This is a transcript of ***Brain Science Podcast*** **#31**, an interview of György Buzsáki about his book, *Rhythms of the Brain*, conducted by Dr. Ginger Campbell. This episode aired February 22, 2007.

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Ginger Campbell: This is the ***Brain Science Podcast***, the podcast for everyone who has a brain, and I'm your host, Dr. Ginger Campbell. On the Brain Science Podcast we explore how recent discoveries in neuroscience are unraveling the mysteries of how our brains make us who we are. For more information including show notes, links to previous episodes, and information about how to subscribe, please go to the website, brainsciencepodcast.com . We also have a discussion forum at brainscienceforum.com , and you can send me email at docartemis@gmail.com .

"Synchrony is an important mechanism to bring elements of a system together in time - it's critical - then I think everybody agrees that it's a pretty important mechanism. The only thing we can add to it is that oscillations do a fantastic job of doing that and they do it almost for free."
- György Buzsáki, author of Rhythms of the Brain

INTRODUCTION

Transcript note: (György Buzsáki's name is pronounced *"Yuri Bi-shock-i")*

GC: Welcome to Episode #31 of the Brain Science Podcast. Today's episode is an interview of György Buzsáki, author of Rhythms of the Brain. (...snip...) In this interview Dr. Buzsáki explains not only why brain rhythms are so important but also why the study of brain rhythms has been relatively neglected compared to some other areas of brain function. This is a complex subject but I think Dr. Buzsáki did a very good job of giving some down to earth examples that I think you will appreciate.
So let's get on into the interview.

(music)

INTERVIEW

GC: György, I'm really happy to have you on the show today..

GB: Same here.

GC: The reason that I asked you to be interviewed about your book, *Rhythms of the Brain*, is that I've had several listeners write to me asking me to do this book; I think several months ago, the first person who asked me about this book wanted me to read it so that I could explain it to them.. (laughter).. I still don't think I could do that. But I thought we might start with some basics for the sake of my listeners who really don't have any background in physics and engineering. Can you talk a little bit about the basics of oscillations, oscillations being another word for rhythms?

GB: Well, nature is full of cyclic phenomena. If you just think about movement of heavenly bodies, the calendar, the life cycles in biology, respiration, heart beat, menstrual cycles.. these are all rhythmic phenomena. And many, many man made objects are also based on rhythms or oscillations, such as clocks, radios, TVs, computers, cell phones, even our electrical lines are transmitted through 60 Hz or in Europe 50 Hz.. and one may think about, that what is the use of all this repetitive phenomena? And one consideration that is it's an artifact, or it's a side effect of how things are put together, or you can think about it differently, that it these are essential parts of the mechanism. So all these man made machines, I've been thinking about, that indeed I can imagine a way how to put together a computer without a one or five megahertz clock just using random timing, but it would be incredibly difficult.

What oscillations do usually is to synchronize. Continuing on this line you can imagine that you can design a car which wouldn't move smoothly, but would speed up and then slow down, speed up and slow down irregularly. And if the average speed of a regular car and this car would be identical, then on a smooth terrain they would do a pretty good job. Perhaps it would be not very convenient to sit in these cars, but eventually they would get in to the goal at about the same time. Now the problem is when the terrain is difficult and adjustments of the car is not so easy. And this is where oscillators come in, because they can be perturbed very effectively.

Now, just to give you an introduction from physics, what usually neuroscience does or biological sciences do, is when they want to quantify something or make it objective they go to other disciplines. And this what of course people who work in neurobiology and are interested in oscillators, they read about oscillators in physics or engineering and usually get two packages.

One of the packages is called "harmonic oscillators." Just think about the pendulum clock, whose motion is almost perfectly sinusoid. Now the good thing about these pendulum type oscillations is that they are very predictable. So, for example, a perfect pendulum oscillator is the orbit of the moon around the earth. What I mean by predictability is that I look at the motion of the moon for a short period of time, and I have the phase information and I can predict the phase of the moon tomorrow or in fact a million years from now. So, when you would like to design something that is predicting events in time, then harmonic oscillators are very useful, and in fact there are many examples in the brain where these particular kind of oscillator are exploited for exactly this purpose.

Now, the other family of oscillators are referred to as "relaxation" or... it's a complicated name, but let's call them "pause oscillators." Now, these are a little different, because here, discrete events repeat with relative long intervals. For example, when you clap your hands, there is a discrete event followed by some silent period. Or I gave an example in my book about the dripping faucet. The drips repeat at certain intervals, and if you have an observation period which is short, within two drops, there is no way to predict the occurrence of next event. Here, the timing precision is not so good but it has other good features, which are convenient for neuron systems - maybe they can be perturbed easily. So if you tap on the faucet, then you can have a premature drop, determined exactly by the timing of your perturbation.

If there are 100's of 1000's of these faucets and we can simultaneously perturb them, then they can be so-called phase reset, so they can start with the same phase, and we have to do this only once and if they are pretty identical then they keep doing the dropping together. This is usually referred to as synchrony and reset-ability.

So the advantage of these relaxation type of oscillators is that they are very effective to synchronize in large numbers if they are identical. I can refer the readers to works of Stephen Strogatz who is a physicist, or mathematician Nancy Kopell.. they have worked quite a bit about these relaxation or pause type of oscillators and how large numbers of these neurons can be synchronized very effectively. Obviously these are just two classes and there are lots in between and we can discuss how they behave when we get to the neuron oscillators.

GC: So, in the brain, do we have any oscillators that really act like either one of these pure types?

GB: Yes.. it's pretty easy to find oscillators ....most of the oscillators in the brain belong to the family of relaxation oscillators. So, if you have a single neuron, for example - it's a very typical pulse type of oscillator - if you depolarize the neuron and you block certain channels that prevent the neuron from habituation or from adaptation, then the neuron will spike forever. And there is one period which is the action potential and then there is a longer period which is the "in between", the charging phase or the incremental phase. Now, the advantage of the relaxation oscillator - so, this is a typical example - a single neuron is a relaxation oscillator.

Now the interesting thing is that when you put many many many many of these neurons together and you measure their mean field activity, this is their average activity, they become sometimes very sinusoid... some variety of reasons - and their collective behavior looks like a harmonic oscillator. So, we have several examples where we know that the elements that are critical in generating the oscillations are made up from relaxation oscillators: however they are tied together in a monolithic form, that they form a harmonic oscillator. So now we have an example that has features of both. And the good features of both is that they can be perturbed effectively, but they are also good timekeepers.

Another aspect of relaxation oscillators that I'd like to mention is that here, one can separate the input phase from the output phase. The output phase means when an effect is going out; like in our faucet case is, the drop of water is the output, and the incremental phase is when the water accumulates - is the time when the system or the oscillator can be perturbed.

So, the separation of the input output allows that there is a relatively long time when the oscillator can be perturbed, or input can be put into the system, and then it's up to the internal mechanisms of the oscillator that determines when the output occurs. So that's another very simple mechanism how many elements of the oscillator can come together and put their effects shoulder by shoulder and have a strong output.

GC: Now in talking about the neuron as an oscillator, it has also a refractory period when it really can't be perturbed.

GB: Exactly. This is why this is the output phase.

GC: In reading your book, I think the only way to really give it a full understanding would be if I was in the office next to you and went through it chapter by chapter and talked to you about it as I went along, because it obviously represents at least several years of effort on your part. What made you decide to write a book about this subject?

GB: Well.. there has been a lot of debate, exaggeration, denial, and misunderstanding about.. regarding the brain rhythms and brain oscillations. As I mentioned, not only in physics but also in engineering and architecture but also in neuroscience many people thought that this was a byproduct, and for many they questioned as how the brain can perform its complicated products despite the fact that there are these oscillators. But, truth is that wherever I looked in the brain, and whatever mechanism I tried to understand, I always bump into oscillations - it's all levels of neuron organization.

I began to think about it seriously - now what kind of advantages the nervous system can have when oscillators occur. And there are lots of fundamental things that can be solved very effectively with oscillators.

One of the fundamental things about sending messages in the brain from one place to another is that we have to code the information, and information coding entails that every message that is transmitted from one place to another must have a beginning and the end. It's the same with coding for DNA; you have to have a beginning code and an ending one. And that's not trivial in a brain which is interconnected and continuously active. For example, if you are looking at events at the periphery, such as the cochlea, then the beginning of the sound and the end of the sound perfectly signals the messages because these are coded or signaled by extrinsic physical stimuli. But these stimuli are not available in the brain especially during cognitive processes when there are no external timers, so the brain has to come up with these internal timers. So, oscillations are perhaps the best solutions for marking the beginning and the end of the messages, because, as we may be talking about a little bit later, every single oscillation reflects or is associated with the fluctuation of excitability. There is always the period or phase of the oscillator when the activity is maximum and when it is minimum. So, when you go from minimum to minimum, then these time periods can beautifully mark the beginning and the end of a message. So this is one attractive feature.

The other attractive feature is quite recent I would say - perhaps it goes back no more than a decade - is that people acknowledge that there are oscillators in the brain. Everybody knows about sleep spindles or alpha oscillations or Parkinsonian tremor, and various things like that. What was not clear until recently is that it's not only that there are a few oscillators with different frequencies in the brain but there is a *system* of oscillators. What I mean by that, is that several orders of magnitude of time starting let's say with the high frequencies - 3, 4, 500 Hz, which is only a few milliseconds of time window - all the way to tens of seconds, or minutes, are covered by neuronal oscillators. And there is no gap. And if you look at the mean frequencies, and the variability of the range of these oscillation generators, they are overlapping in a regular way, and their mean frequencies happen to coincide with a number of life's natural logarithms. And that was an interesting revelation.. that oscillators exist together, or can exist together; they don't have an integer relationship - in other words one oscillator cannot entrain the other one permanently - but because they are related to each other through irrational relationships, irrational numbers, they can never sustain some permanent activities. For the interference between oscillators, between natural brain oscillators, is always transitional. And this was an attractive feature for many, because it's led to the recognition that this is probably the way how you can generate pictures that look like noise, as well as this is a force that keeps the brain going permanently, and it never comes back to the same state. These are the scientific arguments behind trying to write a book.

The other aspect was more practical, namely that when I gave talks in different departments, biomedical engineering, and sometimes physics departments, and neurosciences departments, and to molecular biology oriented people, I realized that many of the knowledge that I was exposed to are available in various specific publications, and people in various disciplines are exploiting the advantages of oscillators including physics, mathematics, engineering, and membrane physiology, systems neuroscience, even clinical neuroscience, but they have never been bound together into a coherent whole. And when I talk about a specific oscillator, then people come up to me and say, "Oh, it is probably very specific to your favorite structure, or to your favorite species, but there are no general rules."

And I realized that to present a coherent synthesized picture, all this scattered information should come together in a single brain, and cross reference across the information, and somehow simplify it. So my goal was to simplify the existing knowledge and to explain it not necessarily to the layman but to those people who have some background in neuroscience or some serious interest in neuroscience and see how a neglected area of dynamics can represent something very important and fundamentally in the brain.

GC: And I think that your book is a good demonstration of the fact that neuroscience today, in order to be done well, really needs to be a multi-disciplinary field, because you really brought in a lot of stuff from other fields, like systems.. like you said, engineering..

GB: Well indeed that's the case and has always been the case that science progresses when it understands ideas from other disciplines and see what are the commonalities. And, as many of us recognize, neuroscience has progressed in one direction and physics and statistics and certain parts of engineering progressed almost independently and made large movements forward in an area that is called today complex systems. The "complex system" offered a very rich toolkit for neuroscience to think about interactions in the brain in a new way. But it also was very important to realize that many of these ideas are important because you can view things differently but ideas and principles that have a common thread across different disciplines are substrate free. But whenever we want to understand the mechanisms we have to translate these interesting principles into mechanisms on a given substrate. So when I learned, and with other people we tried to say, oh, the brain is a complex system which has particular dynamics and it's non-linear, all these things, it didn't tell me anything. It doesn't tell anything to the average reader, because the mechanisms have to be understood and broken down into pieces. And that's where I think the responsibility of neuroscientists lie, that the hand-waving interesting explanations have to be translated into neuronal mechanisms. And this is where I think the new field of neuronal computation and experimental neuroscience must work together to see how the ideas that spring out from your brain, from your head, can be really tied to reality rather than just express imagination.

GC: Before we get into some more details about the brain rhythms themselves, can you sort of review for my listeners what you see, as we see our inner knowledge today, what the functions are being accomplished by brain rhythms? I think you gave me timing, and prediction...

GB: OK, let me start with a very convincing example I think, and the examples are taken from two individuals who are both physicists from (unintelligible) and (unintelligible) who recorded the behavior of the audience in Budapest Hungary after a performance: let me just start ..(starts a recording).. and you will see what happened (sound of a large audience clapping).. it was a very large performance, the audience obviously liked the actors, and the music, and they are expressing their gratitude now. (*Clapping slowly changes from random noise to synchronized...*)

I think it's already clear that after a few seconds the clapping of the whole population became rhythmic. Now, there are a couple of interesting things that I can use and exploit, to explain why rhythms are so useful for the brain.

The first question one should ask is what is the cause of the emergence of the rhythm? And that's a very tough one.. because there is no real cause that we can point out. The word "emergence" is what is being used, because it starts with a random interaction of a few seeds - some people just happen to clap their hands in synchrony, and with the same rhythmicity, and the surge of the sound of these individuals influenced the neighbours, and eventually the rhythmic clapping becomes dominant. So the interesting thing about it is that it has this bi-directionality. What I mean by that is that once the pattern or the rhythm emerges, then it enslaves every single individual in the room so their degree of freedom decreases, they stop doing their self-organized activity and they become part of the population.

Hermann Hakan, who spends a lot of time ... he's a laser physicist from Germany.. he spends a lot of time thinking about these things.. he's talking about "bi-directional causation" and the interesting thing is that what really happens here is that the elements of the system emerge and produce.. the elements of the system give rise to a new quality - we can call it an "order parameter", or the rhythm in this case - and the rhythm will then cause or effect the elements to do one thing, and not another.

So this is a very fundamental thing, and it makes the questions of the skeptics so difficult to answer is that what many brain scientists ask from us is that, for example, I do believe that brain oscillations are important; if you remove the oscillations without affecting anything else and the brain will be affected. But it is not possible, because the reason why the oscillation emerges is because of the behaviour of the individual elements. The two of them are tied in an interesting bi-directional manner.

Now, the other very important aspect of this very simple single oscillator was that it's very cost effective. What I mean by that is that the goal of hand-clapping is to generate a sound as much as possible. Now, if hand-clapping is rhythmic, the surge of the sound is several orders of magnitude stronger than.. at least it's louder ... compared to the random clapping. The important thing is that this increase of the output can be achieved at no cost. In fact, if you would count the number of claps, or the rhythm of the clapping, during rhythmic clapping of the population, or individual clapping when the rhythm is.. the population clapping is random, then the frequency of the individuals is slower. So in this particular case the individual investment and the energy that's being invested is less, yet the outcome is much stronger.

So, now, translating into the systems of neurons, if the goal of computation is to not only compute something but to transfer that information to target neurons, the best way to do that is synchronize them. Synchrony through oscillations comes for free. Here's an example: during a particular type of epilepsy, called petit mal or generalized epilepsy, very many neurons in the thalamus and the neocortex become entrained into 3 Hz spike and wave. This synchrony can be measured, and it's very obvious by recordings, but because it's epilepsy we thought for a long time that epileptic activity is extremely energy consuming. So it came as a surprise when the methods for measuring energy use with fMRI was applied to these epileptic episodes and they found that many investigators in several laboratories almost simultaneously, they found that both signals became negative when the spike and wave epilepsy emerged, meaning that less energy was used.

Now, this was a surprise, but if you understand the mechanisms of how oscillations come about, and what is the investment of a single neuron, then it is not surprising at all, of course, it is almost obvious. Prior to this recognition, we already knew this, because in 1992 we described a phenomenon - we can call it hippocampal ripples - at 200 Hz, very fast oscillation, and we showed that we can get synchrony- very nice and very tight synchrony - without any change of the firing rate.

So what changes? Individual neurons don't change their firing rate at all. What is changing when synchrony emerges through oscillations is the timing of the neurons *relative to each other*, the result of which is that now the impact of the same neurons when they are firing in synchrony is much more effective. And in fact these ripple patterns have been associated later on in several laboratories with the transferring of information from the hippocampus to the neocortex. This was just one single oscillator.

Now, let's try to think about two oscillators. When two oscillators come together with slightly different frequencies, we get an interference pattern. And the best example for this interference pattern has been provided by John O'Keefe from the University College London. He showed, not only that it occurs, but that it's behaviourally very important. What John observed is that individual place cells in the hippocampus oscillate at a frequency slightly faster than the ongoing so-called theta frequency oscillation. The result of this is very precise timing, but the importance of this that was translated into behaviour is that the phase position of the action potential relative to the ongoing clock cycle, reliably predicted the position of the animal. So, here's a convincing case where we go from the basic features of oscillators through physiology all the way to behavioural significance. And then you can pose other questions - how would this be possible without an oscillator? And I can come up with some scenarios that could be done without oscillators, but it would be very expensive energetically and it would involve a lot more computation and would be a lot more complex. But these are two oscillators.

Now let's think about when many oscillators come together. Now, here's a simple rule that applies to oscillations of various frequencies - the brain is a physical system, as we all acknowledge, and information from one place to another goes through axonal conduction delays as well as when one neuron discharges, its target neuron will discharge later, not only because it takes time for the action potential to go through the axon, but it also, when the neuronal transmitter is released, on the post-synaptic neuron, the neural transmitter has to charge the membrane to threshold - so there is a time delay - a finite time delay of how fast the information can go from one place to another.

And brains are very slow mechanisms compared to computers... so, the consequence of this is if it generates a fast oscillation that has a short time period, then the number of neurons, or the proportion of neurons that can be involved in these fast oscillations are relatively small. The oscillation is typically local. Now, when the time period is long, then there is time that activity propagates from one area, from one set of neurons to many other sets of neurons. So a large volume is involved, the result of which is that the synchrony of the population or the proportion of the neurons that are engaged in this rhythmic activity is much larger. This explains the common observation that slow oscillations are always high in amplitude, or almost always high in amplitude, whereas fast oscillators are small in amplitude. But the important consequence for the purpose of our conversation is that slow oscillators can affect fast ones, in such a way that the phase of the slow oscillator, because it involves very large areas, can organize the activity of the faster ones that emerge locally.

So I gave you at least three examples which I think are quite convincing that even though other possibilities also exist to coordinate activity, oscillations provide the cheapest possible solution.

GC: And given the fact that the brain has such high energy requirements anyway, it seems to make sense that it would use the one that would ...

GB: Exactly. If you talk to anybody who works in this field he'll remind you that our brain uses 20% of our energy; with a newborn it's actually 50% and if you look at the smallest mammal, the tree shrew, the tree shrew uses continuously even during sleep, 50% of all the energy to sustain brain activity. It's very expensive. Evolution must be very careful how it allocates resources.

(Interlude)

GC: The oscillating begins with a single neuron - I mean, even single neurons are oscillating - is that correct?

GB: Yes and no - the important thing that we learned over the years is that it's simple to link oscillators together. So every neuron is an oscillator, the issue is how they get synchronized into an oscillation activity. But in fact, one can make an oscillator where none of the elements individually serve as an oscillator. A mechanical clock is a perfect example of that. You need a mechanism that ties all the elements together to make the clock ticking. And many many oscillations in the brain in fact come about that without... if you record from single neurons, you can record from them for long long long times, and you will never see that there is an underlying oscillation. And this is the main reason perhaps, this explains the skepticism of many investigators in neuroscience that deal usually with one neuron at a time. For example, the ripple oscillations that I just mentioned is a perfect illustration of that. If we would be looking at single neurons for five years, there would be no moment in time, perhaps, when we would say, aha - there is a population output here. But if we begin to look at 50 or 100 together, then it becomes absolutely obvious, and we won't miss any of these events. So, in this case, none of the neurons oscillate, but their cooperative activity produces a perfect sinusoid oscillator.

GC: And there isn't any place in the brain that acts like a pacemaker to control these oscillations - that's what you meant when you said they were an emergent phenomenon?

GB: Not quite.. what I said is that there are many ways to produce oscillators. Yes there are pacemakers. For example, our respiration rhythm is determined by a group of neurons in the pre(unintelligible) nucleus in the brainstem that is responsible for maintaining or pacing the respiration. In the case of hippocampal theta activity, for a long long time we thought that there was a pacemaker in the medial septum, and we pointed to one set of neurons that have pacemaker capabilities - in fact many neurons in the medial septum, cholinergic and GABAergic neurons, we record from them in the slice preparation, in the in vitro conditions when they are disconnected from the hippocampus and every part of the brain, they still can maintain oscillating activity. David McCormick describes in slice preparations of the lateral geniculate of the (unintelligible) of the thalamus of the (unintelligible) that isolated neurons can oscillate perfectly.

Now calling many of these or some of these true pacemakers comes with some burden, because in many cases, like in the thalamus even in the medial septum it turns out that yes, individual neurons have the propensity to oscillate, and under certain circumstances they do, but when they are embedded into a physiological substrate or physiological activity their timing is coordinated by various feedbacks. And even if we have an independent set of neurons, let's say in the medial septum, that can fire at 5 Hz, somehow their activity must be coordinated. And in many cases that kind of coordination comes from their target structures, in our case the hippocampus.

So what we call a "clock" or a pacemaker, and what we don't, is a matter of approach. And if you think about it a little bit, we say, Aha, it's good to have a dedicated clock, but when we go back to the problem of energy, then we would say, Aha, if we have to allocate a set of neurons which would do nothing else, just keep time, that's perhaps not so effective than having neurons that can transform information and affect the firing patterns of neurons, and at the same time, in cooperation with others, they can produce an oscillation.

GC: One thing that confuses me a little bit is that you mentioned in the book the importance of the balance between the excitatory signals coming in and the inhibitory signals - that that was a key to oscillating occurring. So, how does a neuron in an vitro preparation that's isolated ever oscillate?

GB: Well, inhibition and excitation are very important in the brain, but it is not required for an oscillation. Obviously the ocean waves don't have inhibition and excitation in this exposit sense. Oscillation always emerges. It's inevitable when you have opposing forces. A push and a pull, like in the swing, is perfect enough to maintain oscillations. In the brain there are many many opposing forces; if you just think about potassium and sodium, that go in the opposite direction in the membrane, for the individual neurons they are perfectly sufficient to maintain oscillation. No GABAergic inhibition, there is.. no inhibitory neurotransmitter is needed for this. But the inhibition is there in a sense that one force tries to counteract the other force.

Now, in the brain, indeed the two most important opposing forces, when it comes to neurotransmitters, is excitation and inhibition. And it is organized in such a beautiful way that if you would take a single pyramidal cell from the neocortex, for example, and count the number of terminals that are excitatory and inhibitory, it turns out that the number of terminals from inhibitory neurons is only a minority. It's about 15 - 20%. But they are at strategically important position because most of these inhibitory terminals are near the soma and the axon initial segment, and these parts of the neurons are critical for generating the output that is the action potential. So it seems that the inhibitory terminals make sure that the timing of the neuron is right. And in fact that's what happens in many cases of oscillations.

Now, if we continue this argument further about the balance between excitation and inhibition, even though the number of inhibitory terminals are smaller, the inhibitory terminals are very active - and in fact they are about 5 times more active than the principal cells. So, we have fewer inhibitory terminals, much fewer number of inhibitory neurons, but their activity is higher, the result of which is that the total number of EPSPs and IPSPs if I can say these terms to your audience, that is the excitatory inputs and inhibitory inputs per unit time, are exactly the same or almost exactly the same when you consider this time in (..?)seconds. So, it seems to be that there is a balanced system. However, this balance is brought about by fluctuation, because if you zoom in in small time windows then we always see that either inhibition or excitation dominates. And the easiest thing to balance the two opposing forces is through oscillations. So that is the reason why inhibition is so important. Without inhibition there would be no computation in the brain. Why? Well, the second law of thermodynamics clearly states that in physical system if you have only collisions then collisions will produce more collisions and the entropy of the system will increase and there will be no order. This applies also to the brain, of course, and any other physical systems, and the brain is a physical system, is that if we had only excitation, and then excitation would produce only further excitation. In fact, in principle, the action potential of one neuron would lead to the discharge of every single neuron in the brain.

Now, you can call it after Shannon, the information approach, or information theory approach, and it works perfectly - at the periphery - at the first senses. It works good at the retina, at the cochlea, perhaps even at the first relay station in the thalamus, but as you go deeper and deeper into the brain, the variability increases, not because the reliability of the brain is not very good, but because other sources of "noise", quote-unquote, come into the picture, and this quote-unquote "noise" is generated by the brain. And the deeper we go into the brain, what we find is there is more and more independence from the environment. The deepest structure in the brain, if there is such a thing as deep, is the hippocampus, or the prefrontal cortex, because they are multiple synaptic connections, far from either the motor output or the sensory inputs, and, they maintain their activity. But this maintained activity is observed almost everywhere. Visual cortical neurons are active, a little bit less perhaps, but they are still active when we close our eyes or when we fall asleep. Many parts of the brain, for example, again, the hippocampus, they are as active during sleep as in the waking state. The number of action potentials of all neurons, that is, the energy they use, is pretty much constant, independent of what happens out in the environment.

Now this is an interesting issue, of course, is because the brain maintains its own excitability, maintains its own activity, in the absence of external information, or external perturbations. And the question is, what is it good for? Well, as I already mentioned the word 'noise' several times, and physicists and computational neuroscientists, they like noise, because many of the systems they produce wouldn't be able to operate without some energy which is usually supplied with the mechanism of noise. But this noise is generated by the internal activity of the brain at a time when the brain cannot rely on outside sources, but this is the time when brain activity moves forward independently, and sometimes it coincides with sleep which is very difficult to understand what kind of processes go on in sleep, but the trivial example for me is that I can ask you to remember your previous interview with say, Christof Koch, and then I'm sure you can recall that information with just one single question and you go through a whole long process of thinking, and that implies that there are cell assemblies that produce self-organized and perpetuating sequences without any further input. And you can think and talk about these events for a long time. And this is all maintained by internally generated activity. Now this is the internally-generated activity that is independent from the outside world and that is the one that interferes with the incoming inputs. This is the source of noise that is annoying when you are trying to understand the impact of a stimulus on the brain. So this noise, which is considered noise for many, is my most important signal. That's in fact the only source of cognitions - the self-generated or inside-generated activity or internally generated activity of the brain is an absolute requirement for cognition. And there has been very little thought about this, and they are very difficult experiments.

(Interlude)

The self-generated or inside generated activity, or internally generated activity of the brain is an absolute requirement for cognition. It is very difficult to approach this experimentally, especially in animals. But if you are seriously interested about how cognitive information is transferred around from one place to the other in the brain, then we have to consider seriously how the self-generated activity is serving some important functions.

GC: Do you think that another one of the functions of all this self-generated activity is to save energy when an actual signal does come in?

GB: I mentioned a couple of times that nature is "designing" quote-unquote various things to be energy efficient, and volume-efficient, and then wiring-efficient and all these things, but we shouldn't forget that certain problems must be solved, so it's a balance between the needs and goals and energy efficiency. So, to try to answer your question, it seems that in fact from this point of view, it's a waste of energy to maintain spontaneous activity - why do we have a lot of neurons firing when we are drowsy? At the same time this activity makes perception less effective, the inputs are not the same so in fact when you are driving on the highway and getting tired, then your brain takes control and your input is becoming less efficient. So from this point of view it's a disaster. But we have to understand and give some good rationale why is it good in the long run for the brain that it has its own fluctuations.

GC: So you'd be like that's a question we haven't totally answered yet..

GB: We haven't answered any of these major questions but at least we understand now from, thanks to the work from many different laboratories, that the activity during sleep is not a random useless activity. But in fact in many structures where this has been looked at, it turns out that the activity of sequences and patterns in the neurons that are being active in our sleep processes are pretty much the same as the ones that have been used in our waking experience. In fact, (unintelligible) has written a book recently about creativity and discussed a couple of things about how, what could be the mechanism of creativity in the brain; according to her, many of the creative people reported to her that they tried to create in an environment which is peaceful, calm, and they try to fall asleep, but not quite sleep, and whenever the associations occur in an interesting and random manner they can bring it back to wakefulness. Sure, I have fantastic associations every single night in my dreams, but I don't have the ability to bring them back to the waking states. These are the states when the activity of the previous day dominate, but at the same time, other things that happened in our previous life will also emerge, and mix with the recently acquired information. Sleep is the best mixing phase because it's noisier so to speak, but perhaps this noisiness is creating, is using something or serving something very important. Can I give you an example?

GC: Yes, go ahead.

GB: The example comes from Jan Born, in Lübeck, Germany, who has been working on these ideas for quite some time, that sleep is this special slow wave thing that I hypothesized in 1989, very important for consolidating memories. He showed, fairly convincingly that if you give a puzzle that requires a few repetitions to solve, and if you give these puzzles to students who can think about the puzzles but only two or three times which is not sufficient to solve the puzzle, and after this they can go and sleep. Then when they wake up, a fairly high percentage of students can solve the task right away, compared with those students who have been engaged doing something else, implying that during sleep, those representations about the unsolved problem went through various synapses and various parts of the brain, and in the morning, they were, so to speak, consolidated, and the answer was available.

GC: That's even more convincing than the experiments that just show that you have a better memory of something you've studied the next day after you sleep than if you don't sleep.

GB: Exactly: there are also many examples that show that sleep provides an advantage and there may be a savings of 10, maybe 15% that interestingly can be enhanced beautifully by oscillations. Again, I can give you an example from the same laboratory, Jan Born's laboratory, where they followed up the idea of ours, that there is a slow oscillation in the neocortex that is capable of entraining these fast ripples that we thought was critical for storing and consolidating episodic memories. So the rationale was, if this is the case, then we can enhance the magnitude of these slow oscillations during sleep. So what they did is, through EEG electrodes that were placed on the scalp, they were applying electrical currents, while the students were in stage 4 sleep. And as a result of the electrical sinusoid stimulation, the power of the slow oscillation increased, and perhaps this enhanced activity increased the probability and timing of hippocampal ripples (although this hasn't been shown...). But this entrainment of oscillations enhanced the ability of sleep for an additional 10% or so - I don't exactly remember numbers - so those students whose brains were stimulated during stage 4 sleep remembered the memorized items even better than those who had just had a regular sleep.

GC: I think that's a good argument for the whole idea that oscillations aren't just epiphenomena.

GB: It is a good argument, of course, but you can always have a counter-argument - aha: oscillations not only produce oscillations but they made neurons fire more synchronously, contact with the balancing partners were discharged more effectively, and these perturbations did not occur in an oscillatory manner but in a random manner, perhaps the outcome would be the same. Now I have spent a lifetime in oscillations, but I'm the first one to admit that this is a very difficult issue to answer for the reasons that I already alluded to at the beginning that it's a bi-directional causation, and the system that oscillates uses every ingredient, and every ingredient when it works perfectly together produces an oscillation. So whether it's an epiphenomenon or not, it doesn't have a trivial solution. However, it. does. not. matter. If you are looking at the practical aspects of this, because they are there, they can be used, they can be useful for a researcher who is interested in how internal activity of the brain or internal generated activity of the brain is generated, and whether oscillations are epiphenomena or not doesn't really matter as long as he understands the processes that underlie behavior and commission.

GC: That's one big reason why I wanted to have you on my podcast - that's the idea that I wanted really to get communicated to my listeners is that this whole idea of oscillations is a very valuable research tool and an important aspect of trying to figure out how our brains work. Like you say it's pretty much a neglected subject so I wanted to bring it to their attention.

GB: I think if you put it in a different way and say that synchrony is an important mechanism to bring elements of a system together in time, it's critical, then I think everybody agrees that it's a pretty important mechanism. And the only thing we can add to it is that oscillations do a fantastic job of doing that and they do it almost for free.

GC: So I don't think that we're going to have a chance to talk about the hippocampus today, which is something we had thought we might get around to but I really appreciate you taking the time to talk with me today..

GB: My pleasure.

GC: It'll probably be about a month before this podcast actually comes out but when it does I will send you the links so that you can share it with others. Thanks again for your time.

GB: Well most welcome..

GC: OK, bye.

GB: Thank you, bye.

(Music)

GC: You probably figured out listening to this interview that Dr. Buzsáki's book is very technical - it's one that will particularly appeal to the engineers among you. But I really appreciate him coming on to the podcast and helping me understand the material and to share it with you

- The End -

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- Self-organizing processes: The sound of many hands clapping Nature 403, 849-850 (24 February 2000)

4. Hermann Haken (his homepage): German laser physicist who studies bidirectional causation

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5. John O'Keefe (University College, London): along with Lynn Nadel he discovered how the hippocampus forms a cognitive map of the world.

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- "Independent rate and temporal coding in hippocampal pyramidal cells " by John Huxter, Neil Burgess, and John O'Keefe. Nature 425, 828-832 (23 October 2003)

6. David McCormick (Yale University): showed that neurons from the thalamus can oscillate spontaneously

- Neocortical Network Activity *In Vivo* Is Generated through a Dynamic Balance of Excitation and Inhibition (pdf)

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9. Claude E. Shannon : founder of Information Theory

10. Jan Born (University of Lübeck, Germany): experiments with how sleep improves both memory and problem solving

- list of publications

11. The Handbook of Brain Theory and Neural Networks, Michael Arbib 2003

12. Encyclopedia of dynamical systems from Scholarpedia