. If we instead ask what the relative frequency would converge to in the limit as we toss the coin infinitely many times, it is unclear why there should be some specific fact about exactly what would happen in that case. Saying what would "probably" happen doesn't help.

Various versions of propensity views exist where probability represents some kind of physical propensity or disposition for a given set up to produce certain results. Karl Popper famously thought that single-case propensities fit the probabilities in quantum mechanics quite well while Gilles (2000) and others develop views that allow long-run propensities that do not apply to single cases and so, for example, a coin tossing setup may have the physical disposition to lead to a coin coming heads roughly half of the time in a thousand tosses without actually having any particular propensity for an individual toss.

Subjective views of probability have a long history, but it took until the 20th century for their most rigorous formulations. Here, probabilities represent the degrees of belief of some agent. You can get a grip on degrees of belief by asking, for example, how much an agent would be willing to bet on the truth of some proposition with stakes of say, $1 if they win the bet. If they would be willing to bet $.50, then it seems that their degree of belief in that proposition is .5. Ramsey (1926), de Finetti (1937), and Savage (1954) are considered among the modern founders of this view.

Each interpretation has its followers and arguments on its behalf. But of course each also has its problems. I myself think it is quite clear that none of these could possibly ground all of our uses of probabilities. As we will see in the next section, a number of authors agree and develop a pluralistic view in which different interpretations apply in different circumstances. A common view seems to be that there are two (or at least two kinds of) correct interpretations – an objective one and a subjective one.

3.1. Classifying interpretations

The project of interpreting probability has a long history. Ian Hacking's *The Emergence of Probability* (Hacking, 1975) is a philosophical history of the origins of probability theory from roughly 1660 until Hume's *Treatise* in 1738. Hacking forcefully argues that both objective and subjective uses of probability have been with us since the beginning. As he puts it, probability is "Janus-faced", named for the two-faced god of the Romans (Hacking, 1975: 12).

A number of philosophers have argued that there are at least two different interpretations or kinds of interpretations of probability that are correct in different cases. Famously, Rudolf Carnap believed there were two useful measures, which he called probability_1 and probability_2 (Carnap, 1945). Probability_1 is the "degree of confirmation" in the sense that, $P_1(X|K)$ is roughly speaking, the logical probability of X given background knowledge K. Probability_2 is a measure of long-term frequencies.

Ian Hacking (2001) says that Carnap has things roughly right, but he calls his interpretations "frequency-based" and "belief-based". Carnap defines his probability measures rather precisely and Hacking purposely does not so it is far from clear that he really has the same thing in mind. I think the best way to read Hacking is that he does not believe that there are just two useful interpretations. Rather, he thinks that there can be a variety of slightly different things that we might mean but that they can basically be categorized into two categories. Hacking argues against "dogmatism" which says there must be exactly one of these interpretations that is correct in all cases or even all cases in science.

David Lewis (1980) thinks that Carnap was right that there are two kinds of probability, but he disagrees about what they are. He calls the two interpretations "chance" and "credence" where "chance" refers to objective, single-case probabilities made true by non-mental features of the world. Single-case quantum probabilities are the ideal case for objective chances, but Lewis assumes that these quantum chances can "bubble up" to larger, macroscale phenomena. But they are not the same as the actual frequency of some type of event nor are they simply defined by something like a long-run frequency. Exactly how Lewis can get these chances within his philosophical system is a long and difficult story, but it suffices to say that these chances, if they exist, are objective in the relevant sense. On the other hand, Lewis also defines "credence" as a probability measure. These are the subjective probabilities of Ramsey and de Finetti, which Lewis says measures reasonable degrees of belief.

Donald Gilles (2000) takes at least four different kinds of interpretations seriously, but he classifies them into two groups – objective and epistemic. Frequency and propensity accounts are classified as "objective" while the classical and subjective accounts are classified as "epistemic". Gilles classifies the logical account of probability as a version of classical probability and thus it counts as epistemic.

Once we allow for a pluralistic view of probability, it is easy to slip into thinking that objective probability refers only to the fundamental, irreducible chances posited by theories like quantum mechanics. But this is a mistake. Frequency views already show us a way to have mind-independent probabilities "in the world" that are consistent with determinism, but this is certainly not the only way. Other accounts can be found in the literature that are meant to apply in special circumstances such as "deterministic probabilities" (Strevens, 2003), "counterfactual probabilities" (Lyon, 2011), "deterministic chances" (Glynn, 2010), and "mechanistic probabilities" (Abrams, forthcoming). Elliott Sober has argued (Sober, 2000, 2010) that we might simply treat probabilities as fundamental postulates in a theory thus rendering them objective. We can call this the "no-theory theory" of probability. Each of these interpretations tries to capture the possibility of objective, macro-level probabilities that are consistent with an underlying deterministic dynamics.

3.2. Objective and subjective probability

There are numerous ways of trying to spell out the meaning of "objective" and "subjective" but a rough characterization might be that objective probabilities are meant to be "in the world" while subjective ones are meant to be "in our heads" or at least dependent on features of our knowledge or beliefs. This doesn't seem to be a straw man characterization as both sides seem to accept this kind of division while arguing that one side of the division makes no sense or can't be useful at least for certain, special cases, for example, in scientific applications.

While something like the objective vs. subjective distinction seems to be very common, it is not that helpful in understanding many kinds of probabilities. This is because the natural way of reading the distinction does not provide a neat classification for existing views. Individual interpretations often have a flavor of both (and sometimes try to avoid key features of each) such that classifying the interpretation doesn't really tell us much and in fact, can be misleading. There are at least two primary reasons for this problem: 1) Subjective probabilities cannot merely represent purely psychological states of agents. These states could not hope to follow the axioms. For example, since no one is logically omniscient, no one is clever enough to have a degree of belief 1 to all of the statements that are logical truths. Real agents like us aren't that smart. Instead of representing purely psychological states, subjectivists think of probability as some kind of measure of "reasonable belief" or idealized belief. Yes, your degrees of belief are functions of what you yourself belief, but also functions of the way the world is. Arguments that degrees of belief must follow the axioms show what rational agents *should* do – not what real agents *actually* do (Hájek, 2011). Some subjective probabilities thus have a flavor of objectivity to them. It is a mind-independent fact that A and B are exclusive if they are and subjective probabilities must respect this. Thus rational credences satisfy some of the features of objective probabilities.

Second, it seems that we want to locate some probabilities such as the probability of a coin toss coming up heads or a gas diffusing into a larger volume box or a gene being expressed in a given location in a given time interval as being "in the world". These should be objective probabilities. Surely the probabilities of statistical mechanics, such as the fact that the probability of an ice cube melting in warm water is very high, are not dependent on our psychological states. So these probabilities are objective. But at least in some of these cases, we have deterministic models for how these work. Given the exact initial conditions, only one outcome is possible. Thus it seems that if there are probabilities in these cases, they must be subjective at least in the sense that they are based on incomplete information about the phenomena. Yes, we can use probabilities to predict the outcome in a particular case. But if we knew more, we could make better predictions. Thus the probabilities seem subjective or at least have a subjective flavor to them.

In fact, statistical mechanics is a very good model for how to think about gene expression. Paulsson (2005) implies that the stochasticity of gene expression derives from the collisions of molecules inside the cell. While we do not have proof that this is the case, it is a reasonable hypothesis. But even if this is true, it would not immediately answer our question about the interpretation of probabilities in gene expression since after all, there is a long history of debate about the interpretation of probabilities in statistical mechanics. For example, in just one recent volume on probabilities in physics (Beisbart and Hartmann, 2011), Uffink (2011) argues that we should understand these statistical mechanical probabilities as subjective, while Lavis (2011), Callender (2011), and Maudlin (2011) all disagree. However, each of these three authors defends a very different account for the source and interpretation of these objective probabilities. Even if we accept the link between gene expression and statistical mechanics, we are still left with many fundamental questions unanswered.

Probabilities that seem to represent objective features in the world are consistent with underlying deterministic dynamics, which apparently leaves no room for objective chance. Subjective degrees of belief must be reasonable degrees of belief, which are guided by objective features of the world such as physical symmetries. Therefore with even the briefest of careful inspections, the objective/subjective distinction seems to break down.

3.2.1. Classical and logical interpretations

To see a specific example of how the distinction can quickly break down, let's examine the classical theory of probability as expounded by Laplace and others. Laplace is clear that what makes two cases "equally possible" is our evidence with respect to these possibilities. As he says, probability "is relative, in part to our ignorance, and in part to our knowledge" (Laplace, 1814, p. 6). This is clearly an epistemic view. To get probabilities, Laplace endorses a "Principle of Indifference" which says that if you have no evidence favoring one possibility over another, they should have the same probability. Clearly different people can have different evidence and so assign different probabilities to the same phenomena. But Laplace did not intend his view to be subjectivist in the personalist sense of Ramsey or de Finetti who think that agents with exactly the same evidence might nevertheless have different degrees of belief. Laplace aims to be capturing an objective fact about our uncertainty of the situation. These objective facts are typically characterized by symmetries in the system in question. The symmetry of the two sides of a well-balanced coin or the sides of a fair die is a property of the objects in question and thus if physical symmetries guide our probabilities, then it seems that they are objective.

Descendants of the classical view include the logical views of Keynes, Jeffreys, and Carnap. In fact it was Keynes who clearly articulated and named the "the Principle of Indifference" (Keynes, 1921). Keynes considered probabilities to be degrees of partial entailment. Here, the relevant symmetries that determine probabilities are logical symmetries that arise from our language. While Carnap calls his logical probabilities "degrees of confirmation" and uses them to model evidence, they are meant to represent objective facts about just how much evidence one proposition provides for another. Jeffreys (1939) started a program which today is called "Objective Bayesianism" in which probabilities fundamentally represent degrees of belief and uncertainty as in all Bayesian views, but in his view, prior probabilities should be common to all and thus he was opposed to "Subjective Bayesianism". The obvious problems with classifying well-developed views such as Objective Bayesian views as either objective or subjective shows the inherent problems with such categories. I agree that some uses of probability have this "logical" flavor. But with our pluralist view of probability in mind, it still might be that the probabilities in molecular biology do clearly fall in one category or the other.

4. Final discussion

The categories of objective and subjective to classify probability statements have always been with us even if the words haven't. Incidentally, the meaning of these words has definitely changed through time in philosophy. Nadler (2006) points out that they have nearly the opposite meanings in Descartes (1984)′ *Meditations* as they do today. Zabell (2011) attributes the change in usage to the popularity of Kant's usage.

From the very beginnings of the development of probability theory, probability has played both roles. There have been individuals such as Richard von Mises or Karl Popper who have insisted that subjective probabilities are meaningless. Others, such as Bruno de Finetti, insist that all probabilities are subjective. But a more nuanced view is called for. What we can say is that it would be a mistake to think that just because our model is stochastic, the probabilities must therefore represent irreducibly objective chances. There is no reason to think that our models represent all of the relevant variables in the sense that even if we included more information about the exact state of the various molecules involved this would not change the probabilities of the various outcomes. This could very well be a case where a stochastic model can do a very good job of representing a deterministic process. In fact, given that we do not want a biological model to represent everything about the world (such as the precise temperatures of each molecule or the effects of gravity due to an orbiting asteroid), it may well be that the best possible model is in fact a stochastic one.

A natural response upon seeing this conclusion is that we should infer that the probabilities in question are therefore subjective; that our model is only stochastic because we are ignorant. I think this is also a mistake. It may well be true that an omniscient Laplacian being with unlimited computational powers would have no need for a stochastic model of gene expression. Perhaps the being would use models of molecular interactions more directly. Perhaps it would even use quantum mechanical models and have no need for simpler "higher level" models. But this does not mean that the probabilities are subjective.

Subjective probabilities are standardly interpreted as degrees of belief. Degrees of belief are often interpreted as something like betting quotients. It is, at best, unclear how these could play a role in science. How could the scientific explanation of phenotypic heterogeneity in an organism cite our degrees of belief about its internal states? Our models of gene expression do not vary between different cognitive agents. If one scientist is more willing to bet on a certain pattern of cellular differentiation than another, this does not change the model that the scientific community thinks is best. But these are natural implications of the subjective view of probability.

My inclination if I were forced to choose is that "objective" is a much better term than "subjective" to describe these molecular probabilities. They represent facts about the world and not about our beliefs. They do not vary between agents. They are robust under various kinds of perturbations of the parameters. Given the history of the objective vs. subjective debates and what I think the proper uses of these terms are, "objective" seems to me the better choice. Even if we are not being forced to choose and we have say, "neither" or "both" as options, it still may be that "objective" is appropriate. However, we should not simply stop there. It can be extremely misleading to say that these probabilities are objective without further, detailed discussion of what this means.

Various "objective" interpretations of probability have been developed: actual frequency views, hypothetical relative frequency in the limit views, propensity views of various kinds, and plausibly, the classical, logical, or Objective Bayesian views can also be called objective interpretations. All have severe problems as general views of probability and I think that none of these interpretations as described by their defenders does a very good job of capturing what the probabilities mean in the models of gene expression that we are considering.

The most natural interpretation of "objective" is that the process involved is genuinely indeterministic. Fundamental, irreducible, stochastic dynamical laws would get us objective probabilities. But we cannot draw this conclusion in our case. While a number of philosophers as well as physicists, statisticians, and others have tried to develop interpretations of probability that are consistent with "deterministic chances", others simply declare that the project is hopeless on its face, or have general arguments against the very possibility, and every view developed so far developed has its critics. But I do not wish to just add another interpretation to the list. I have no interpretation to offer here. I am merely pointing out that the problem is not an easy one.

Typically, those who object to the very possibility of deterministic chances have in mind something like the following argument:

an omniscient being would not use the stochastic models of gene expression that we are examining. Therefore, the probabilities in our models must be the result of our ignorance and therefore they must be subjective (or at least, not objective). If this is simply what you mean by subjective, I have nothing to say. I agree; they do not represent fundamental, indeterministic laws of nature. However, this view of subjectivity is so extreme that it would classify processes like the melting of an ice cube, the diffusion of a gas in a box, or the movement of proteins in a cell, in the same way that it treats the "probability" in the claim, "I will wait and call my mother tomorrow, she is probably asleep right now" – namely, as fundamentally about our degrees of belief. This is far too high of a price to pay and introduces far more problems than it solves.

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