

The adventures of Mimi the microglia :

A trip through the brain



By **Cogni'Junior**

a project of Cognivence

and Fresco

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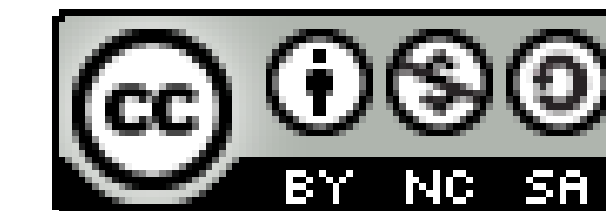
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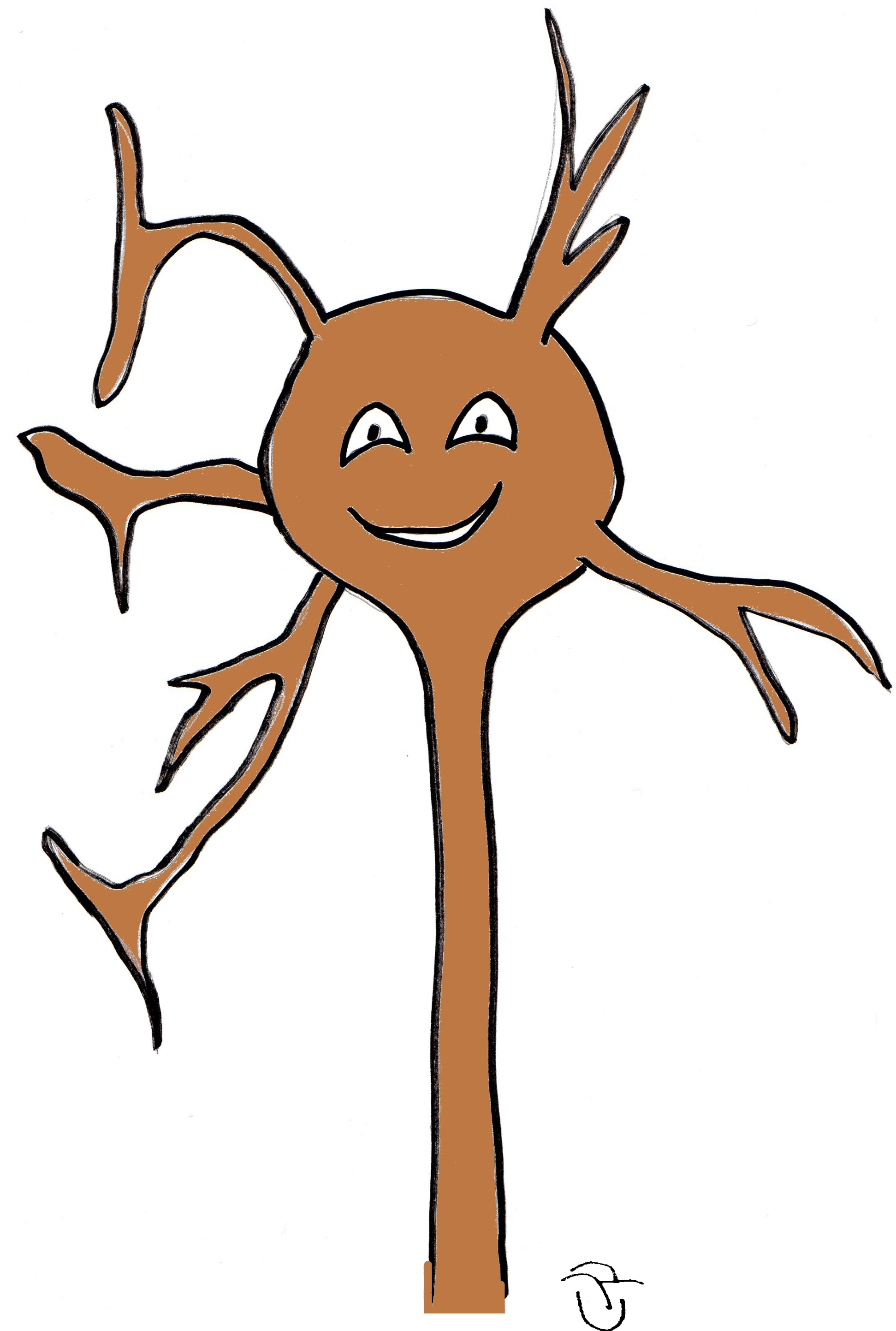
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Drawing :

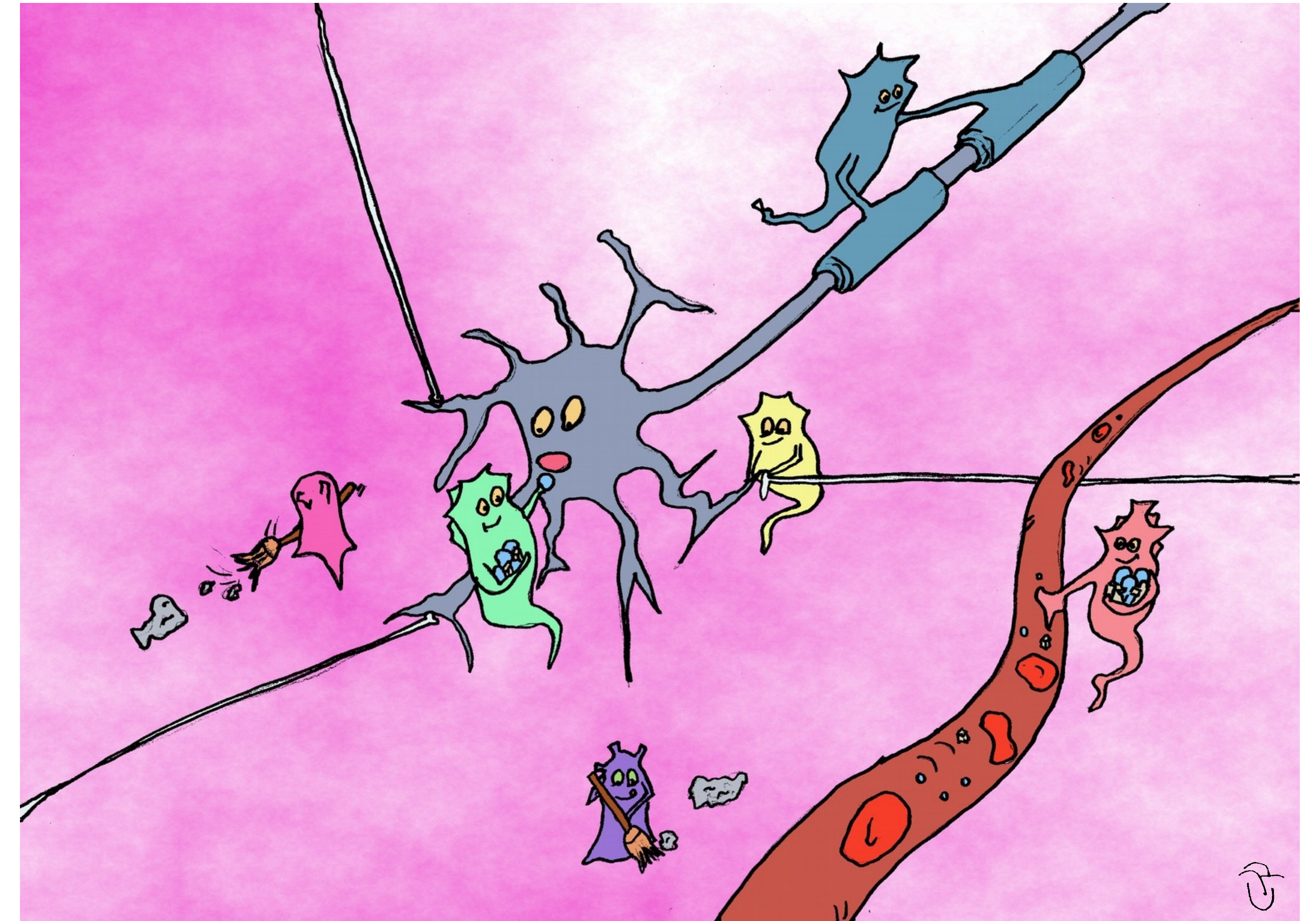
Roselyne Chauvin



“Hi! I’m Nino. I’m going to tell you a story. But first, let me introduce you to my world. It’s a very, very small world. I live inside your body. Actually, inside your brain! ”



I'm a neuron. There are plenty like me! Cousins, sisters, brothers... we're a big family! But neurons are not the only ones around here, there are also glias, who take very good care of us. Some of them feed us, others help us do our work... and then there are the small ones, who clean and protect us.

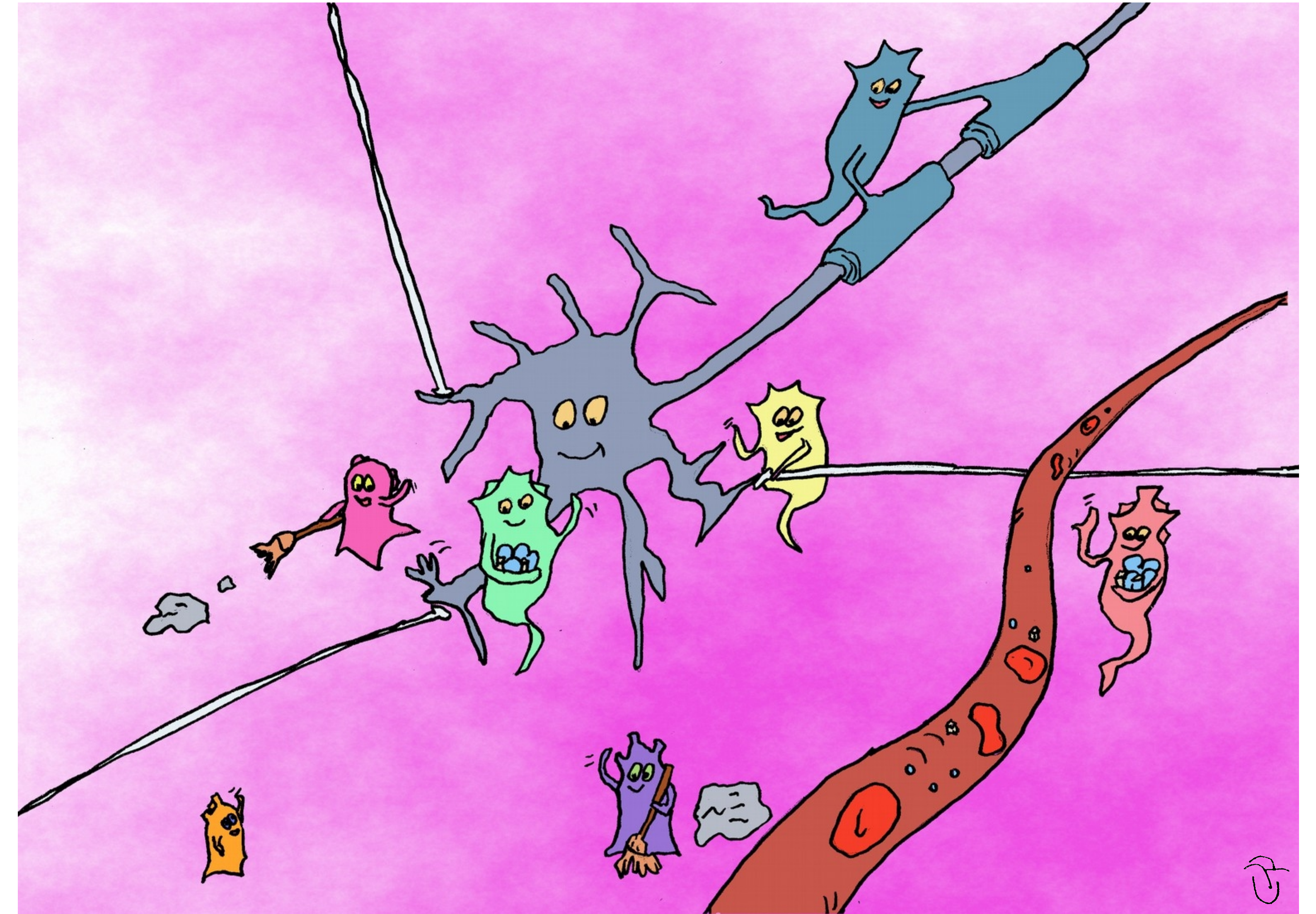


Take a look at Mimi for example.



She's quite small... I'm going to tell you her story.

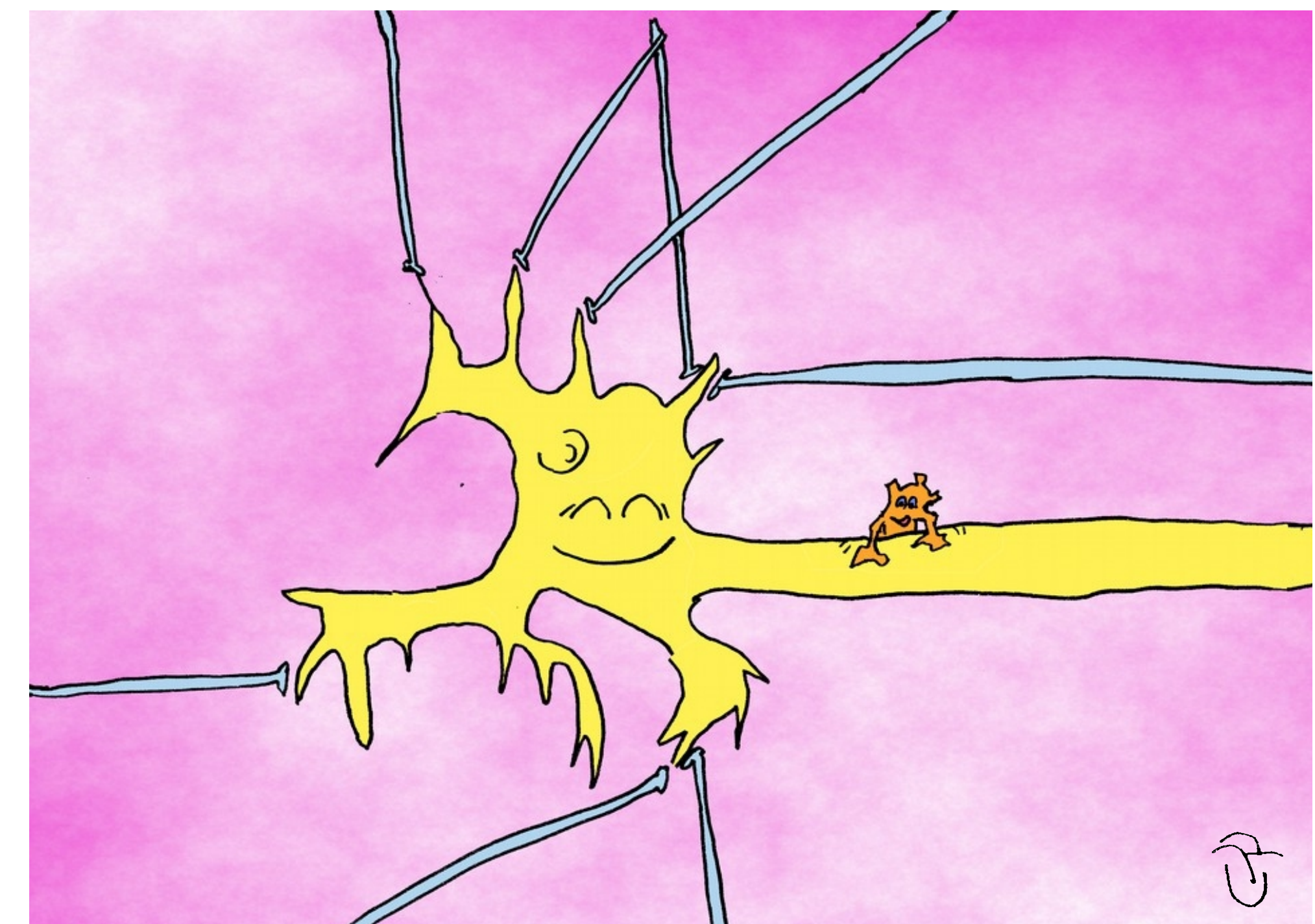
Mimi's days all look alike. She wakes up early in the morning and says hello to everybody: "Hello Astride! Hello Louis! Hello everybody!"



Louis is the neuron Mimi is taking care of. She cleans him, and Louis loves it.

She begins with his head, because it's the easiest part: it's big, it's round, it's the soma.

Then she cleans the neuron's big straight arm, his axon.



Then she cleans the neuron's hair, his dendrites.

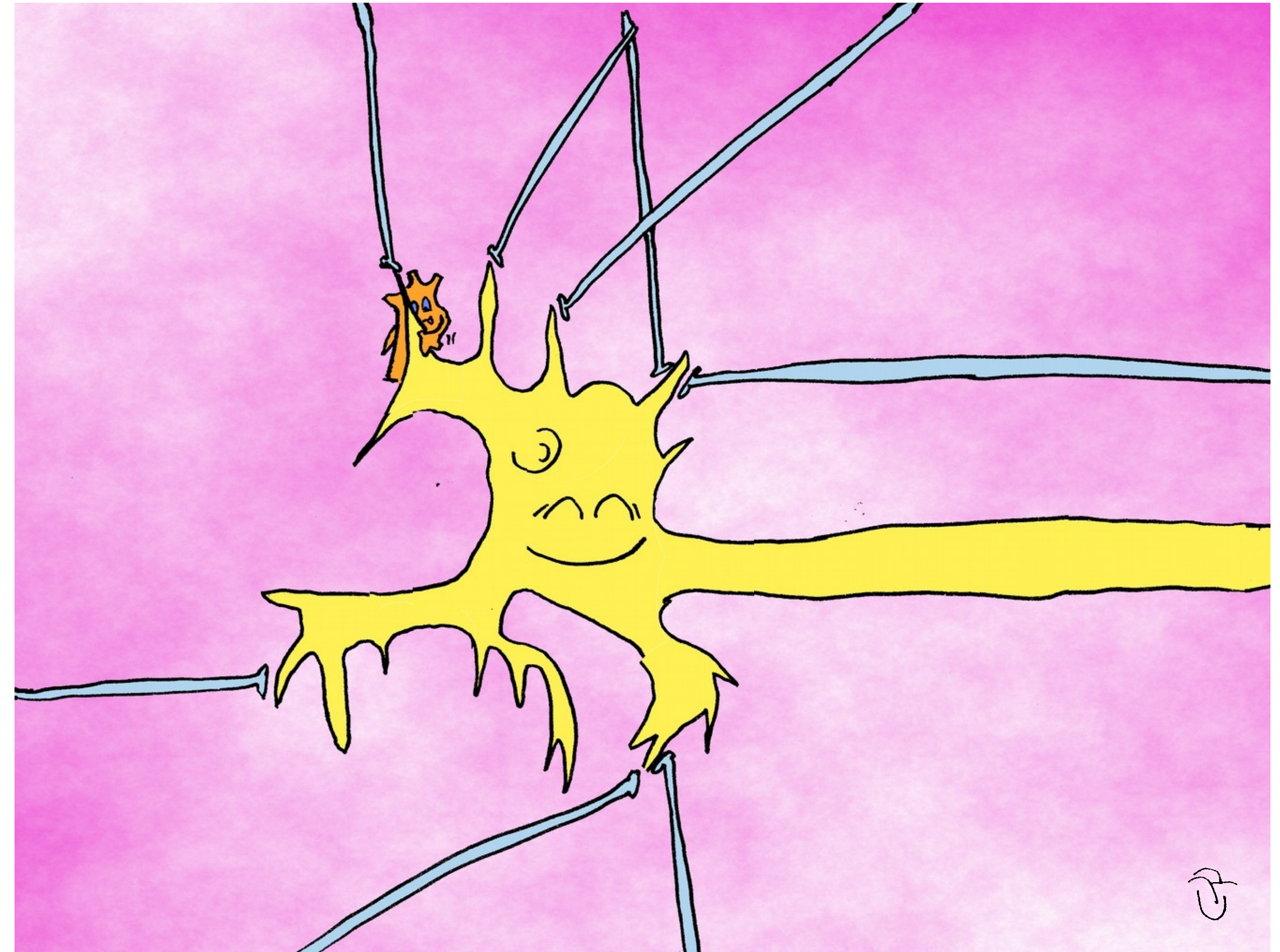
Mimi bends herself in every direction; so as to clean all the small spots... it's exhausting! Today, Louis has worked a lot, and he is complaining about having some tingles in his hair. Mimi is massaging him.

“Mimi, can you massage me a bit harder please?”

Louis asks

— Sure. Is it okay like this?

— Very well! I'm feeling better. Thanks Mimi!”



With this, Astride the astrocyte comes with the afternoon tea:

“ Mimi! Louis! Little break!

— Yeaaaaah!

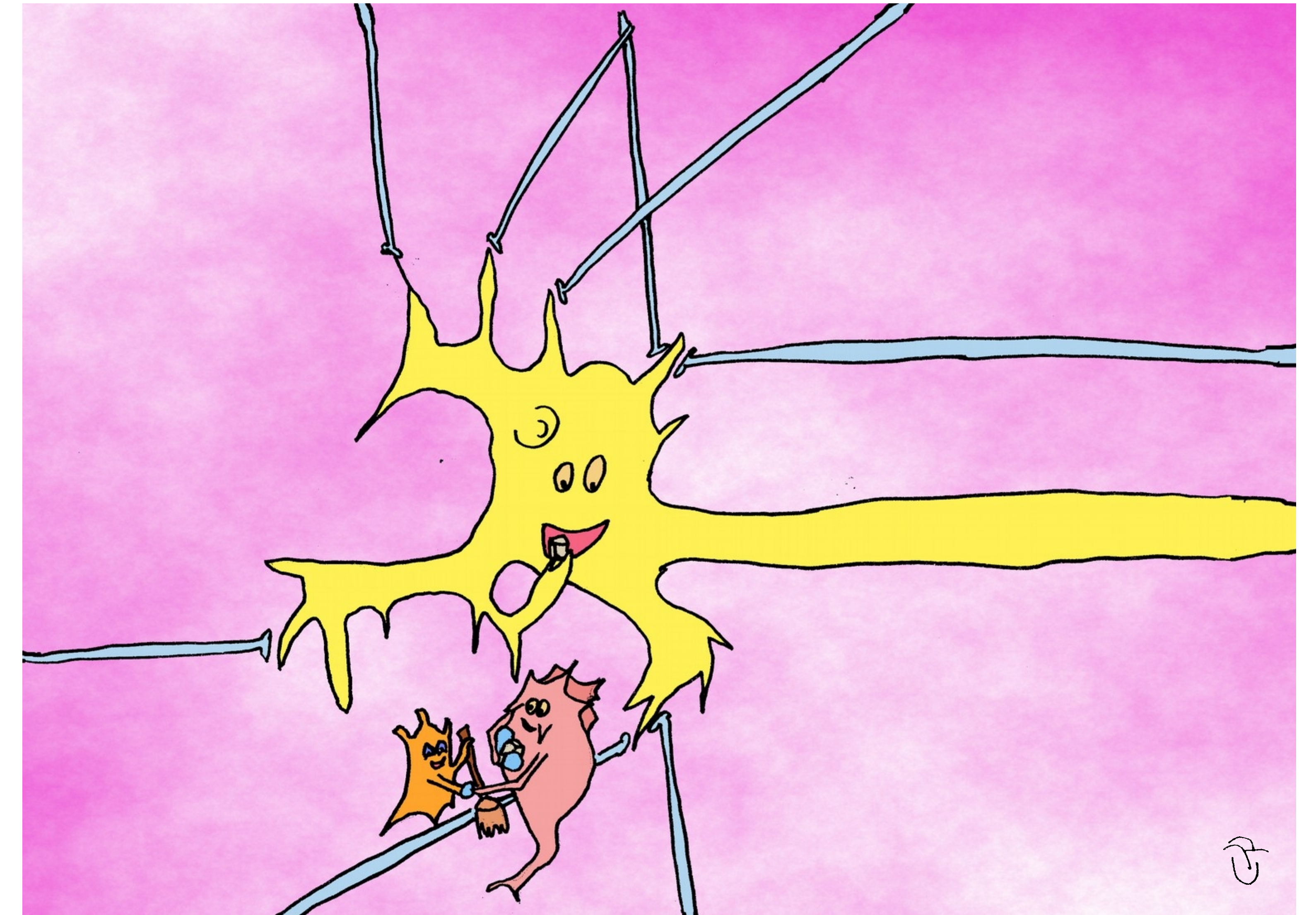
— It looks like you have a lot of work...

— Yes but the pace is slowing down, it's getting much better for me! Louis answers.

— As for me, I've not finished yet, Mimi says, sadly. What about you Astride?

— You're the last ones, after this I'm done with my tea delivery! I'm going to take a little nap. Good luck Mimi!

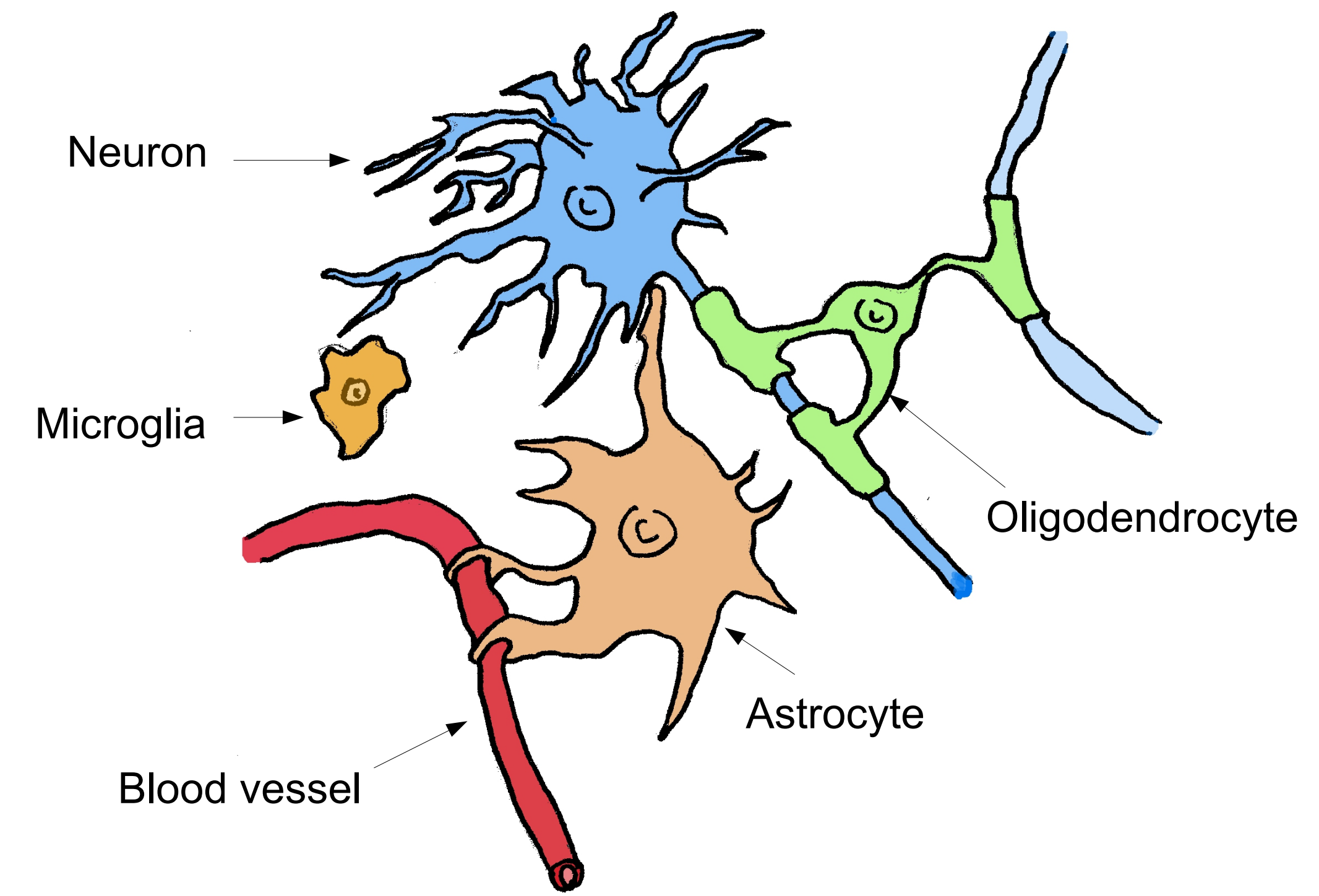
— Thanks Astride.”



To go further...

Neurons are brain cells which process information. But the brain is not only made of neurons. In animals, neurons are actually the minority, because they represent only 10% of the cells. The other 90% are glia cells, which take care of the neurons. Without glia cells, the neurons could not survive. In humans, the proportion of neurons and glia cells depends on the brain area. Depending on their size and form, glia cells are divided into three categories: astrocytes, oligodendrocytes and microglia.

Mimi, the main character of our story, is a microglia. She is an immune cell, surveying the brain for damage and infection, identifying and engulfing dead cells and debris. That is why we say that they are "cleaning" the brain.



In our story, we also meet other characters: Louis, a neuron, and Astride, an astrocyte. Astrocytes are also glia cells : they take glucose and oxygen from blood vessels that are spread all around the brain. They distribute these resources to neurons and other glia cells, which can not feed themselves. That is why Astride is delivering tea to Mimi and Louis.

Even after the tea break, Mimi is feeling really tired! But she goes back to work.

Then, she sees another microglia coming. It's Boulie, and she doesn't look like she's working! Boulie is wandering around and she looks happy.

She comes close to Mimi and asks her:

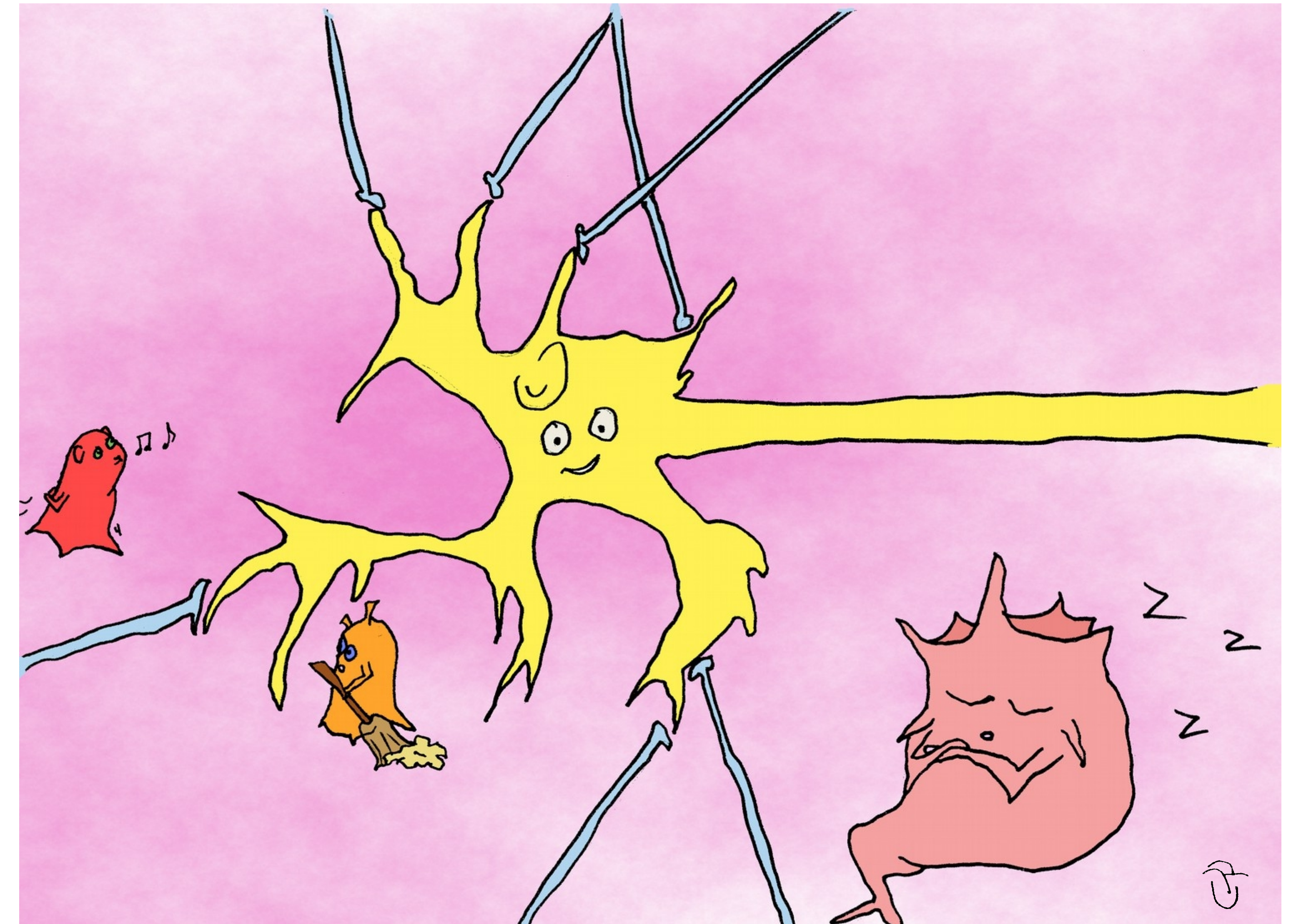
“_ What are you doing? Why don't you take a break to have tea?”

_ I've already had it...

_ That fast?

_ Yes, I still have work to do.

_ Won't you rather come and play with me?”



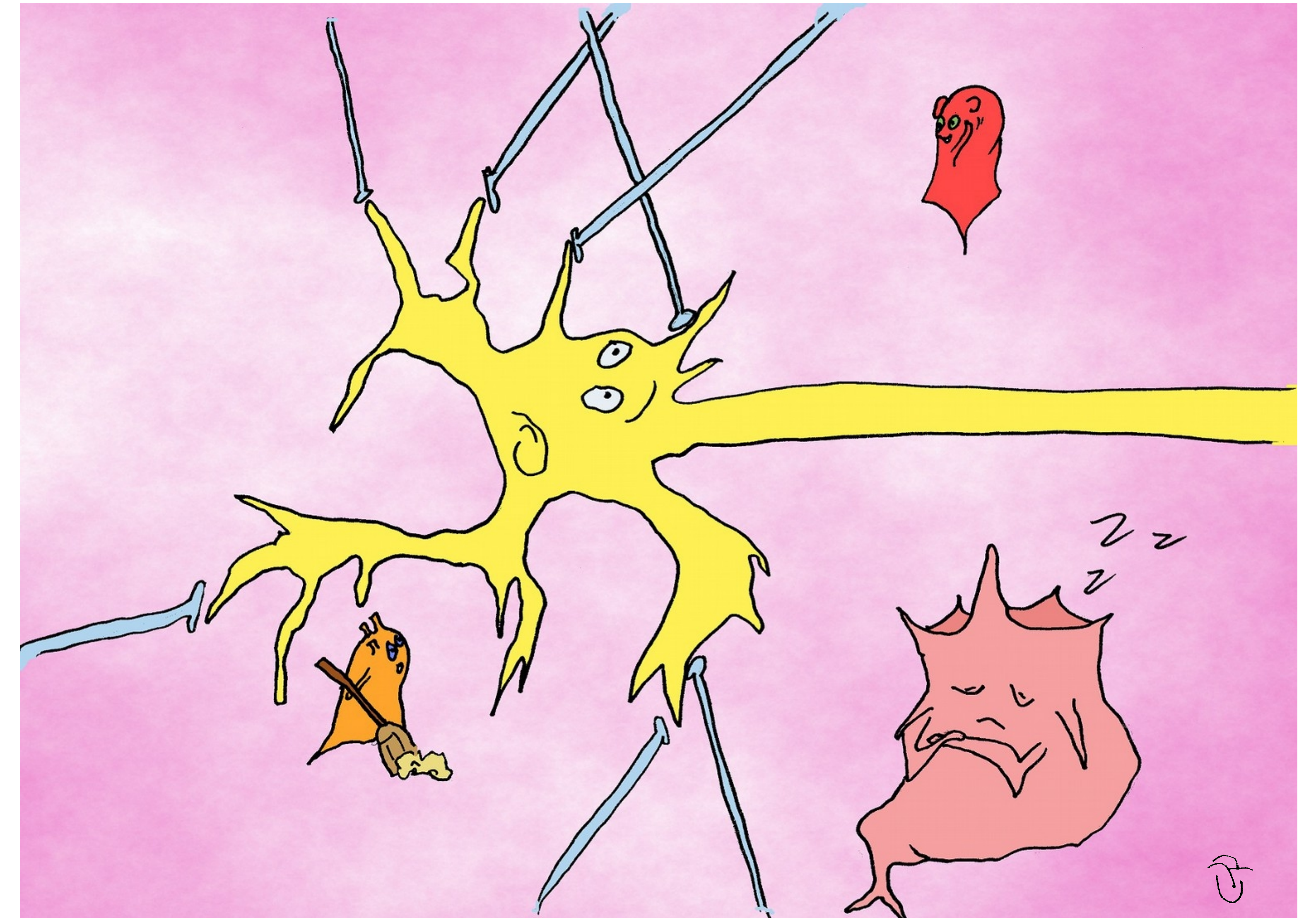
Mimi would like to, but she doesn't know if she's allowed to.

“_ You should ask the chief! Boulie says.

_ But who is the chief here?

_ I have no idea... Well, I'm going to play!”

Boulie goes away, whistling. Mimi doesn't know what to do. She turns to Astride, but she's already asleep.



She then asks Louis:

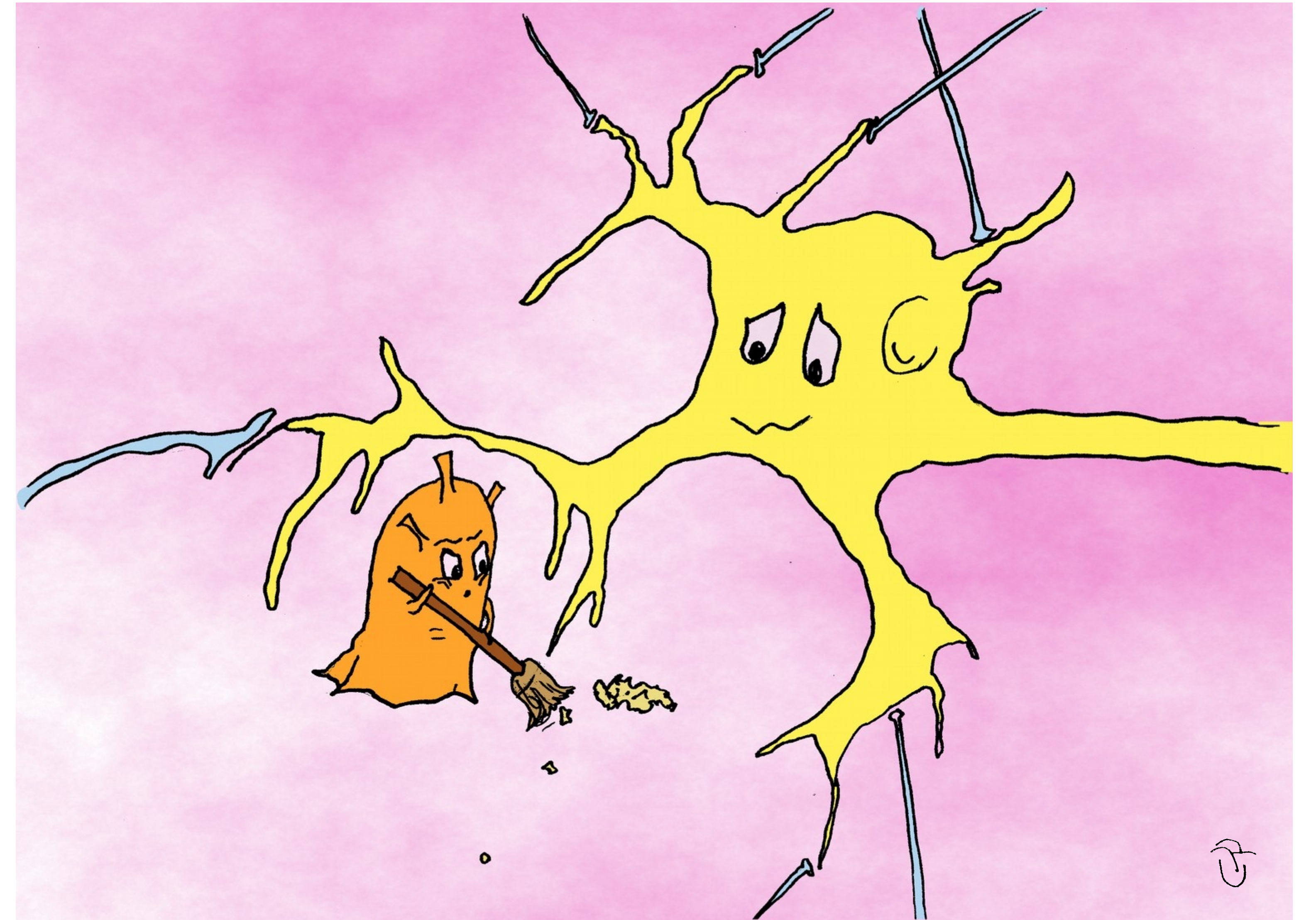
“Louis, do you know who the chief is?

_ I don't know, but every day I receive orders, so they must come from somewhere...

_ Where do you get your orders from?

_ They come from the neurons that are touching my hair.

_ But there are so many neuron arms touching your dendrites...”



Mimi stares at all the axons holding on to Louis' hair.

“_ Who is the one who gives you orders?”

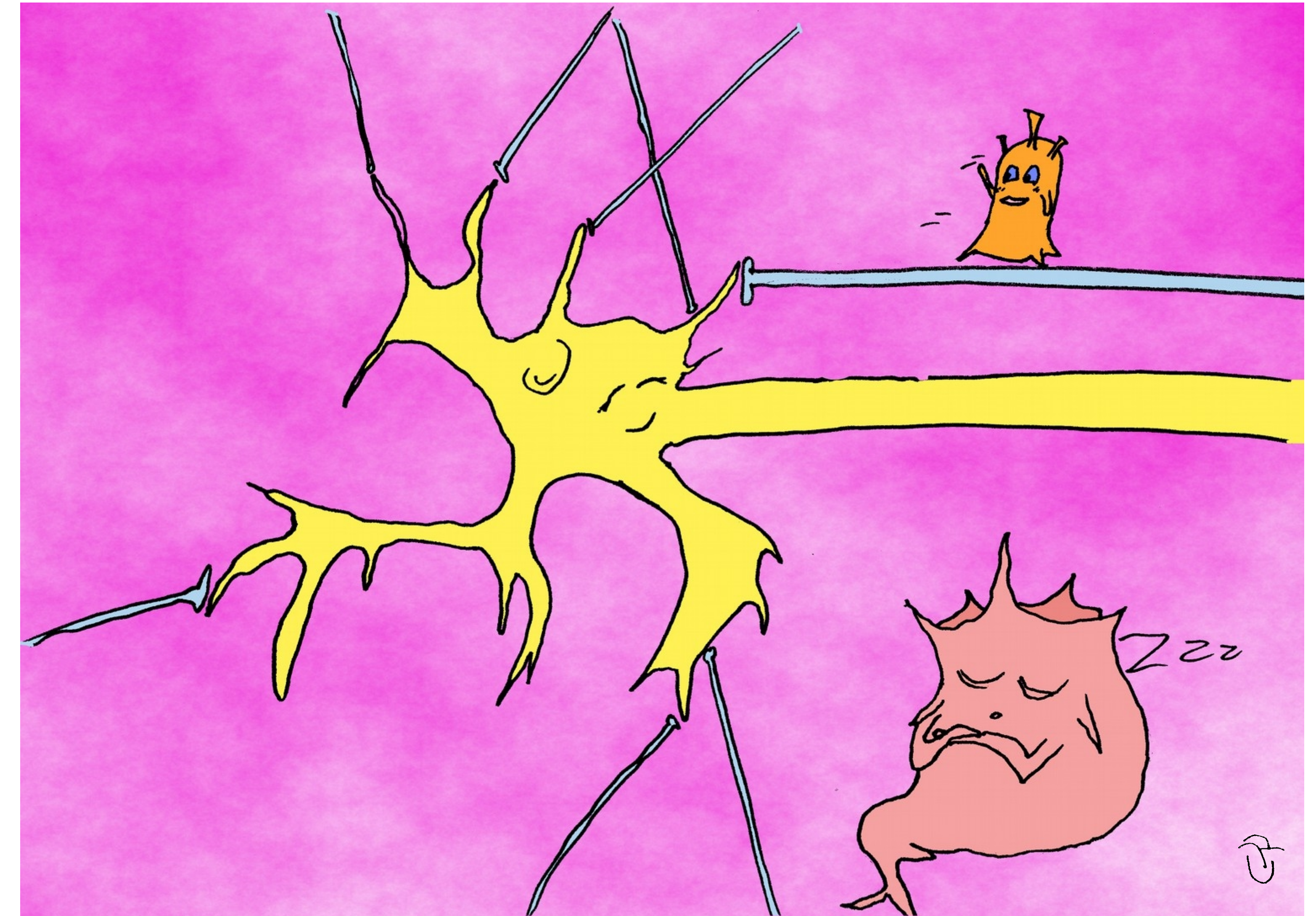
Louis started questioning.

“Here! I've just received a message, it came from *this* axon. Quick, follow him, you might get to the chief.”

For an instant, Mimi stares at Louis then Astride who is sleeping deeply. Eventually, she says:

“Okay, I'm going to have a look.

_ Come back quickly, Mimi. I'm going to miss you! ”



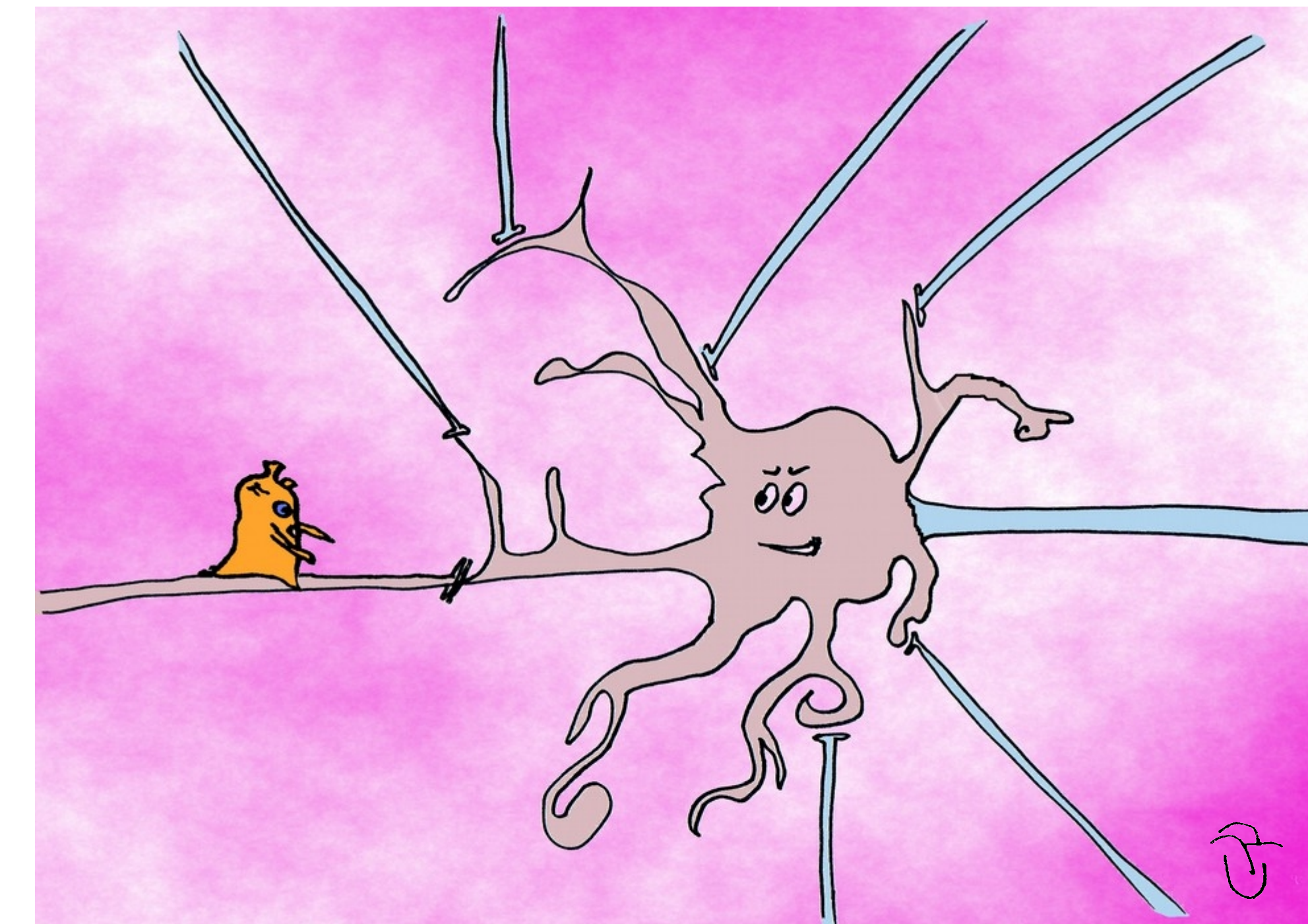
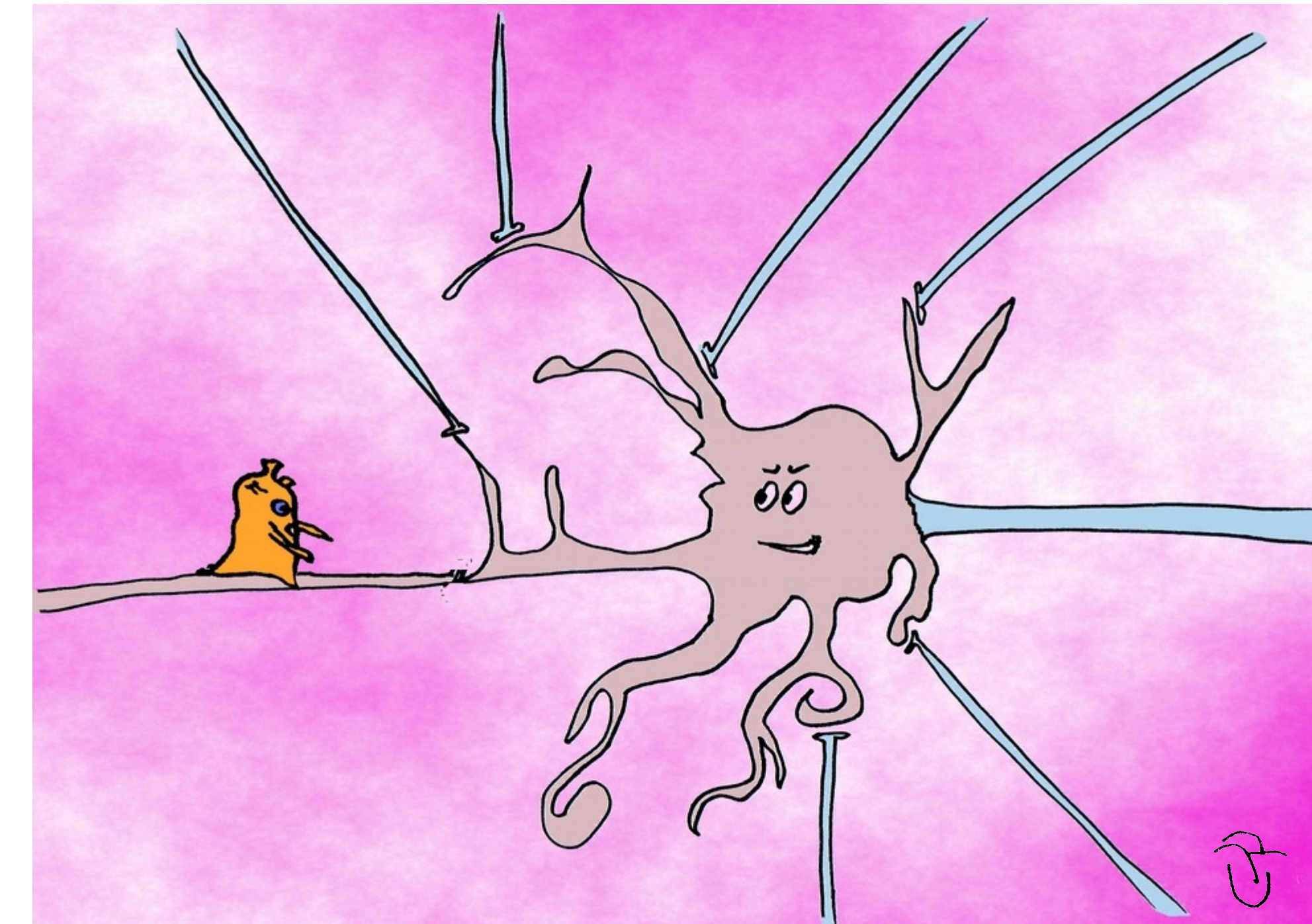
Mimi follows the axon Louis pointed out. She arrives to another neuron.

“Hi! Louis told me you just gave him an order. Are you the chief?”

“The chief? No! I’m Louis’ brother; I’ve just sent him an order that has been transmitted to me. It came from the axon at the end of this dendrite.”

“Maybe the chief is on the other side?”

“Maybe. Good luck!”

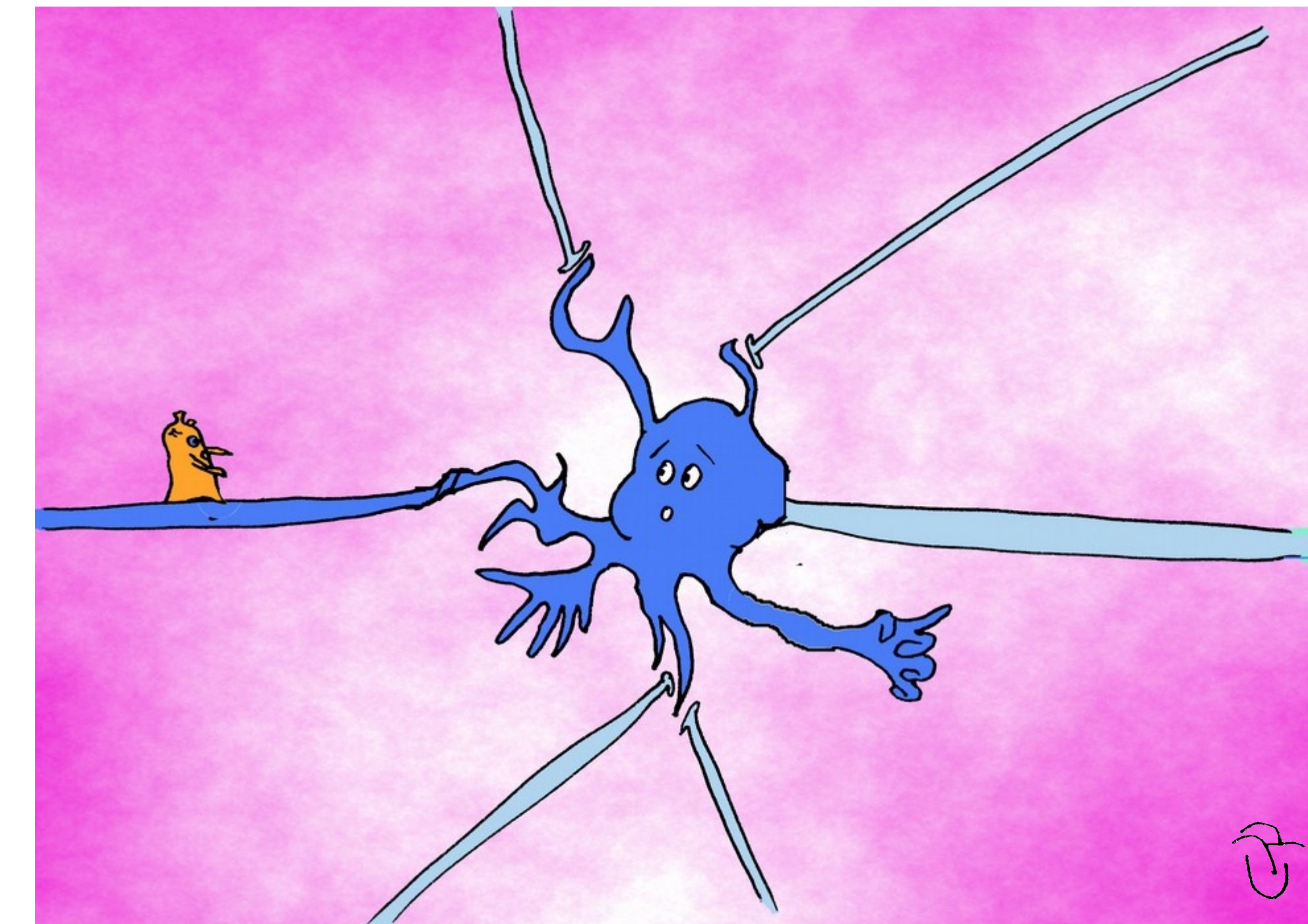
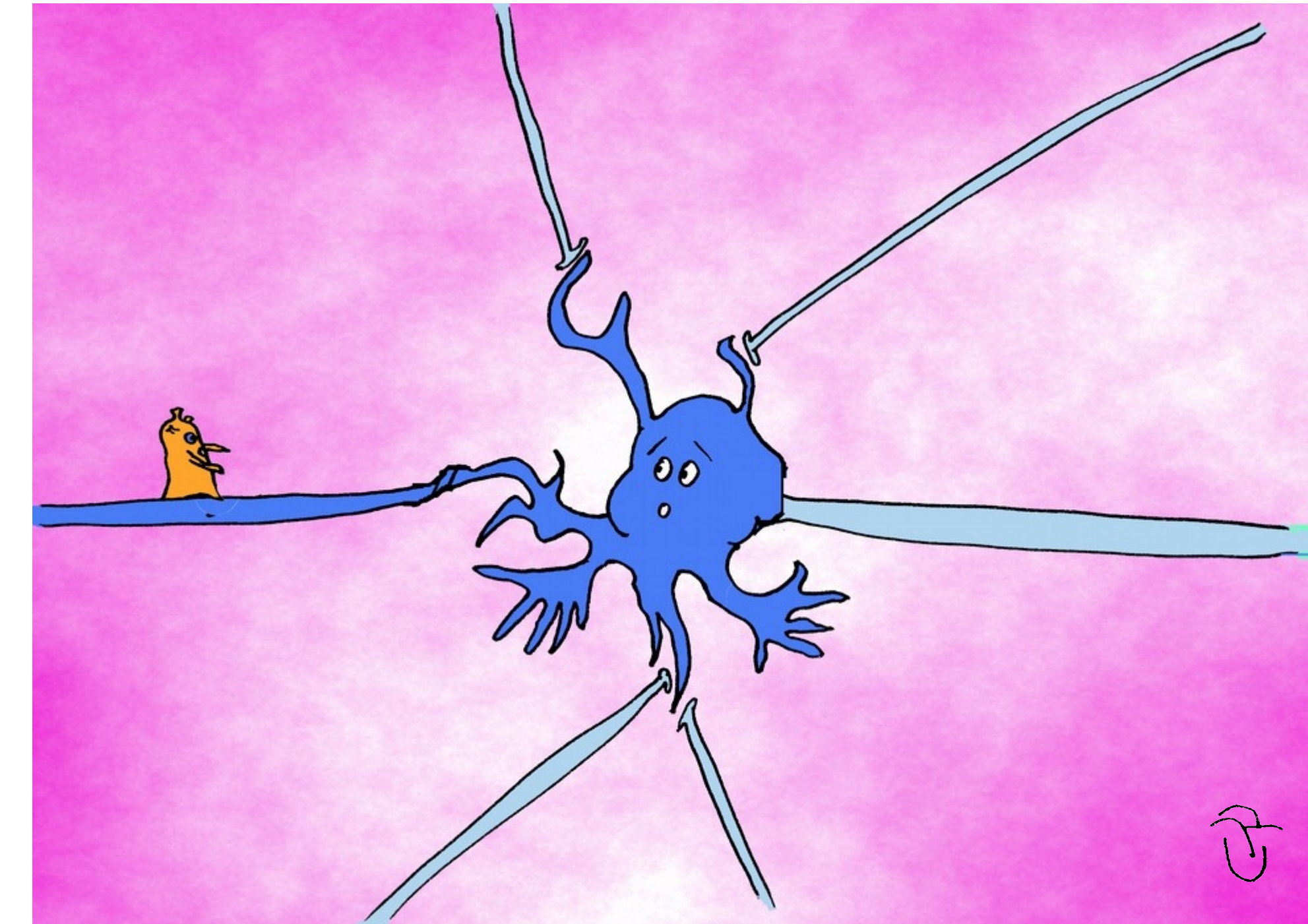


Mimi passes on. She arrives to another neuron.

“Hi! Are you the chief?”

“I’m not the chief, no! I’ve only sent orders, which were transmitted to my cousin, and then to his brother Louis. But I also receive orders! From there!”

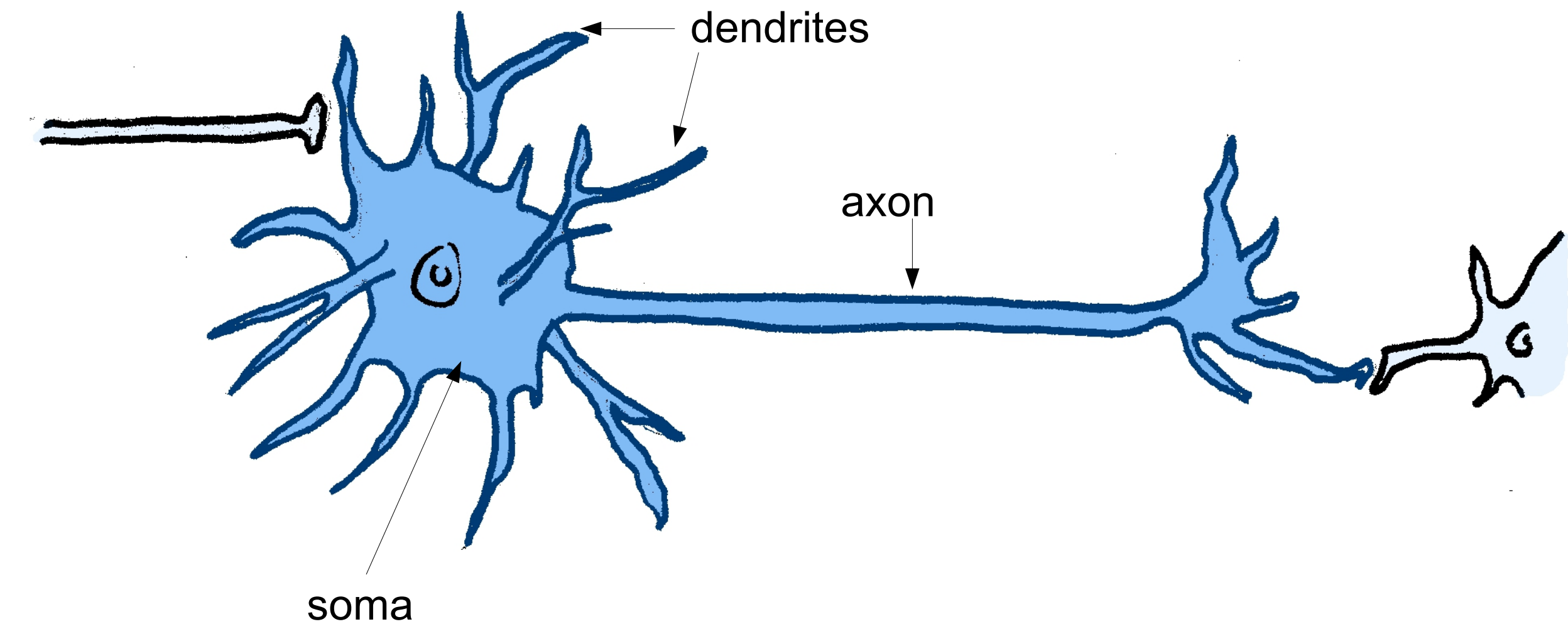
Mimi then arrives to another neuron, who does not even know Louis and who also receives orders from another neuron.



To go further...

In our story, we see Bouli wandering, and Mimi travelling, whereas Louis, the neuron, and Astride, the astrocyte, stay in the same place. We are representing the fact that microglia are mobile cells, capable of moving throughout the brain. Travel is not possible for mature neurons, nor for astrocytes, because they are organized in a network comprising of themselves and neurons.

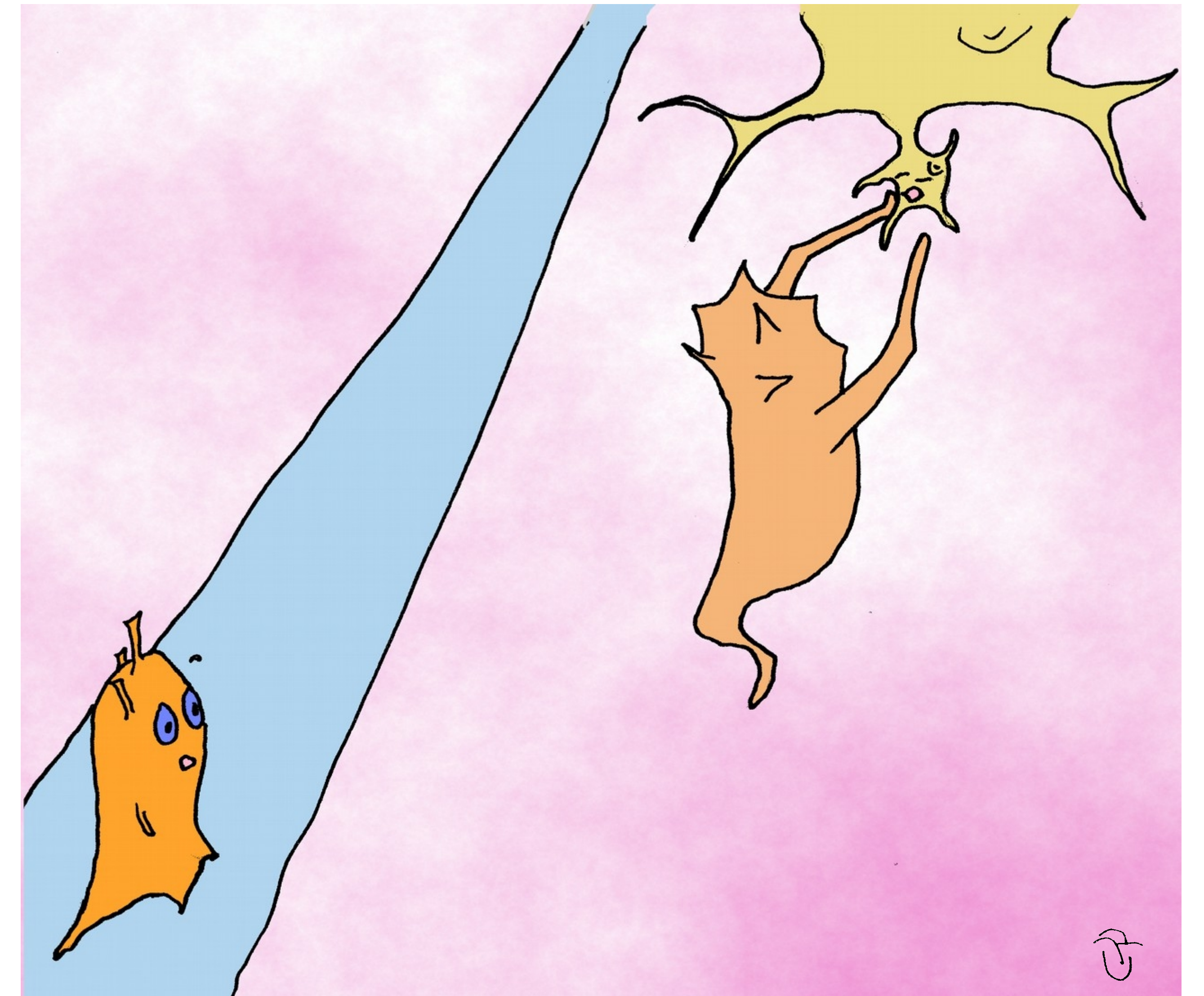
In this part of the story, we also learn more about neurons. They have a specific shape. What we call their "head" is their *soma*, on which there are "hairs" or *dendrites*. From the *soma*, the long "arm" that is extended is the *axon*.



When Louis and the other neurons say that they receive "orders", they are talking about neural information that is transmitted from neuron to neuron. This process follows a specific sequence, from the dendrites, to the soma and finally to the axon, at the end of which a connection is established with the dendrites of another neuron, and the "orders" are communicated.

Mimi doesn't understand how she's going to find this chief that nobody has heard of. She keeps walking and looks around her. Suddenly, she sees something strange: a neuron is being born! Mimi stops and watches this beautiful spectacle.

Mimi has listened to Louis recollecting about his birth, but she has never seen one. An astrocyte is delicately grasping the newly born baby neuron who looks a bit lost, his big eyes opening to this world, the brain, his house.



“Hello, the astrocyte says to Mimi, you look new around here. Are you lost?”

—A little bit...

—Well, you’re here in one of the birth centers. We put infant neurons into the world and we take care of them. Have you already seen the birth of a neuron?

—No, it’s the first time. Actually, it’s my first trip.

—Oh, and where are you headed to?

—I’m looking for the chief. What about you? What are you doing?

—I’m feeding the baby neuron so that he becomes big and strong.

—Is he going to become as big as Louis?

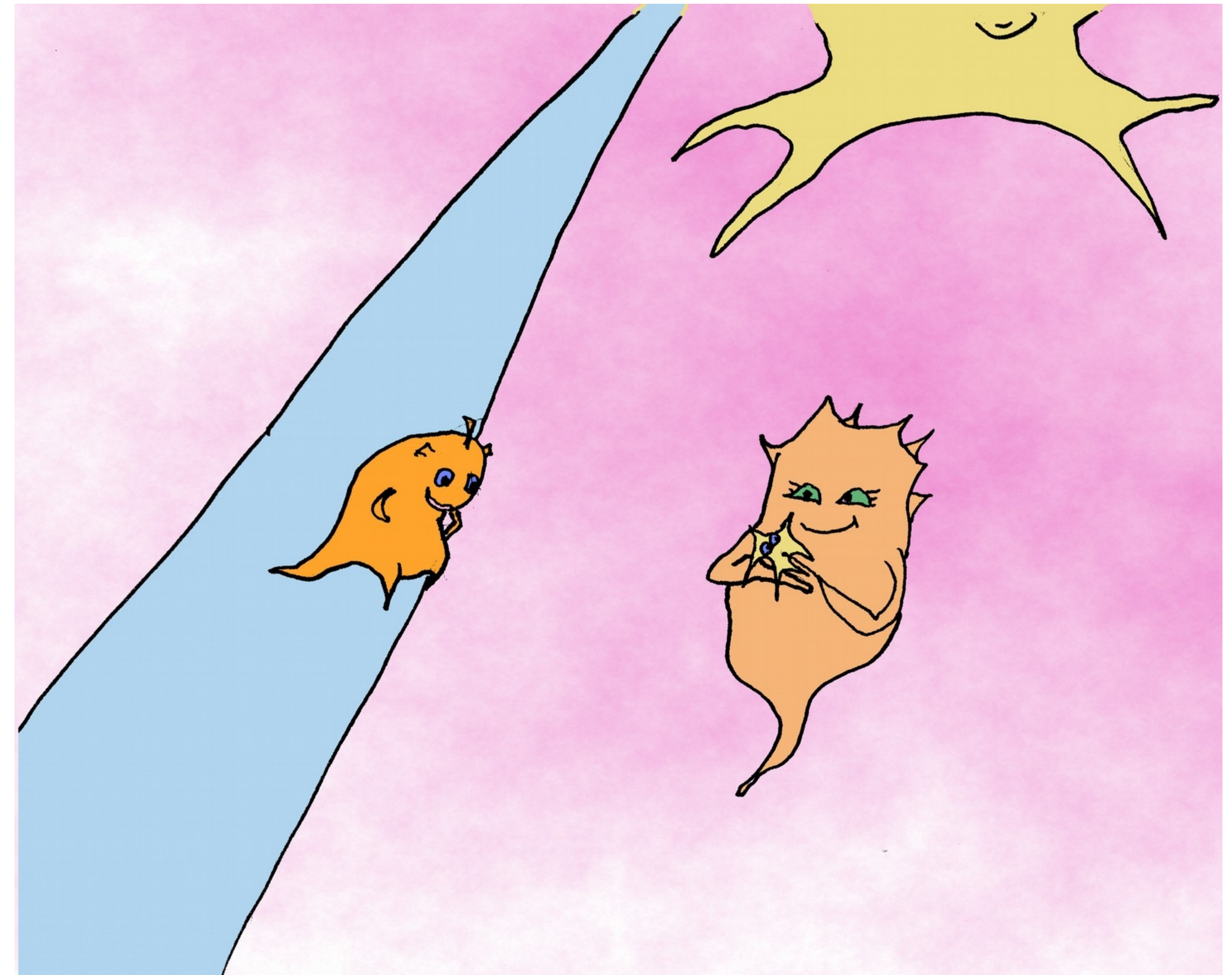
—I don’t know Louis.

—He’s the neuron I’m taking care of.

—So he’s an adult?

—Yes.

—This neuron is just a baby. Usually, babies go and try to find their place in the brain. But this one is going to live here. For now, I have to take good care of him so that he can grow up.



“He doesn’t only need food. Look!”

The baby neuron’s arms begin to grow and they reach out to the other neurons around him.

_He needs to reach his friends?

_Exactly, to be part of a network. A network is the group of all the neurons that are touching each other. My role is to help him make his own.

_Why does he need to make a network?

_To chat with his friends, send and receive messages.

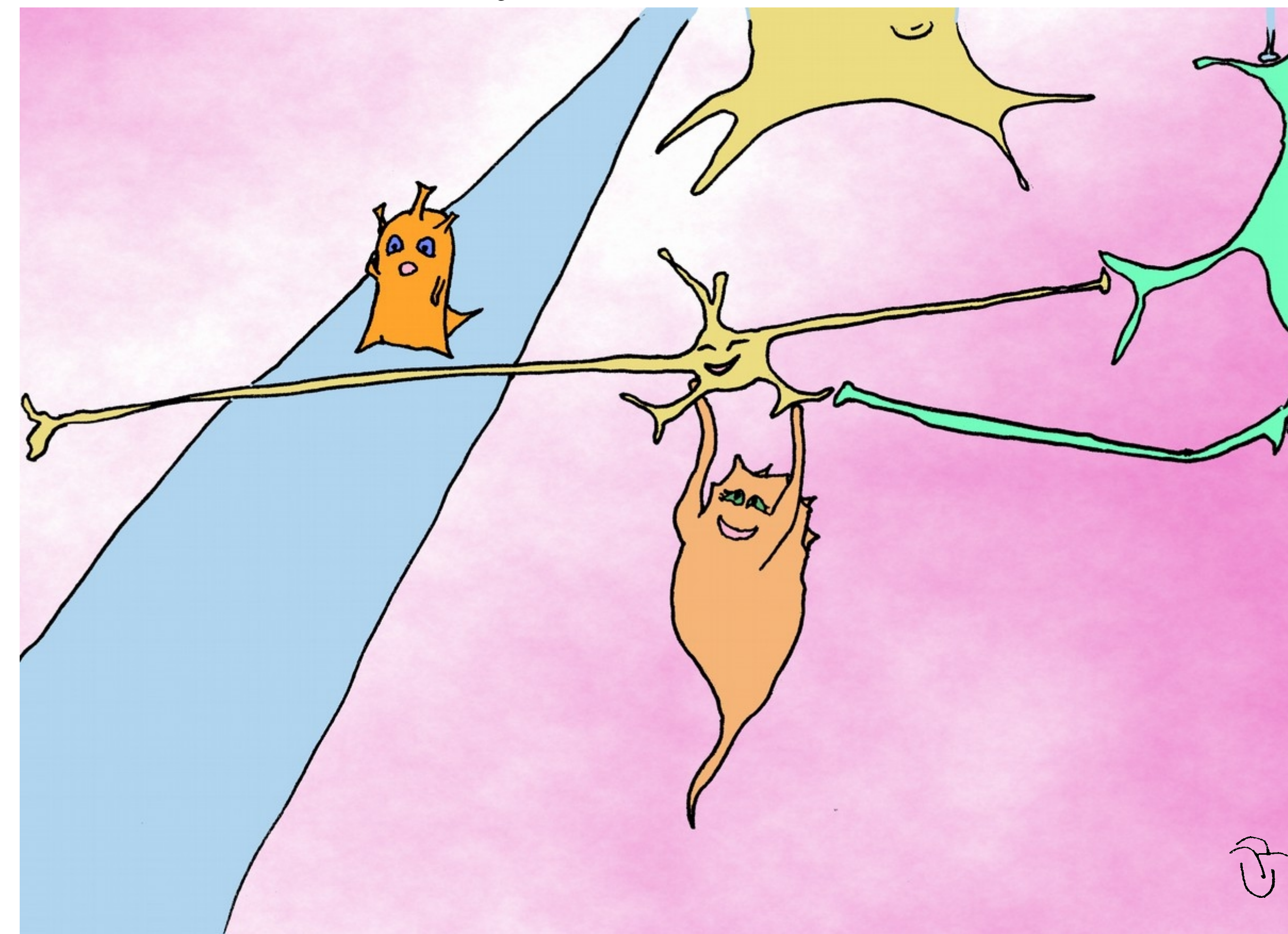
_Like Louis! Mimi exclaims. I saw it when I was coming here, when I followed the neurons’ axons to find the chief. By the way, do you know who he is?

_Sorry, I can’t help you: I don’t know!

_Well, I’m going to keep searching.

_Good bye Mimi. If you find the answer to your question, come back to tell me. See you little microglia!

_All right, see you then! Thanks for showing me how you take care of a baby neuron!”



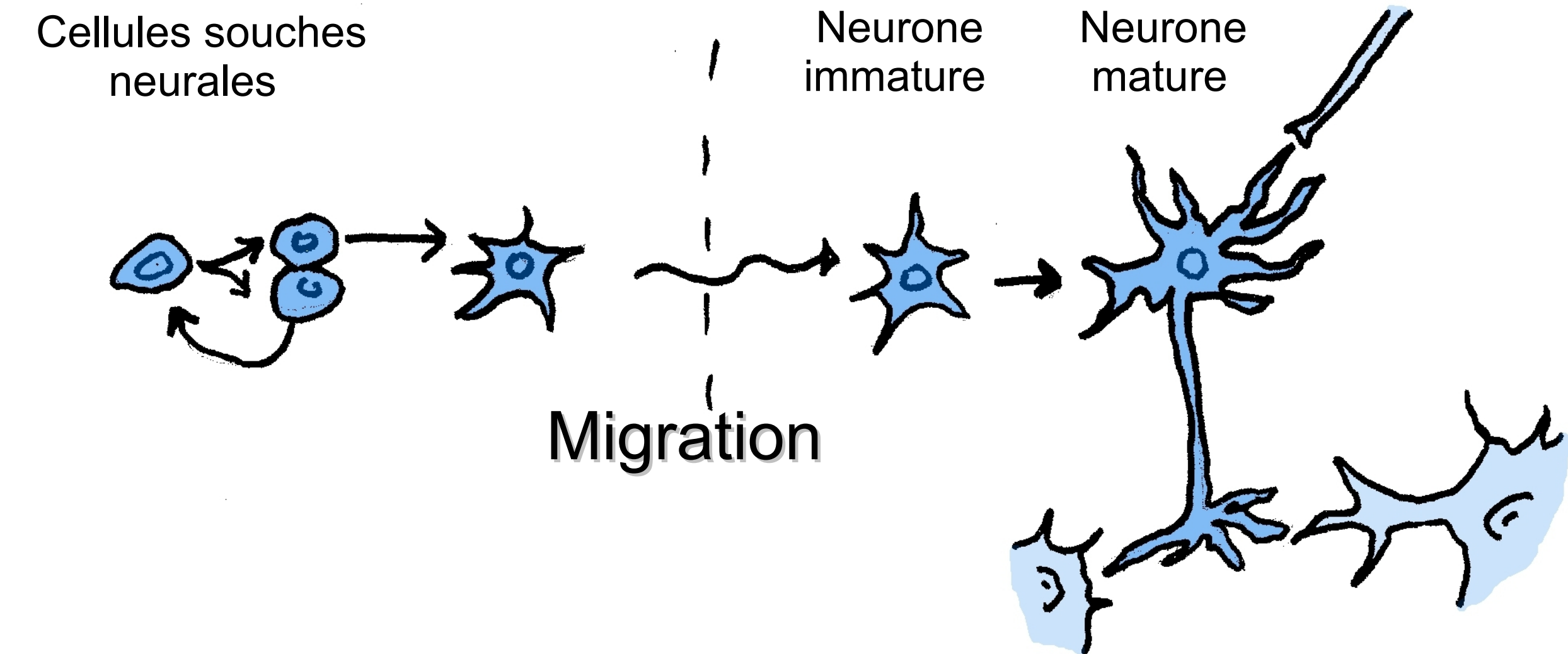
To go further...

Mimi is surprised to discover that "baby" neurons exist in the brain. The birth of new neurons is rare in the brain. For a long time, scientists thought that, from birth, we have a limited number of neurons, that die little by little during life.

However, it has been discovered more recently that new neurons are created in two areas: the hippocampus (which can produce 700 neurons per day), and the olfactory bulb. This is of high interest to scientists who hope, one day, to help people recover from brain lesions using neurons created in adulthood.

Lieu de naissance
Ex : hippocampe

Lieu de résidence
Ex : lobe frontal



In this episode of the story, we also discover a new role of astrocytes: they guide the migration of new neurons and help them make their first connections with other neurons. This is really important because a neuron that is not part of a network, and not connected to other neurons, would be eliminated.

Mimi starts her trip up again when she suddenly hears:
“Mimi! Hi! What are you doing around here?”

Mimi recognizes Bibli, a microglia friend who sometimes comes and work near her area.

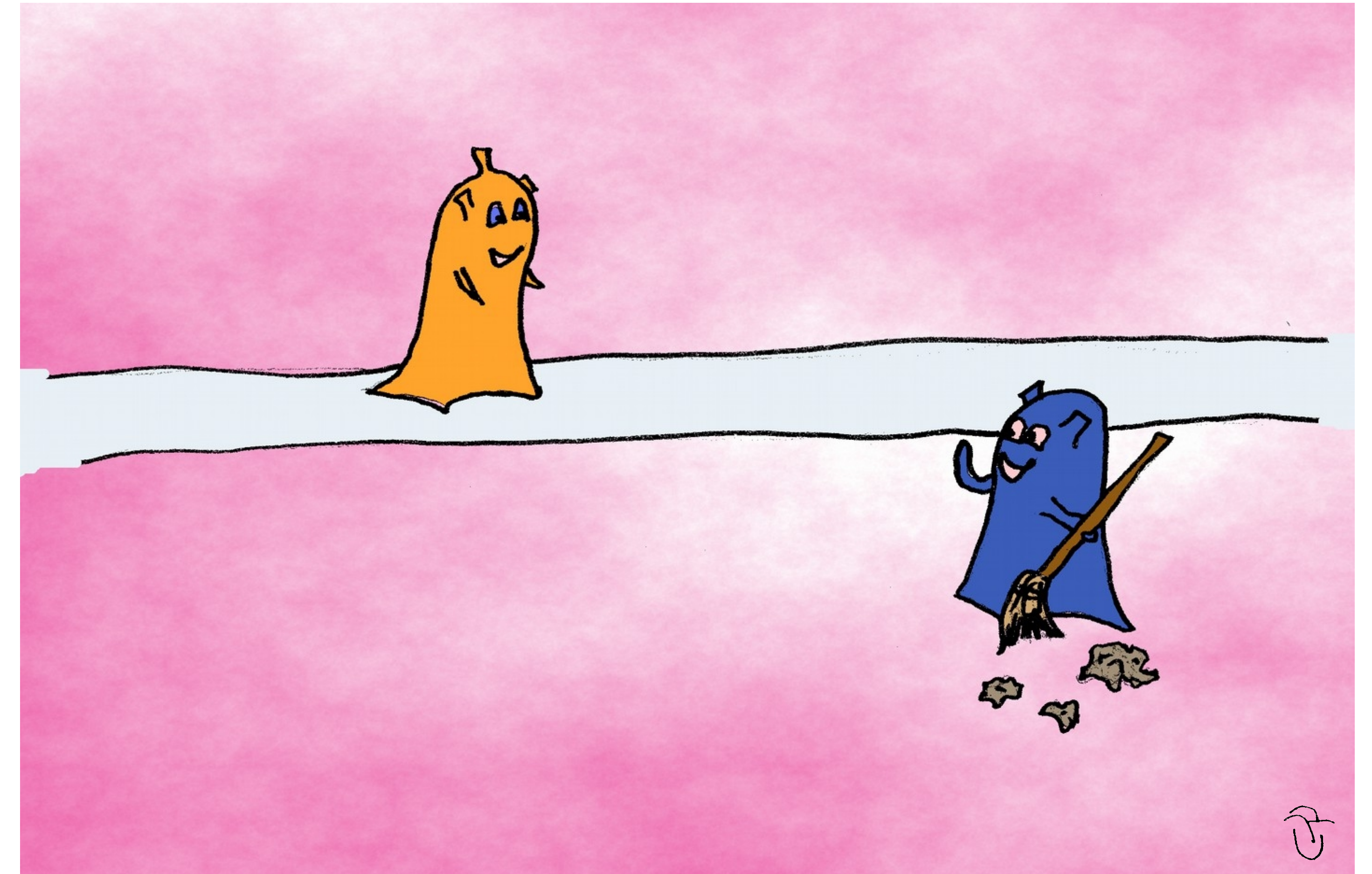
“Hi Bibli! I’m happy to see you! Guess what, I’m looking for the chief of the brain.

Mimi is aware that Bibli knows a lot of things. Maybe he can help her.

“Do you know where I can find him? I’d like to take a vacation but I don’t know if I have the right to do so.

“That’s a good question! I don’t know. But hang on, it interests me aswell! Can I come with you?”

“Sure!” Mimi says, proud to have the opportunity to help Bibli discover something new, him who already knows so many things.



Mimi starts telling Bibli about her trip, when suddenly they hear screams: “Help! Help!”. The two microglia run towards the place where the screams are coming from. They find a tall neuron, with all dendrites trembling...

It’ me! Nino! Your narrator!

“_ What’s happening?” Mimi asks

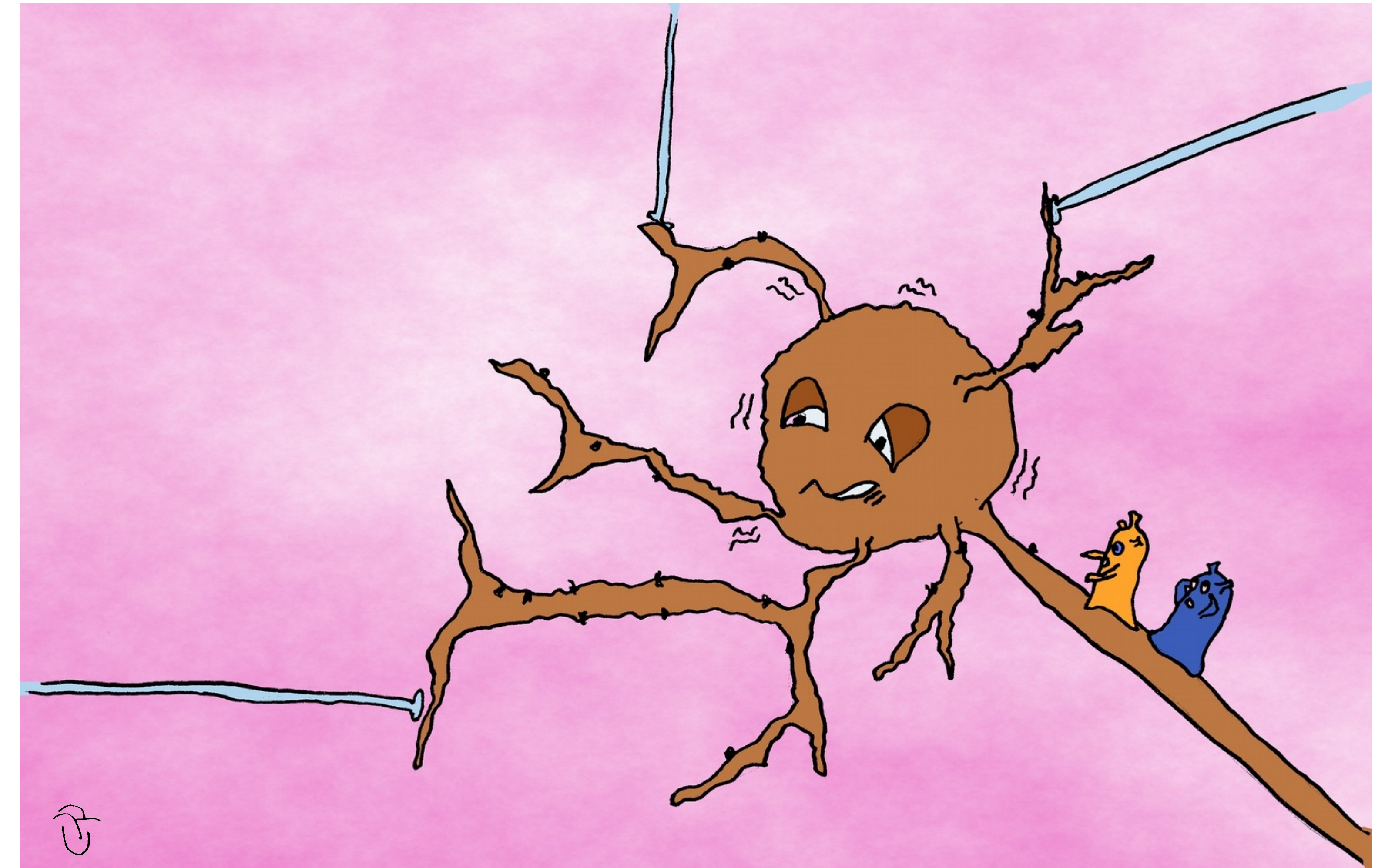
I answer rapidly:

“_ Don’t you see? I’ve been attacked by microbes! My dendrites are very damaged. This needs to be fixed!

_ Yes, yes, of course, Mimi says, as she starts to panic. But... but... the two of us are not enough to do it! We need some help!

_ We must call for backup! Bibli exclaims

_ Yes, yes, indeed, Mimi responds. Microglia, microglia, over there!”



All the microglia around the place arrive.

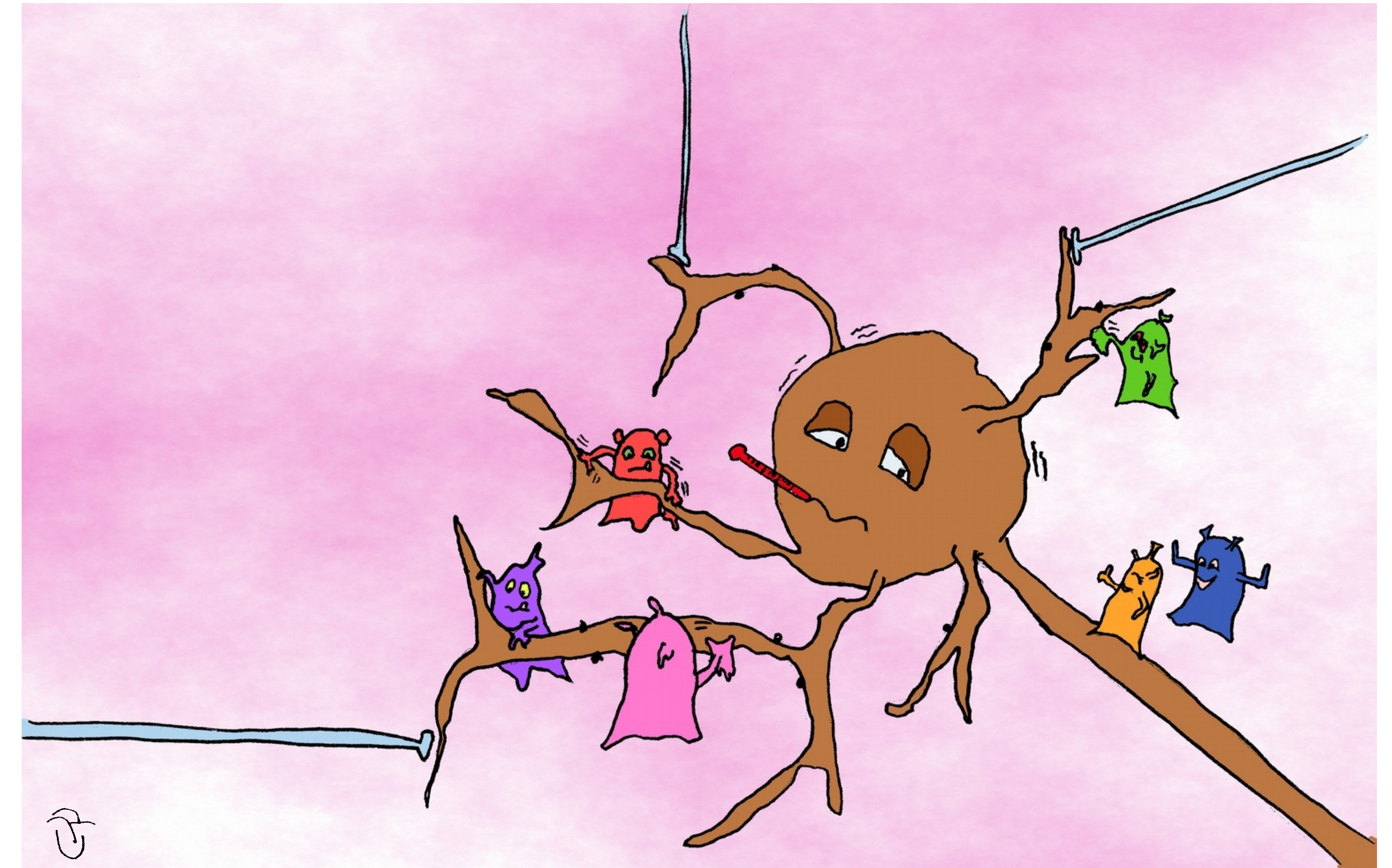
“_Come on microglia! Mimi says in a determined voice, we need to repair everything, as quickly as possible! Hurry up!”

The microglia are beginning to clean me everywhere. A couple of minutes later, I stop trembling.

“_I feel better now!” I say to them.

Yet, Boulie keeps cleaning me without any reason. Everybody can see that there is no microbe anymore and Boulie begins to hurt me.

Boulie is cute, Boulie is nice, but Boulie often does silly things!



“_ We must clean... we must clean... we must clean...
Boulie says without stopping. It ain't clean, it ain't
clean, it ain't clean... We must clean more... We must
clean more... We must clean more...”

_Careful Boulie! Mimi says to her, if you clean too
much, you're going to hurt Nino!

_You told me to clean, so I'm cleaning!” Boulie
answers, a little offended by Mimi's remark.

_ Yes, but now, you're hurting Nino instead of ridding
him of microbes!”

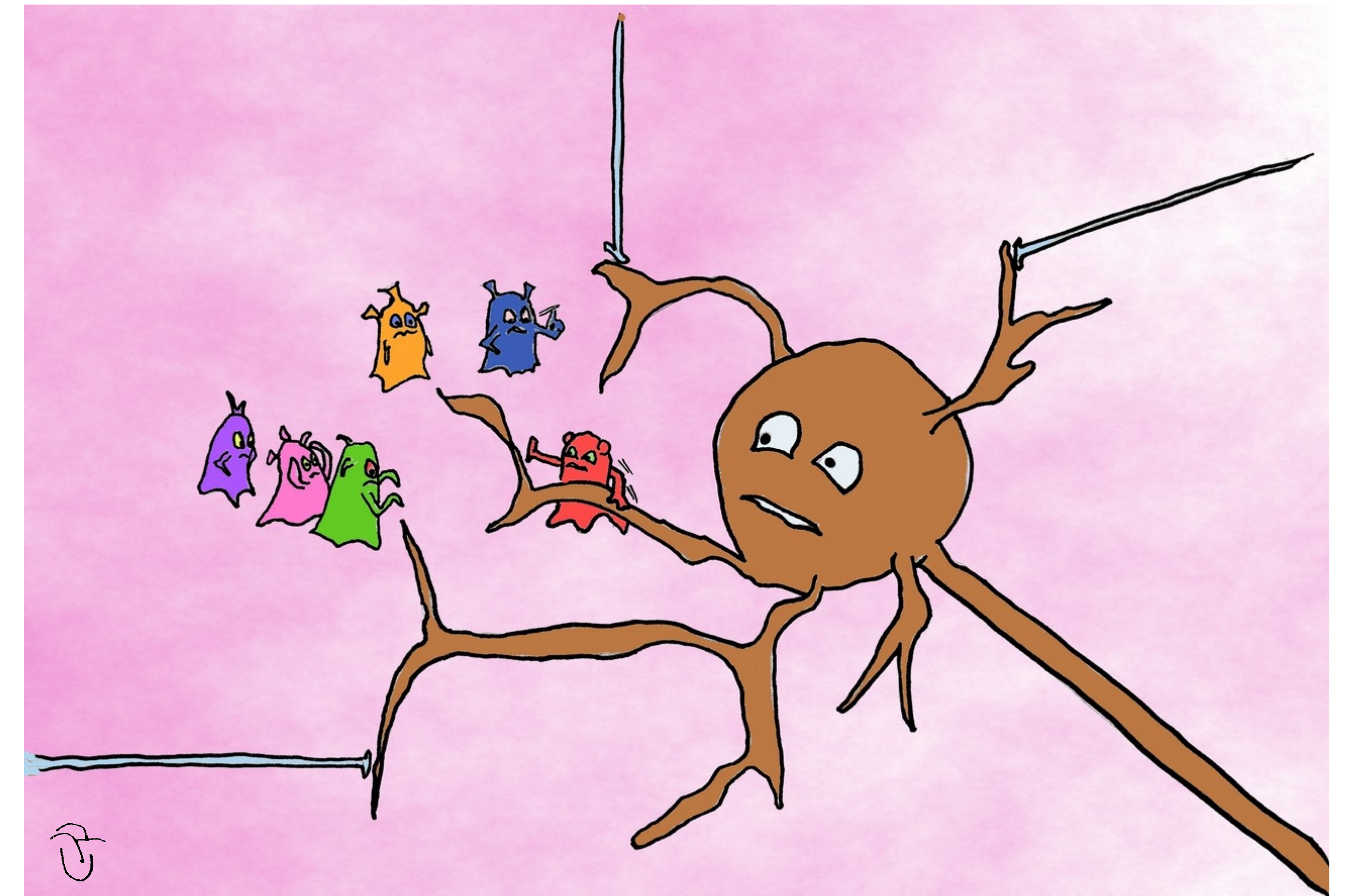
The microglia move closer to Boulie to make her stop,
but she pushes them back nastily:

_Leave me alone, you don't know how to do it
properly.”

Mimi moves closer too, but Boulie pushes her back.

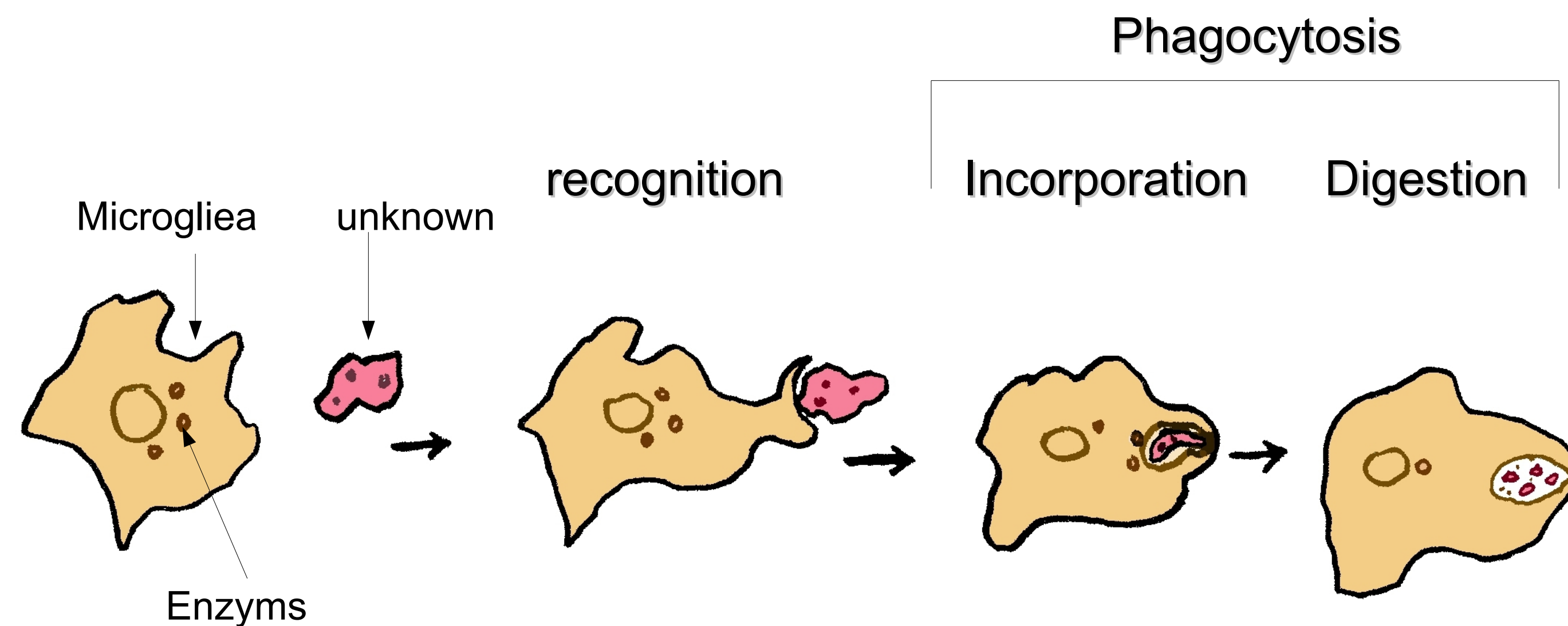
Then, Bibli becomes very red, very angry with Boulie's
behavior. He says:

“_ Boulie, you stop now, you must listen to us. We are
all telling you to stop, you're hurting the neuron.
Finally Boulie calms down.”



To go further...

The brain, like any organ of the body, can be invaded by a virus or bacteria. With Nino's disease, we discover microglia actively cleaning. For real, they will catch germs responsible for infection, engulf and digest them. We call this process "phagocytosis".



We also learn how microglia get organized to fight important infections: a microglia that has discovered a problem will release signals in the brain (cytokines), that will attract other microglia toward the infected area. When the brain does not function properly (like in Alzheimer's or Parkinson's disease), we actually find a large and abnormal number of microglia.

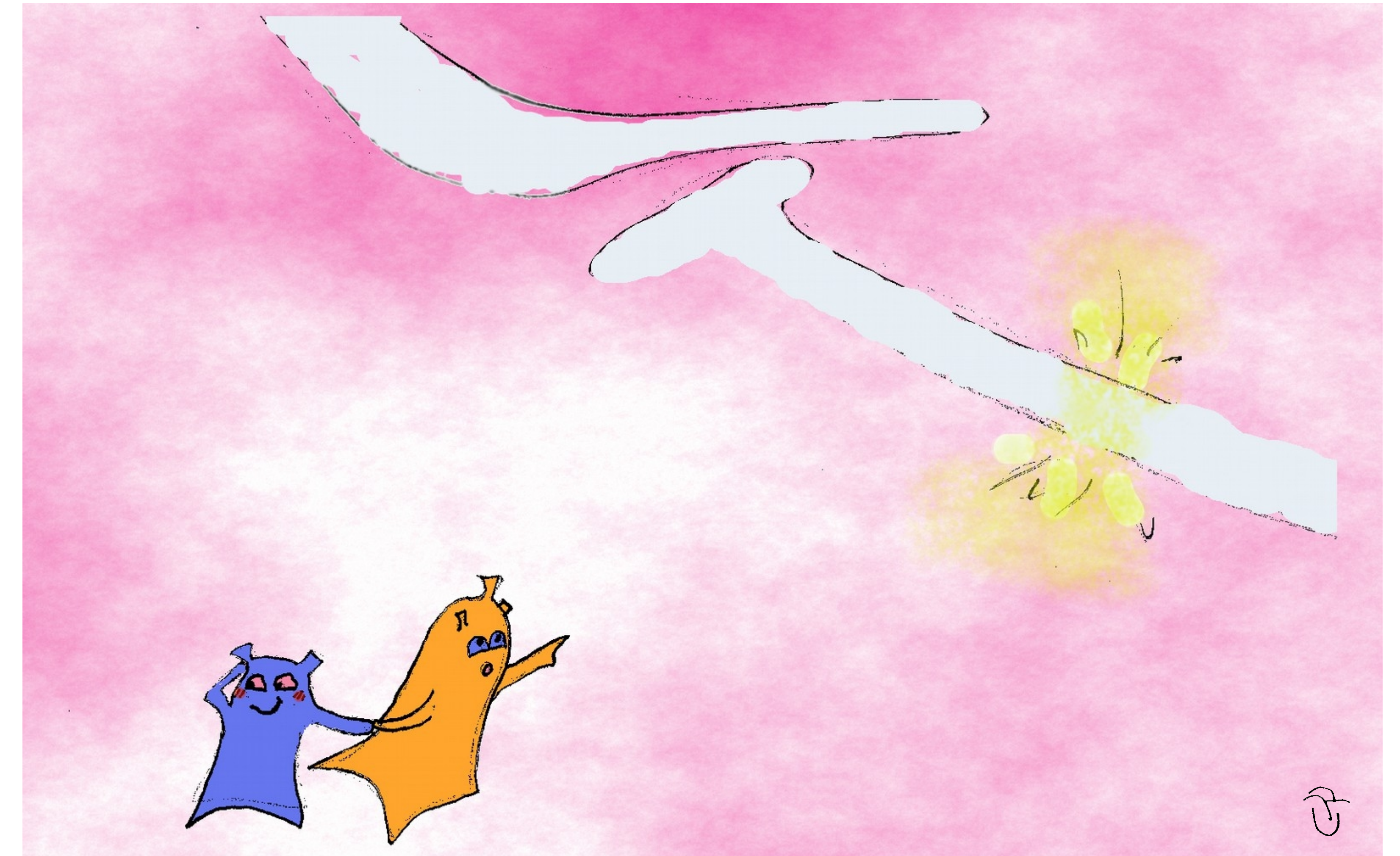
Furthermore, Boulie adopts a strange behavior, illustrating a deleterious function of microglia's activity. Even though microglia are in charge of defending neurons, they sometimes release toxic substances which kill neurons. In the case of neuropathic pains, microglia might release toxins that make the neurons hypersensitive, provoking intense and chronic pain. Currently, we don't know the cause of this abnormal change in microglia's behavior.

I thank them, and all the microglia leave. Mimi, very moved that Bibli stood up for her and smiles at him. Bibli blushes... He reacted in order to protect Mimi, but he didn't want it to be noticed. Actually, it's been a long time Bibli is in love with Mimi!

Mimi doesn't notice it. Indeed, she focuses on something luminous in the axon, going at them very fast.

Mimi catches Bibli:

“_Oh, look, a light! Come, I want to see the fireworks!”

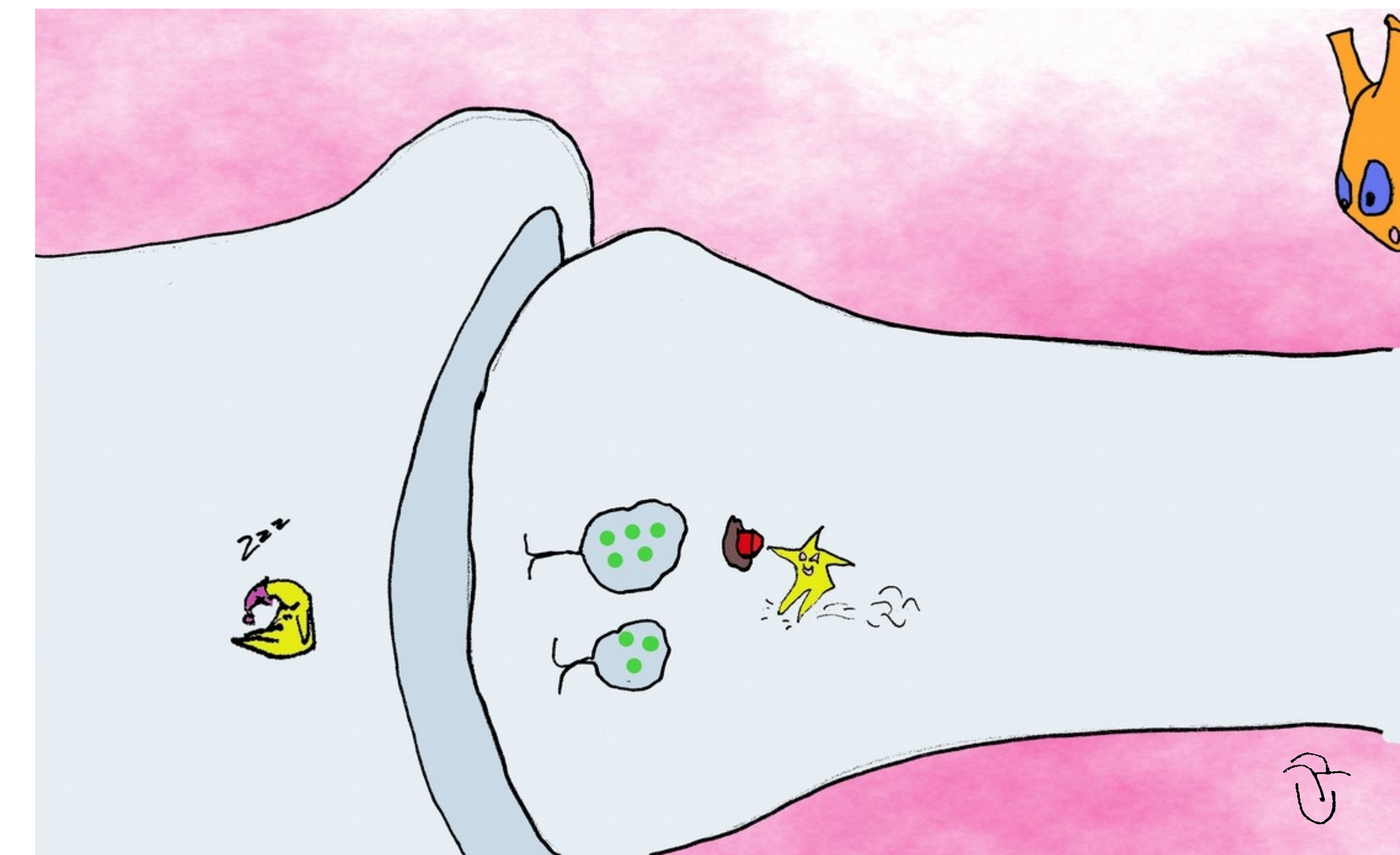
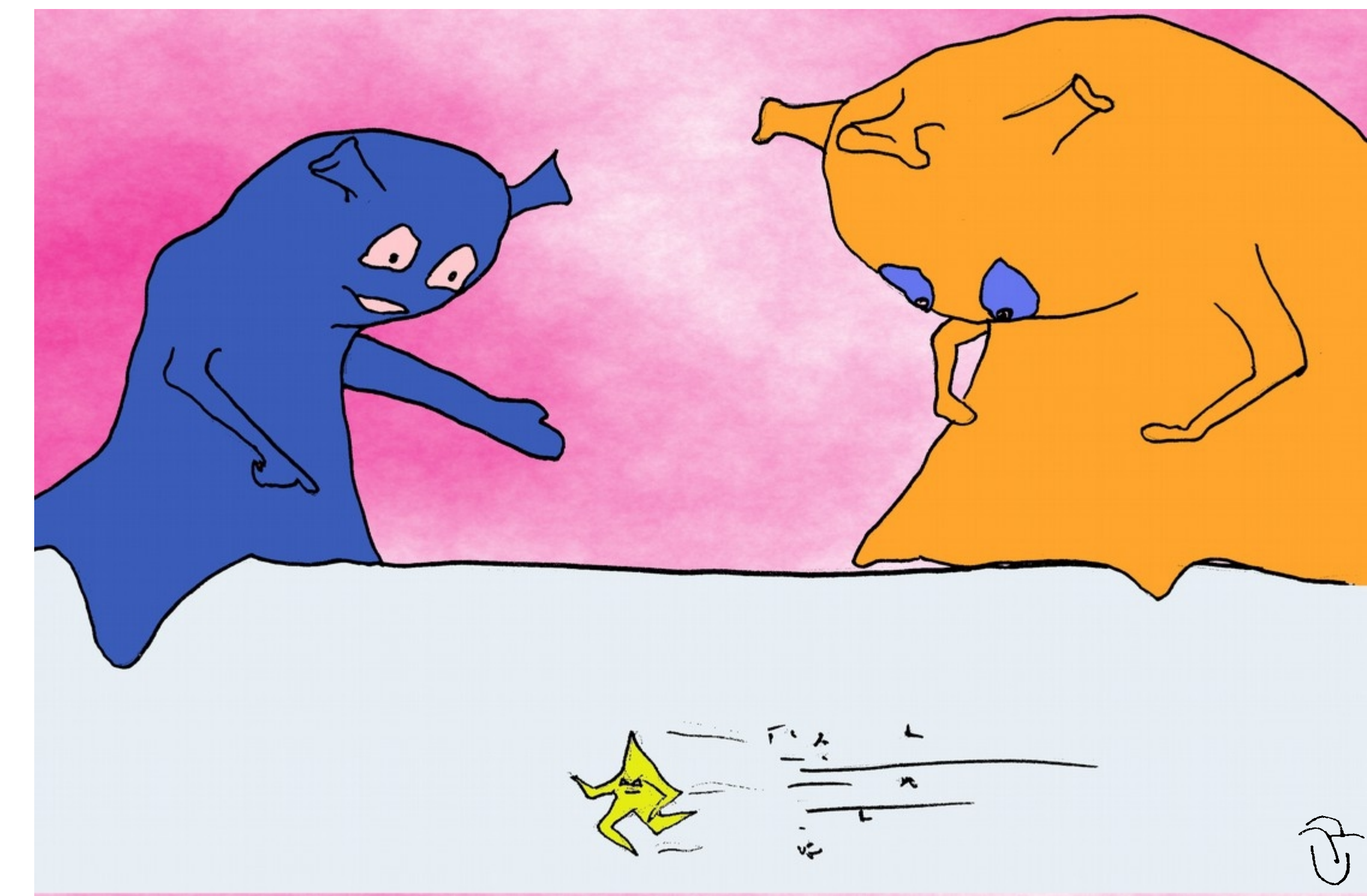


She runs with him, following the light to the end of the axon, because she loves to see the fireworks made of small pearls.

_Have you ever looked precisely at what happens? Bibli asks her.

Mimi leans and she sees that this light is a small star; the action potential. When it arrives to the end of the axon, the star pushes on a big red button. Bags of small pearls, neurotransmitters, are then released in the synapse; that is the slit between the axon and another neuron's dendrite. Mimi lifts her head and observes the firework of pearls she likes so much.

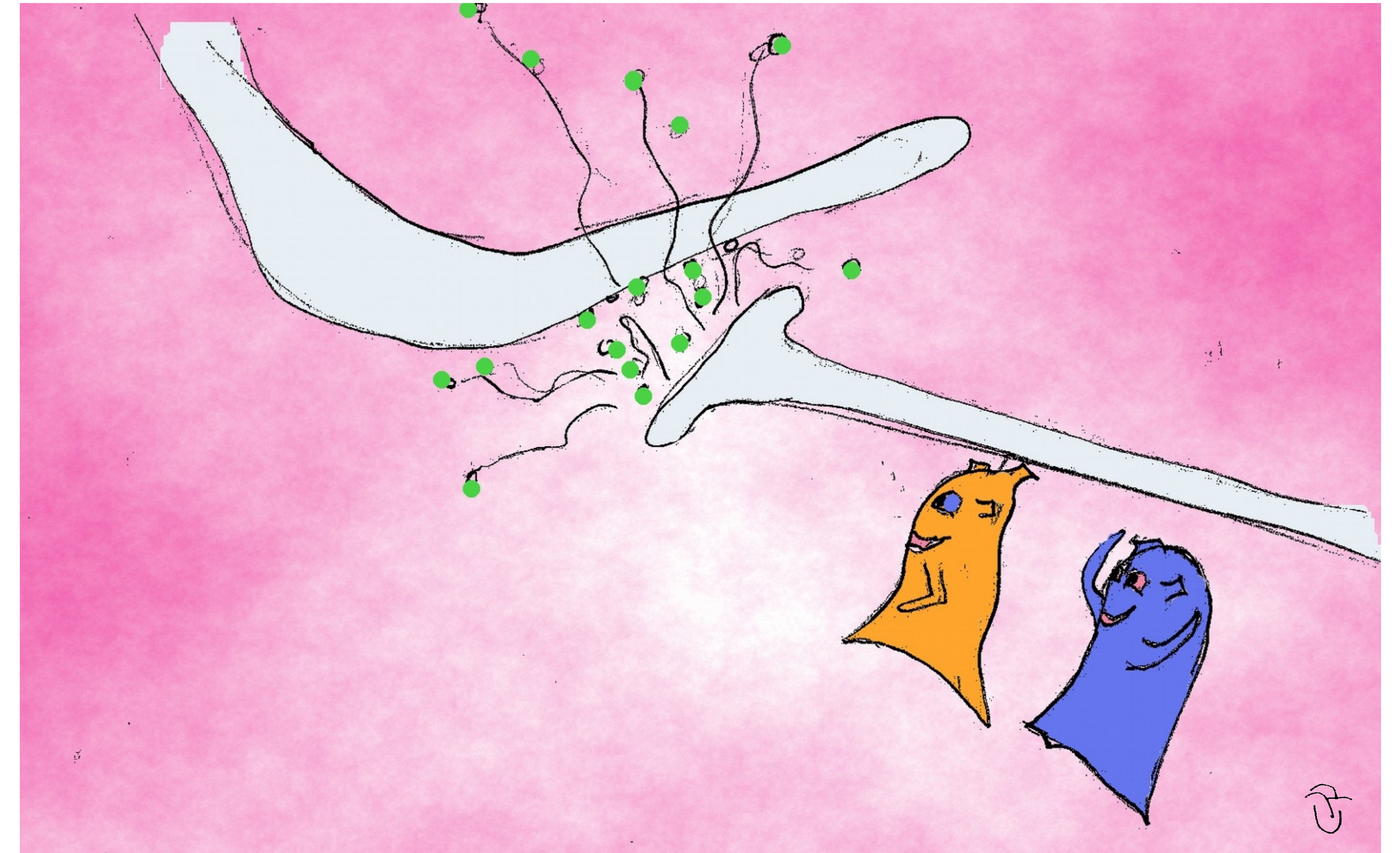
Together, the two microglia exclaim:
_How beautiful!



The pearls spread into the synapse. Some jump onto the dendrite of a neuron close by or move nearby, but others stay attached to this one. It is the signal of taking over for the star standing on this dendrite. She begins to run towards the head of the other neuron.

At the end, some pearls go back to the previous neuron and an astrocyte comes and patiently gathers up the remaining ones.

Mimi is disappointed that the firework is already over, and she shares this feeling with Bibli. He reassures her, showing her a new star on another synapse.



Together, they watch fireworks exploding all around in the brain.

_There really are a lot there, which means neurons are talking a lot to each others. At my place, with Louis, it's rarer, Mimi says.

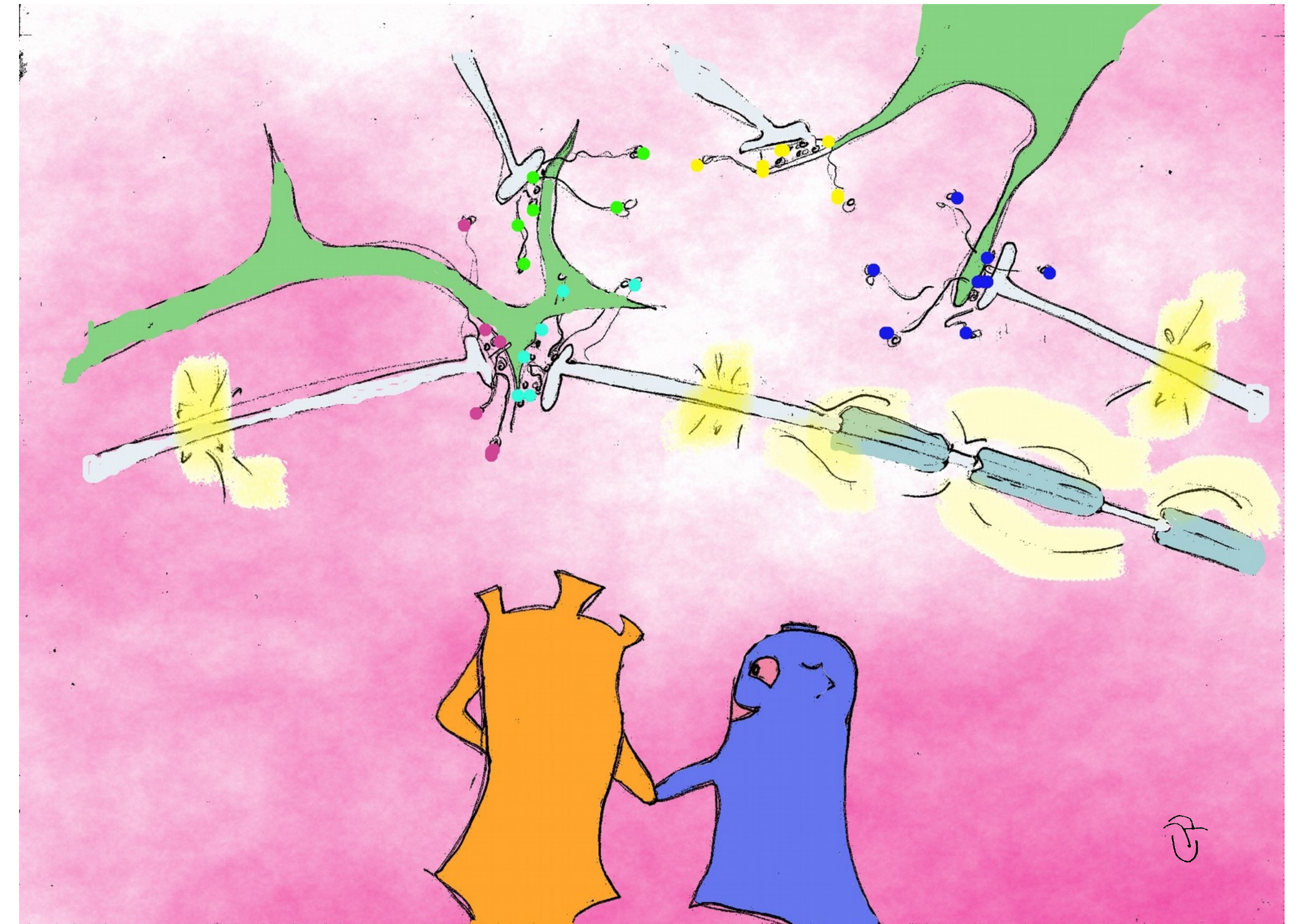
_Yes, it depends on the place, and moment, Bibli explains.

Mimi, is surprised and exclaims:

_Look, some lights are going faster than others! They look like shooting stars!

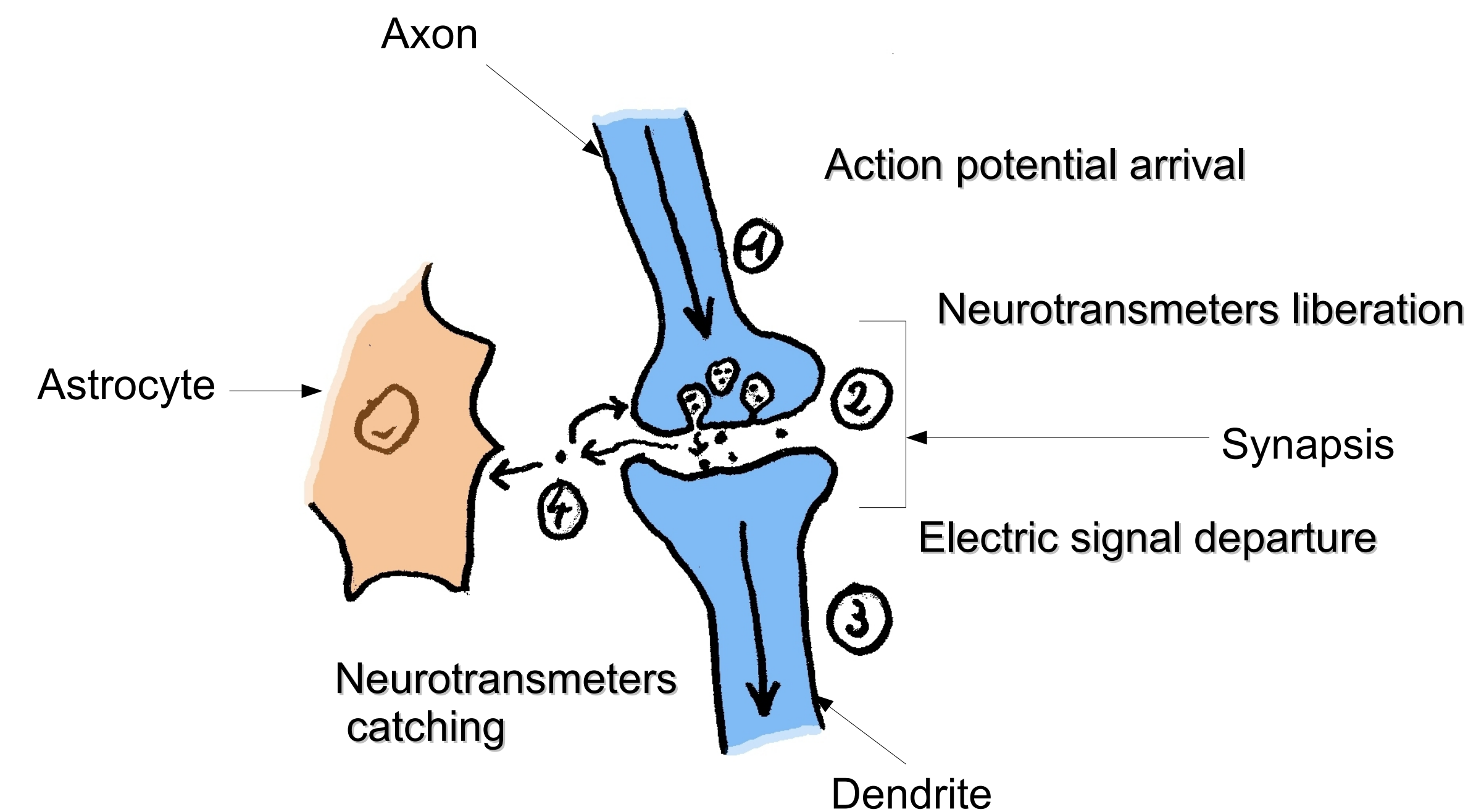
_Yes, Bibli says, you're right, I've never noticed that. That's weird, let's go see!

Once again, Mimi is very happy to have discovered something Bibli doesn't know. Sometimes, she feels like Bibli has an answer to everything.



To go further...

A synapse is a little space between two neurons, fundamental for their communication. Neurons form complex networks, and have multiple connections with each other. Information transmitted by neurons takes two forms: an electrical and a chemical one. When the information is inside the neuron, it is an electric signal, or "action potential". To illustrate this concept of electricity, we talk about "light" in the story. The action potential, generated by one neuron, passes through the axon. When it reaches the end of it, it causes the release of neurotransmitters (here the "pearls") in the synapse. This neurotransmitters are captured by receptors on the dendrites of the neuron at the other end of the synapse. Depending on the quantity and type of neurotransmitters this neuron receives from the first one, and from several others in the brain, it may or may not produce an action potential.



Adrenaline, dopamine and serotonin are neurotransmitters. We should note that only one proportion of the neurotransmitters released will reach the second neuron. Some of them are eliminated, others are being captured by astrocytes, and some will go back to the first neuron. These different processes, which regulate the amount of neurotransmitters and influence the communication between neurons, is really important when to explaining and try to cure several diseases, such as depression.

Mimi and Bibli move closer to an axon where stars go very fast.

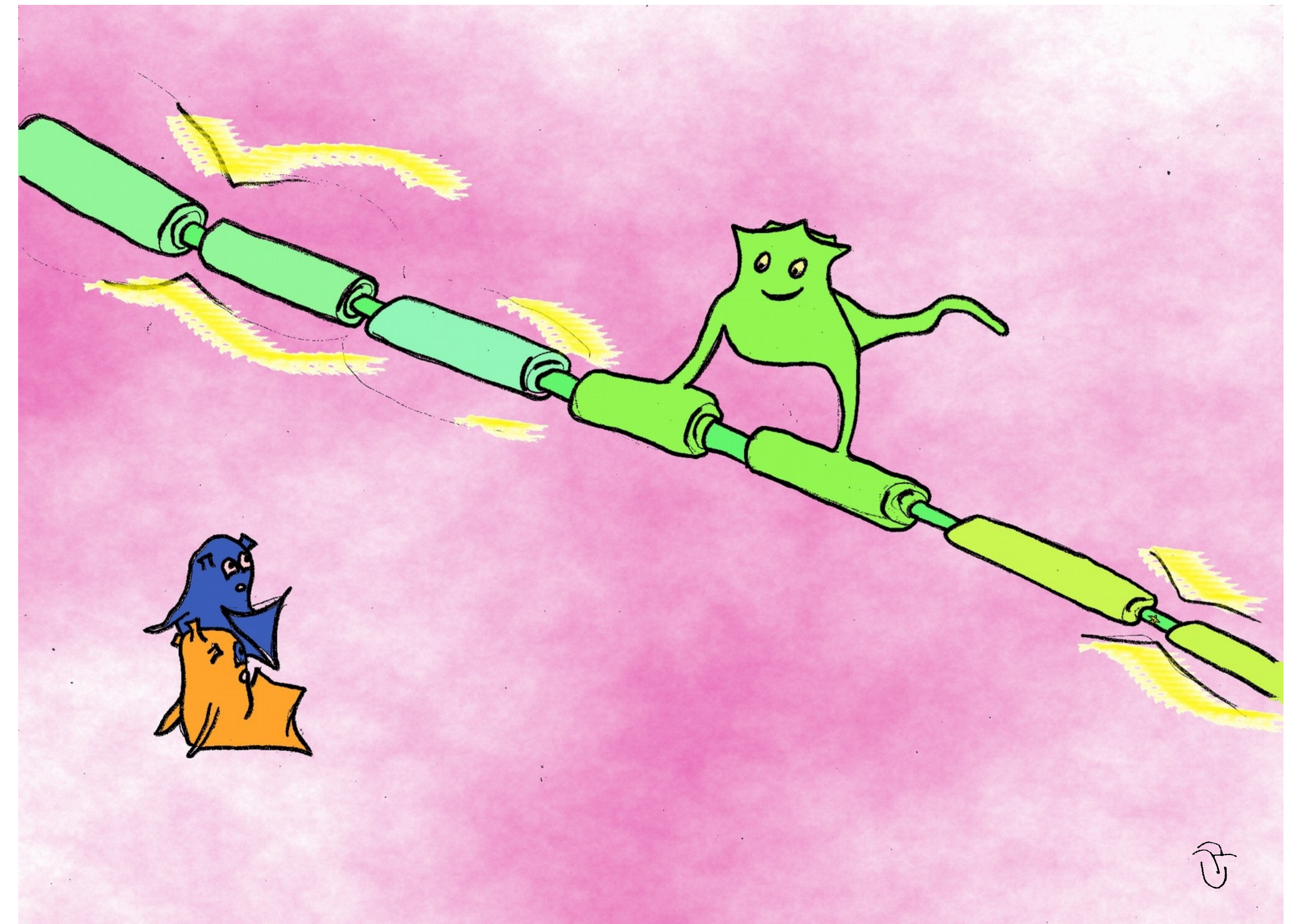
“Oooooow, Blibli exclaims. Look, it’s even more beautiful! They’re going so fast we almost don’t see them.”

They sit down comfortably to watch this spectacle, peacefully. Bibli whispers:

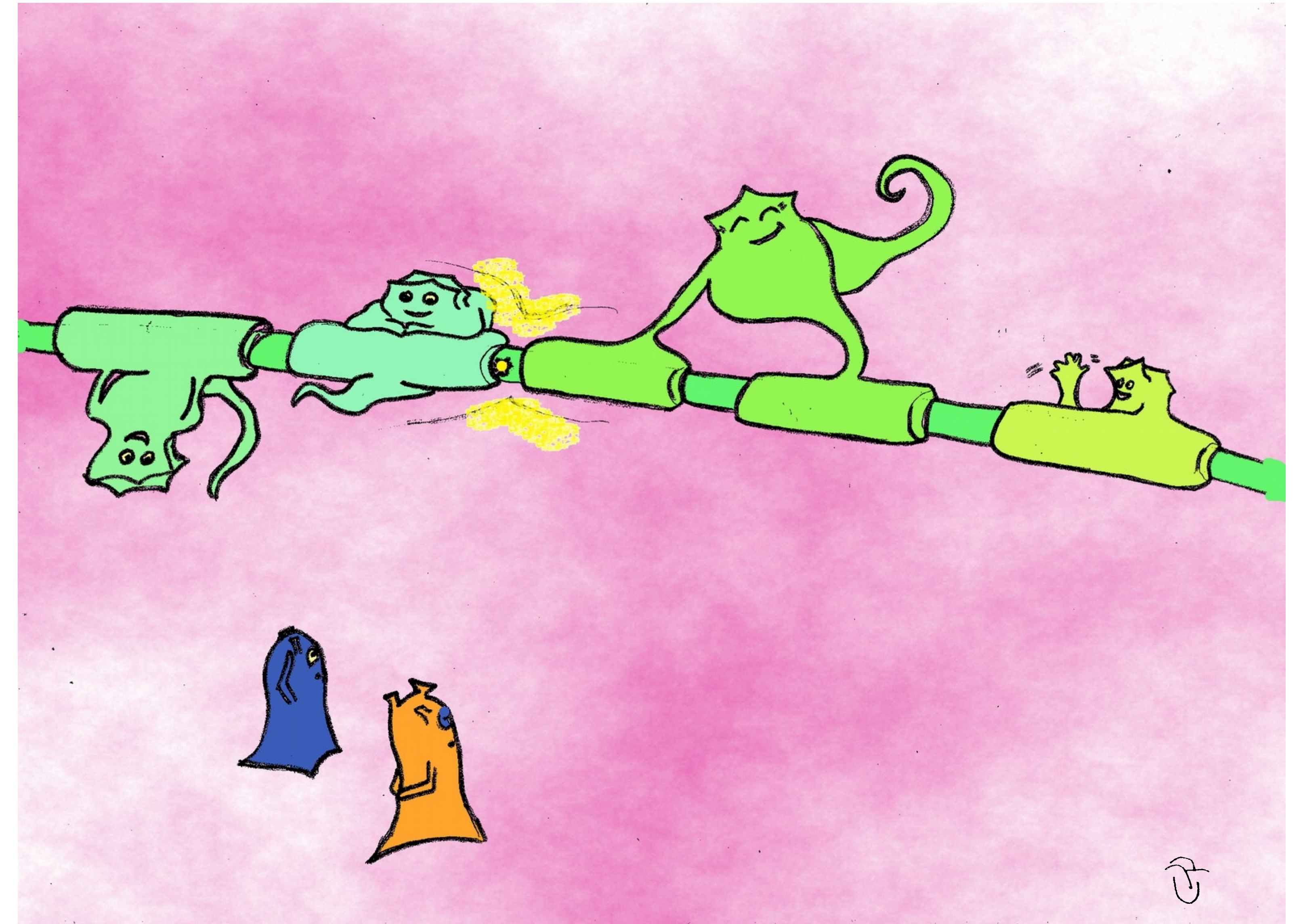
“I’d like to know how it works. Those lights are so quick they must have something special.”

With these words, a small character hidden behind the neuron breaks away to call out to them:

“Actually, those are the same lights as everywhere else!”



Mimi jumps in front of this appearance:
“But who are you? We thought we were alone here.”
Mischievous, their interlocutor bursts out in laughter.
He’s followed by more laughs coming from nowhere.
“To be alone in the brain, little microglia? But this is impossible, we are everywhere.”
All around Mimi and Bibli, tens of eyes are blinking.
Mimi, delighted, smiles to them:
“Who are you?”
The closest character to them answers:
“My name is Oli, I’m an oligodendrocyte. We are neurons’ friends, we wrap their axon up and speed up the lights.”



_So, it is thanks to you that those luminous messages go so fast? Bibli asks.

_Exactly! Thanks to me, those stars become shooting stars.”

Tens of exclamations raise:

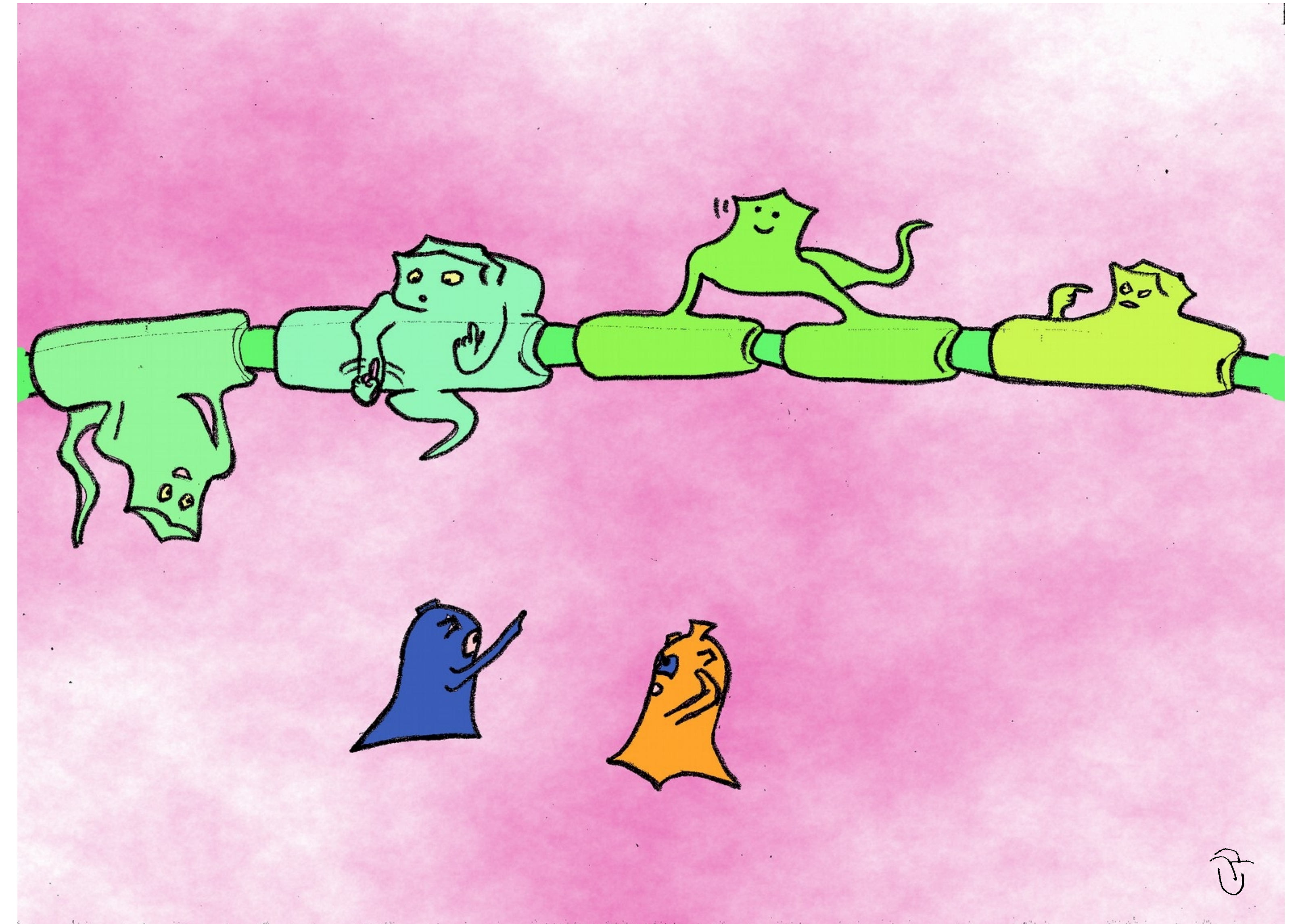
“No, it isn’t thanks to him, it’s thanks to me!

_No, to me!

_To me!

_Without me, there wouldn’t be any communication!”

One by one, the oligodendrocytes surrounding the axon crane their head to observe Mimi and Bibli. From the neuron’s head up to its synapse, each portion of the axon is surrounded by an oligodendrocyte. These begin arguing with each other about which one is the most important of all.



“Oh dear, Mimi says. I don’t understand anything.
_ Stop arguing ! Bibli exclaims. It’s simple, in order to know which one of you is the most important, we just have to ask someone who knows how all that works.

_ Oh, you want to talk to our Big One.

Mimi jumps:

_ Your Big One ? You have a Big One, like a chief?

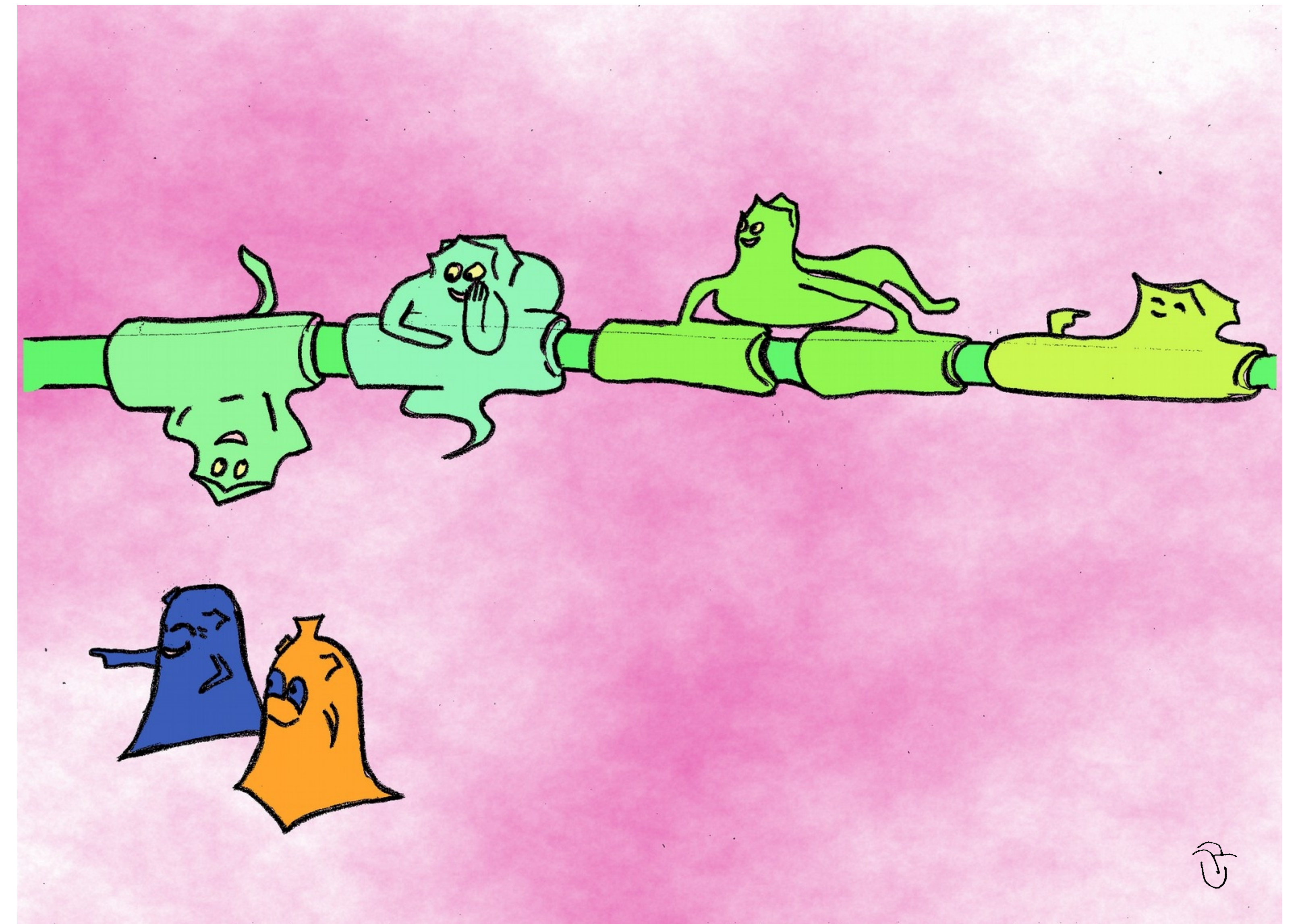
_ Not exactly, she is the neuron we’re wrapping up, Oli says. You can go and see her by going up her axon.

Very excited, Mimi and Bibli hurry up the axon. Around them, luminous messages are flying in the opposite direction and the oligodendrocytes stare at them, whispering:

“They’re gonna talk to the Big One.

_ I bet she’ll say i’m the most important.

_ No, it’s me!”



Mimi and Bibli finally arrive at the neuron's head.
“Hi! Mimi says, breathless. Are you the Big One?
_Hello, little microglia. Yes, that's the name my oligodendrocytes friends give me.

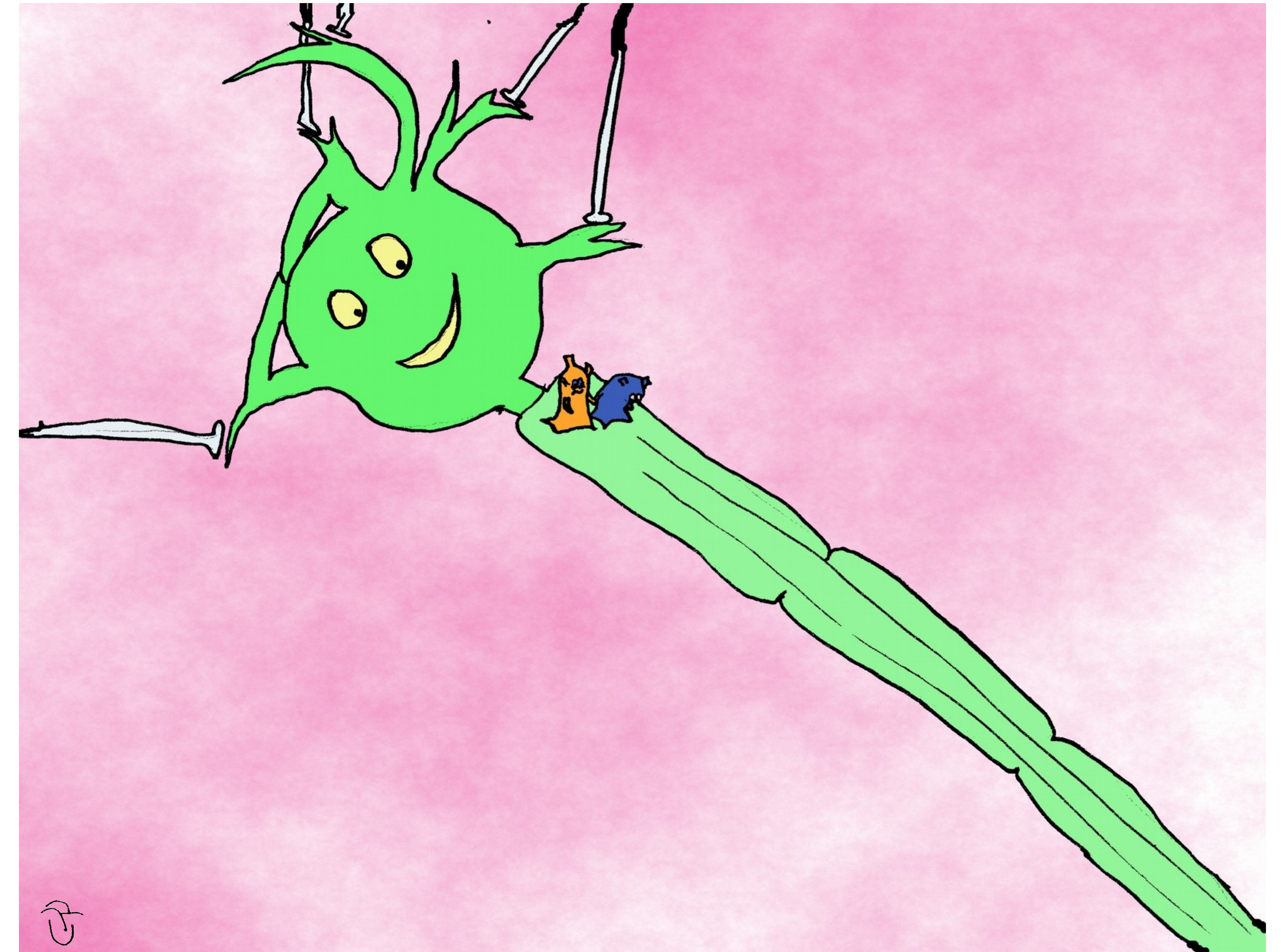
_But you're not the chief?

_No, I'm sorry. The oligodendrocytes call me like that simply because I'm much taller than they are.”

From the other end of the axon, Oli shouts:

_Big One, can you tell those microglia I'm the one making the lights go faster?”

Protesting cries arise immediately. The Big One has a clement smile.



“So? Bibli asks, impatient to know.

_Well, the neuron answers, to tell the true, all my oligodendrocytes are important. If only one of them stops wrapping up around my axon, I wouldn't be able to communicate so fast. But whatever I tell them, there is still one to believe he's more important than the others.”

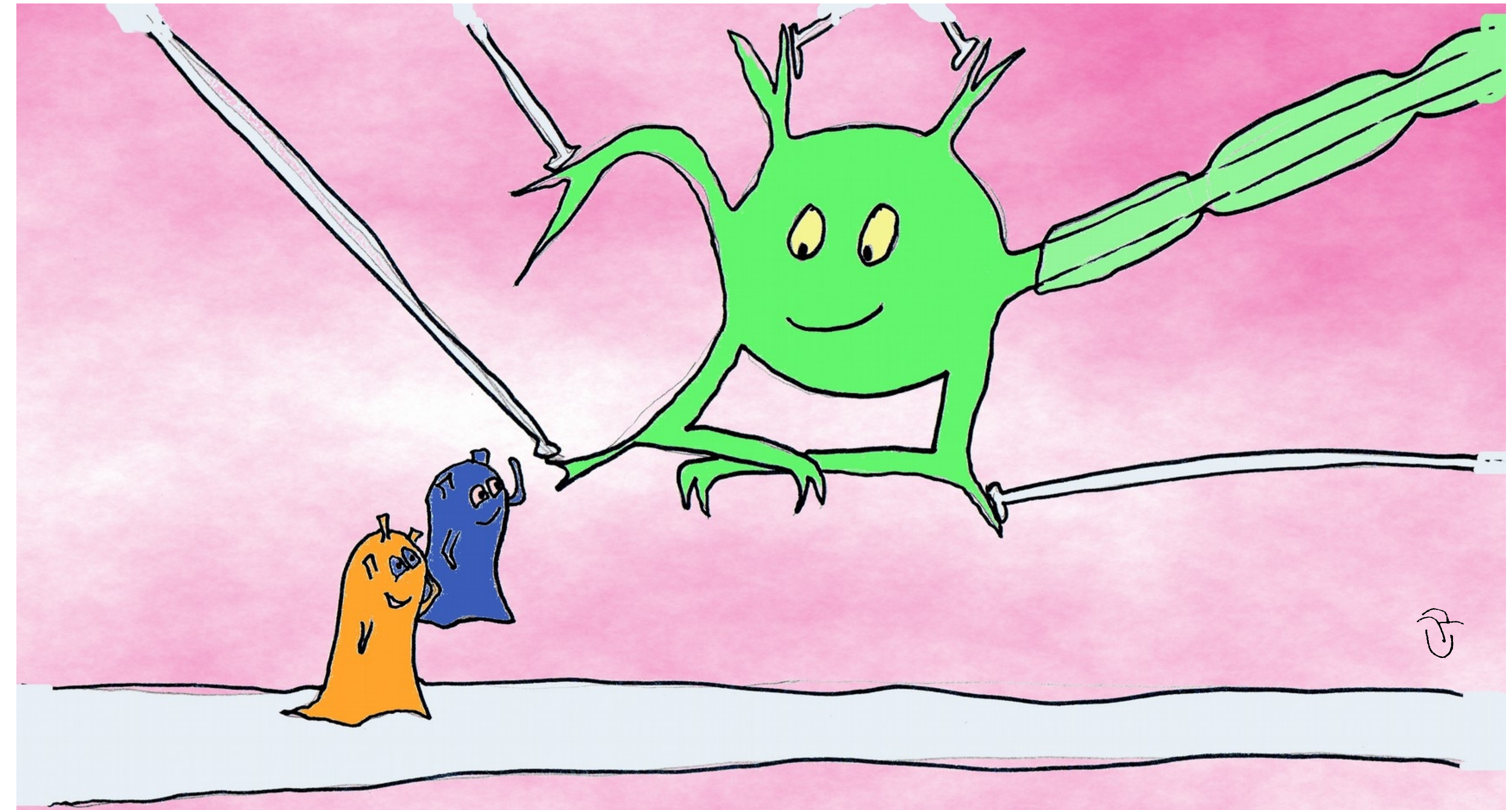
Mimi and Bibli look at each other. They think this neuron looks very wise.

“By the way, Bibli asks, don't you know who the chief is? We'd like to ask him if Mimi could go on holiday.

_No, I don't know, but you should go ask the neuron at the end of this dendrite. He communicates a lot so I think he's someone important.

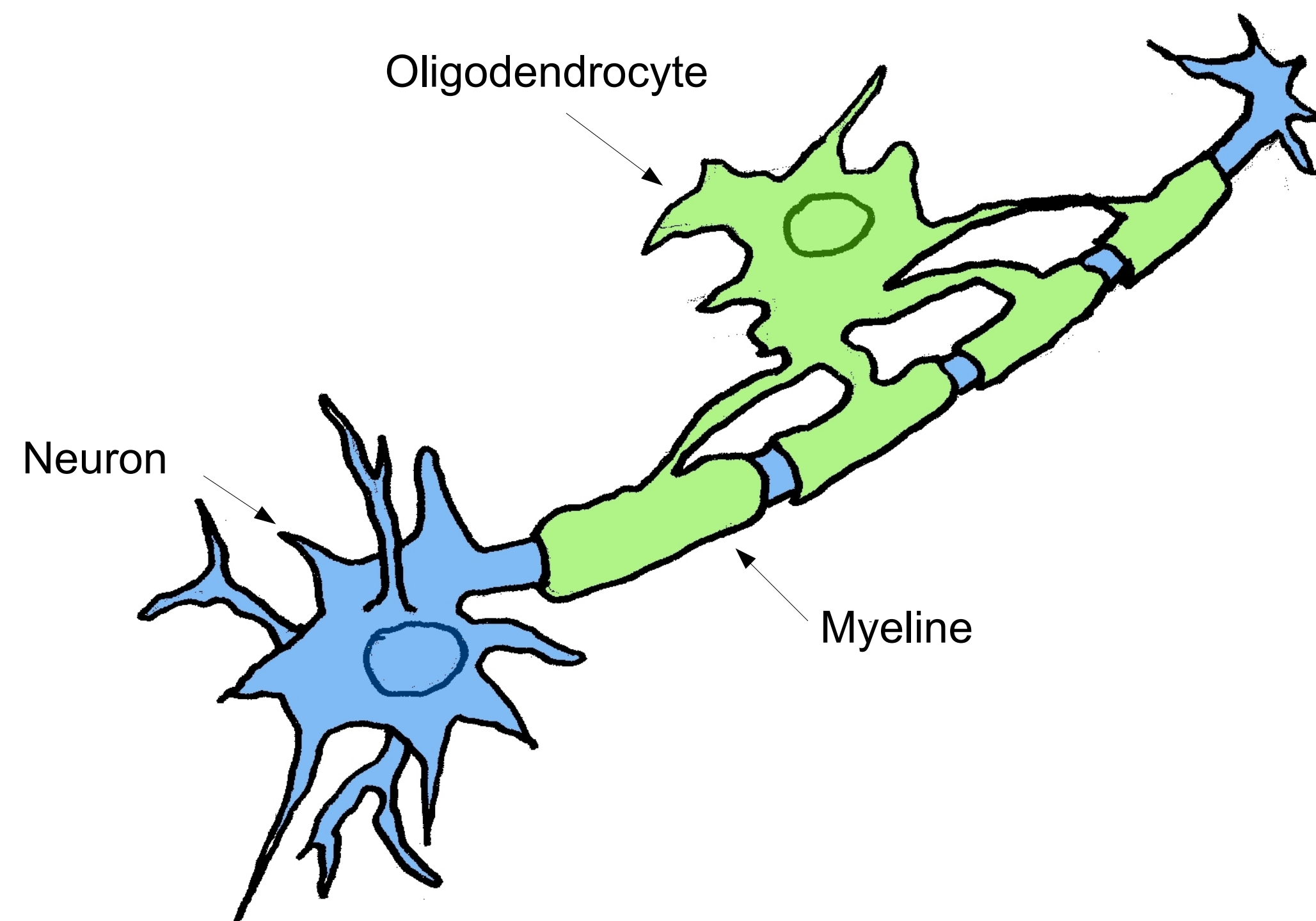
_Okay, thank you!

As Mimi and Bibli move away, stars continue to fly by and, distantly, tens of oligodendrocytes say goodbye to them.



To go further...

Like microglia and astrocytes, oligodendrocytes are also a type of glia cell. They enwrap the axon of certain neurons with strips of myelin. This substance prevents the conduction of electrical signals.



Therefore, the action potential has to «jump» between the parts of the axon that are free from myelin. This speeds up the transmission of neural information. For example this is really beneficial in the case of reflexes, when information has to be transmitted very quickly.

In the disease called multiple sclerosis, neurons start to malfunction and die because their myelin deteriorates. In some cases, astrocytes might release a toxic substance affecting the glia cells which produce myelin, causing their degeneration. Interactions between glia cells and neurons are still poorly understood and, sometimes, very surprising!

Bibli and Mimi carry on. And that is when, walking through an axon, Mimi hears her name:

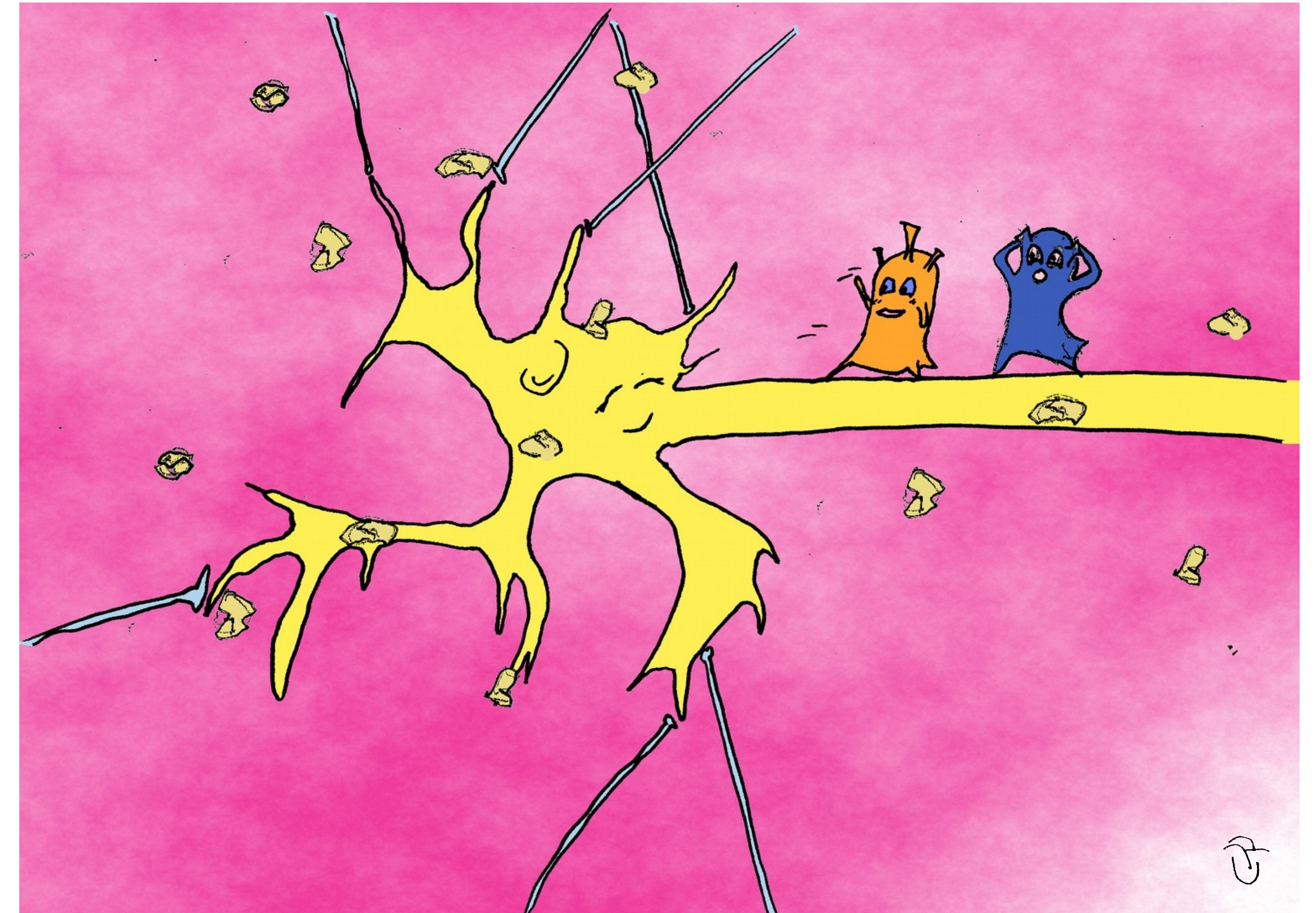
“Mimi!

_But... It’s Louis! Mimi exclaims.

_Mimi, there you are! I missed you! Hi Bibli, it’s been a while since I last saw you.”

Mimi has finally returned! But she looks around her and realizes that Louis is very dirty...

After her long trip, she finds herself with even more work...

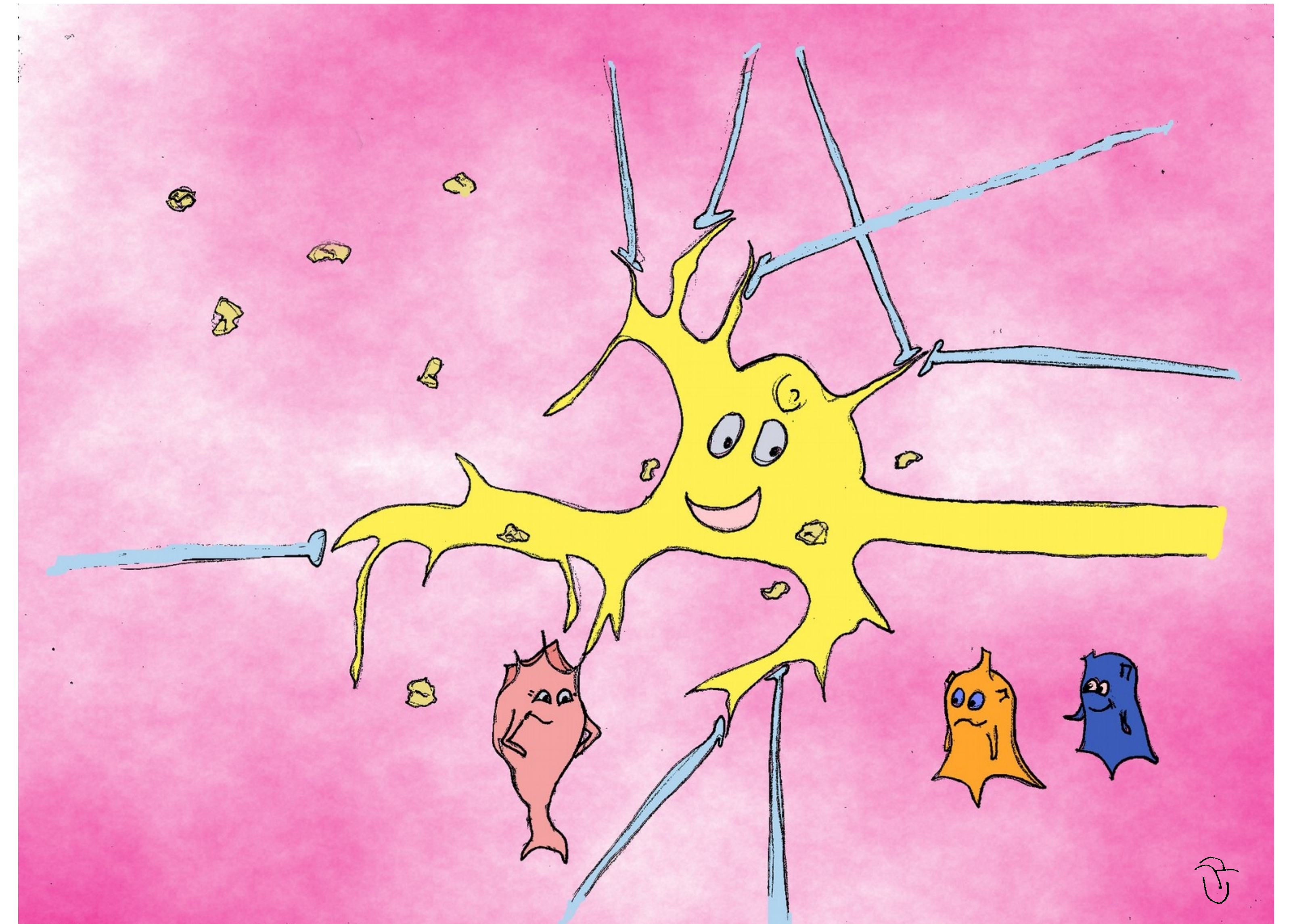


Then Astride, the astrocyte, perfectly awake, says to Mimi with big eyes:

“So then, you were gone looking for the chief?”

—Yes Astride, I wanted to go holiday! But I hadn’t found him... Actually, it seems that there is no chief in the brain. Everybody speaks, everybody listens, and it works!

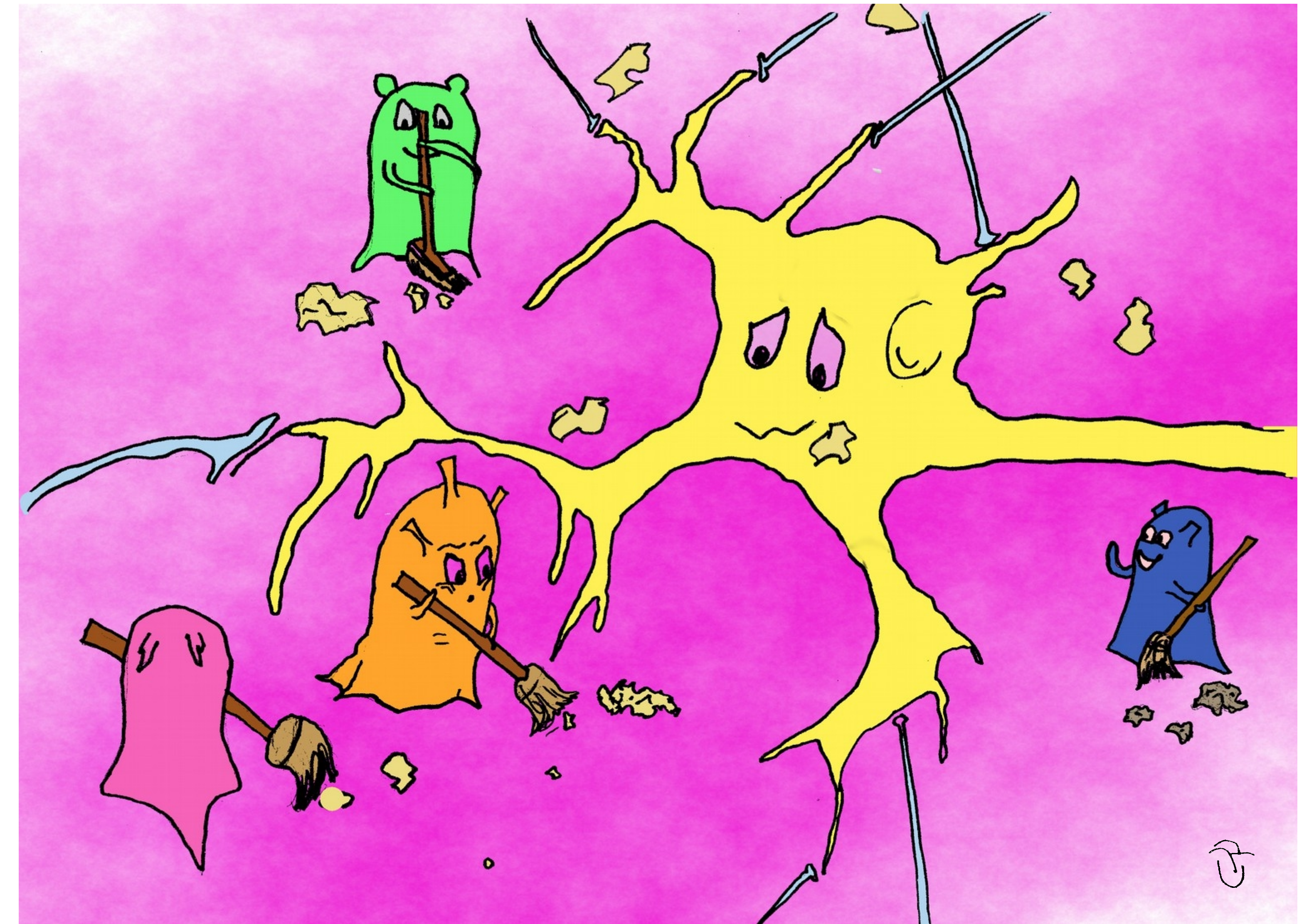
—But you just had to ask me, little one! I would have told you there is no chief in the brain! But it’s good you traveled to discover it by yourself.



Then Mimi stares at Louis all dirty and sighs. Bibli knows Mimi has to clean everything and she feels guilty for being gone so long. So, he calls all the other microglia to help. A lot of microglia help Mimi clean Louis, who is all clean in no time at all.

Then Astride says:

“See Mimi, in the brain, everybody has a role, a job. The neurons talk to each others, the microglia clean, the astrocytes distribute food and help others, oligodendrocytes speed up messages. We don’t need a chief; everybody knows what there is to do! And if you have any problem, or you’re swamped, others come and help you.”



In the end, Mimi is happy she went for her trip. She discovered a lot of things with Bibli, and now, she knows she can rest whenever she needs!

This is the story of how Mimi discovered there is no chief in the brain, how everybody has a role and how this system works in harmony.

