Welcome to the Huberman Lab Podcast,
where we discuss science
and science-based tools for everyday life.
I'm Andrew Huberman, and I'm a professor of neurobiology
and ophthalmology at Stanford School of Medicine.
Today, my guest is Dr. Noam Sobel.
Dr. Noam Sobel is a professor of neurobiology
in the Department of Brain Sciences
at the Wiseman Institute of Science.
His laboratory studies olfaction and chemo sensation.
Olfaction is, of course, our sense of smell.
Chemo sensation is our ability
to respond to chemicals in our environment.
Today, you are going to learn some absolutely incredible facts
about how you interact with the world
and other people around you.
For instance, you will learn that humans
can smell things around them as well as dogs can.
In fact, humans are incredibly good
at sensing the chemical world around them.
You also learn, for instance,
that every time you meet somebody,
you are taking chemicals from that person,
either from the chemical cloud that surrounds them
or directly from the surface of their body,
and you are actually applying it to your own body,
and you are processing information
about that person's chemicals
to determine many things about them,
including how stressed they are, their hormone levels,
things that operate at a subconscious level
on your brain and nervous system,
and that impact your emotions, your decision-making,
and who you choose to relate to or not to relate to.
You will also learn that tears, yes,
the tears of others are impacting your hormone levels
in powerful ways.
You will also learn that every so often,
actually on a regular schedule,
there is an alternation of ease
through which you can breathe through one nostril
or the other, and that alternation
reflects an underlying dynamic of your nervous system

and has a lot to do with how alert
or sleepy you happen to be.
The list of things that Dr. Noam Sobel's laboratory
has discovered that relate to everyday life
and that are going to make you say,
wow, I can't believe that happens,
but then go out into the real world
and actually observe that that happens
in ways that are incredibly interesting,
just goes on and on.
In fact, his laboratory discovered
that we are always sensing our own odors.
That's right, even though you might not notice
your own smell, you are always sensing your own odor cloud,
and throughout the day,
you periodically smell yourself deliberately,
even though you might not realize it,
in order to change your cognition and behavior.
I first learned of Dr. Sobel's laboratory
through a rather odd observance.
That observance took place when I was a graduate student,
many years ago, at UC Berkeley.
At the time, Noam Sobel was a professor at UC Berkeley,
as I mentioned before, he has since moved to the Weissman.
Well, I was walking through the Berkeley campus
and I saw people on their hands and knees,
but with their head very close to the ground
and their eyes were covered, their hands were covered,
their mouths were covered,
and only their nose was exposed.
And what I was observing was an experiment
being conducted by the Sobel laboratory,
in which humans were following a scent trail.
That scent trail was actually buried some depth
underneath the earth,
and yet they could follow that scent trail
with a high degree of fidelity.
It was from that experiment and other experiments done
in Dr. Sobel's laboratory at Berkeley and at the Weissman,
involving neuroimaging and a number of other tools
and techniques that revealed the incredible power
of human olfaction and humans' ability
to follow scent trails if they need to.

And that of course led to many other important discoveries,
some of which I alluded to a few moments ago,
but you are going to learn about many, many other
important discoveries in the realm of olfaction
and chemo sensation that have been carried out
by Dr. Sobel's laboratory
through the course of today's episode.
And by the end of today's episode,
I assure you that you will never look at or smell
the world around you the same way again.
Before we begin, I'd like to emphasize that this podcast
is separate from my teaching and research roles at Stanford.
It is however, part of my desire and effort
to bring zero cost to consumer information about science
and science related tools to the general public.
In keeping with that theme,
I'd like to thank the sponsors of today's podcast.
Our first sponsor is Roka.
Roka makes eyeglasses and sunglasses
that are of the absolute highest quality.
I've spent a lifetime working on the biology
of the visual system and I can tell you
that your visual system has to contend
with an enormous number of challenges
in order for you to be able to see clearly.
Roka eyeglasses and sunglasses were designed
with the biology of the visual system in mind.
So no matter whether or not you're wearing them for sport,
whether or not you're wearing them for work
or for socializing, you can always see with crystal clarity.
Their glasses are extremely lightweight.
So most of the time you don't even realize
that you're wearing them.
I wear Roka readers at night
and sometimes when I drive at night
and I wear Roka sunglasses throughout the day,
except of course I do not wear them
for my morning sunlight viewing.
If you'd like to try Roka eyeglasses or sunglasses,
go to Roka, that's Roka.com and enter the code Huberman
to say 20% off your first order.
Again, that's Roka.com and enter the code Huberman
at checkout.

Today's episode is also brought to us by thesis.
Thesis makes custom new tropics
and new tropics is a word that I do not like
because it means smart drugs.
As a neurobiologist, I can tell you
that there is no neural circuit in your brain
for being smart.
There are neural circuits for focus,
there are neural circuits for memory,
there are neural circuits for creativity
and there are neural circuits for task switching.
Thesis understands that there's a diversity
of neural circuits that support different brain body states
and therefore have designed new tropics
that are customized to achieve specific brain body states.
If you go to the thesis website and take a brief quiz,
they will design a new tropics starter kit.
Some of those new tropics that they'll send you
are designed to enhance your focus,
others for clarity, others for creativity and so on.
To get your own personalized new tropics starter kit,
you can go to takethesis.com slash Huberman
and take a three minute quiz
and thesis will send you four different formulas
to try in your first month.
That's takethesis.com slash Huberman
and use the code HuberminuteCheckout
to get 10% off your first order.
Today's episode is also brought to us by Helix Sleep.
Helix Sleep makes customized mattresses and pillows
that allow you to get the best possible night's sleep.
So if you go to the Helix website,
you can take a very brief quiz,
it only takes about two minutes and answer questions
such as do you tend to sleep on your back
or your side or your stomach?
Do you tend to run hot or cold throughout the night?
Maybe you don't know the answers to those questions,
but they'll match you to a mattress
that's ideal for your sleep needs.
For me, that was the Dusk DUSK mattress,
which is not too firm and not too soft.
And I've been sleeping on it for more than two years

and it's the best sleep that I've ever had.
If you'd like to try a Helix mattress,
go to helixsleep.com slash Huberman.
Take that two minute quiz
and they'll match you to a customized mattress
and you'll get up to $350 off any mattress order
and two free pillows.
Again, if you're interested,
you can go to helixsleep.com slash Huberman
for up to $350 off and two free pillows.
And now for my discussion with Dr. Noam Sobel.
Dr. Sobel, Noam, welcome.
Thank you.
Must say I am extremely excited for this conversation.
I've been a huge fan of your work
for more than a decade or two.
Yes.
Kind of frightening.
Yeah.
We overlapped at UC Berkeley some time ago,
although we did not meet.
Although we lived in the same apartment.
And we just learned that the amazing apartment
that you moved out of was the apartment
that my girlfriend and I at the time moved into in 2006,
I believe.
So we've shared quite a few things.
And today I'd love for you to share with us
all about the amazing landscape of chemo sensation
in particular olfaction or sense of smell
and some related perceptual abilities
or subconscious abilities, including pheromones, et cetera.
To get everybody on the same page,
I'd like to just start off by asking
what are the major components of our ability to smell?
Obviously, where I like to think it involves the nose
at some level, it does.
To what extent is that mixed in with other senses
like taste?
And perhaps more importantly,
what about the chemicals that we are sensing
through this thing?
And for those of you listening and not watching,

I'm tapping my nose that we are not aware of,
that the chemicals that we're inhaling
making sense of without our awareness.
If you could just give us the top contour
or even deep contour of you like of the parts list
and the various roles they play.
So you've asked a lot of questions at once.
I'll start with a little comment on the way
you said smelling through our nose, which we indeed do,
but we also smell through our mouth actually.
There's a process referred to as retro nasal olfaction
where odorants come up through the back of our throat
and out of our nose the reverse way.
And we smell things that way as well.
And in fact, a big part of the contribution of olfaction
to food and taste comes from that,
from retro nasal olfaction.
But primary olfaction is referred to as ortho nasal olfaction
that is through our nose.
We sniff and sniffing is a big thing.
Well, I have a sense we might talk about that a lot today
in all sorts of contexts.
So we sniff in through our nose
and to answer your general question
of the organization of the system.
So molecules, airborne molecules travel up our nose
a distance in the human of about six or seven centimeters
to about here where they interact with,
I will use the word sheet of receptors,
but sheet is a bit misleading here.
It's not a sheet, it's very convoluted.
We have about seven million such receptors
lining a structure known as the olfactory epithelium.
This is the sensory surface of the olfactory system,
the olfactory epithelium.
Again, about probably about six or seven million receptors
in the human.
In the human, probably of about 350 different kinds.
So that's amazing.
That means a meaningful percentage of your genome
is devoted just to this,
just to the kinds of olfactory receptor subtypes
you have in your nose.

By the way, I can share an amusing story.
I would imagine amusing stories are good for podcasts.
So that number of six or seven million receptors
is probably not very well grounded.
It's hard to count, but it's reasonably grounded.
And there was this thing roaming around in the literature
about bloodhounds having a billion receptors
in their nose, which is why they're so amazing.
And this number was, you know,
it sort of propagated through the literature.
And our lab has written over the years,
a few review chapters,
and we were repeatedly writing the olfaction chapter
for a very large, one of these large textbooks,
the Gazanaga Handbook of Cognitive Neuroscience,
I think it's called.
And we had that in there as well somewhere.
And one time when we're renewing the chapter
for a new version of the book,
I told the graduate student who was leading that
at the time, Araya Sharoon.
She's now a professor at Tel Aviv University.
I told her, check that, check that reference out.
Where in the world did that come from?
And we started going back and back and back.
And it turns out it comes from a textbook,
an Australian textbook.
And we found the author of the textbook
and we wrote her and said, look, there's this thing
in the literature of a billion receptors in the bloodhound.
Where did that come from?
And surprisingly, she answered me.
And I was hoping to get a reference, right?
But it wasn't a reference.
And this is where it really becomes funny for us
because she said, I was once at a lecture
of an olfaction geneticist by the name of Doron Lancet.
And he said that in the lecture.
Now, this is really funny because she's in Australia.
This is all over the world, this number.
And I'm writing her from Israel.
And Doron Lancet is in the building next to me.
He's in Weizmann Institute of Genetics.

I mean, he used to be, he's retired now.
And he had meaningful contributions
in the history of olfaction.
So I picked up the internal phone and I said, hey, Doron,
did you say that there's a billion receptors
in the bloodhound nurse?
And he said, what's a bloodhound?
So this was totally made up, right?
It totally made up and it propagated.
I mean, you can probably go into Google
and type like a billion receptors in the bloodhound
and you'll get a lot of hits.
But there was absolutely no evidence for that.
Amazing.
And not just amazing in light of what it tells us
about olfaction in bloodhounds or otherwise,
but amazing because it sheds light on just how much
of what is in textbooks, scientific and medical
is absolutely wrong.
Things propagate and, you know, you set yourself in, right?
So we fixed that in that version of the,
and so to finish the line, so Doron's interact
with these receptors here in our epithelium
where they undergo what is referred to as transduction,
that is the odorants are dock at a receptor
and turn into a neural signal or enforce the receptor
to respond in a neural signal.
And this neural signal, in fact, action potentials,
not gradient potentials of any kind,
propagates via the olfactory nerve.
Now this is a nerve that goes from our epithelium
right here behind the forehead.
No, it's, well, yeah.
Yeah, here.
Through the thinnest part of our skull,
an area referred to as the cribriform plate,
which is perforated, it has a lot of holes.
The nerve goes through those holes
and synapses at the first target in the brain,
which is the olfactory bulb.
In humans, that forms an interesting point of sensitivity
because a lot of people lose their sense of smell
due to trauma because of that structure.

Yeah, a head-hit type trauma.
Well, yes, although you denoted hitting
on the front of the head,
which is where all this real estate is,
but actually the more common cause
for losing your sense of smell for trauma
is the back of the head
because of what's referred to as a contricue injury.
So as your listeners probably know,
our brain is floating in liquid in CSF,
in cerebrospinal fluid inside our skull.
And when we get hit in the back of the head,
the brain has this forward and backward movement
in the liquid, in the skull.
It sort of crashes.
It can crash against the front of the skull,
which is why you also have, in a contricue injury,
you also often have frontal damage.
But what happens is that this generates a shearing motion
on the cribriform plate,
and the olfactory nerve is severed.
And if it's completely severed, it's lost forever.
Because my understanding is that the olfactory sensory neurons
are among the few central nervous system neurons
in adult humans that can regenerate
or replenish themselves.
Right, so again, there are a few questions.
Yeah, that's okay.
So first of all-
We will spin many plates simultaneously.
If it's completely severed, completely,
then yes, you're lost.
Forever.
Yeah, if it's completely severed,
because even if you'll have regeneration
at the basal cell level at the epithelium,
they won't manage to find their way back to the bulb.
If you have partial or something left,
or something shows up in a short while after the injury,
then you have a good chance of recovery.
Because they grow along the trajectory of the other axons
or pioneering the way for them.
Assuming, yeah.

Interesting.
And so basically the timeframe,
and you know, it's funny,
I get a lot of emails on this,
although I'm not a medical doctor,
but I get a lot of emails
from people who have lost their sense of smell
because it's very distressing.
And now more people know this because of COVID,
that it's very distressing.
And basically the rule of thumb is that
if you don't get it back within a year to a year and a half,
you'll never get it back.
My understanding of the statistics on olfactory loss
and COVID and other viral type infections is that,
first of all, I had, I experienced that when I got COVID.
Including total anosmia?
For one day.
And not total, it was just,
there was a remnant of an ability to smell,
or perceive the smell of a lemon,
and I was huffing as hard as I possibly could.
I actually, there's an over-the-counter remedy,
and this is not pseudoscience
because there's a number of papers published about this
on PubMed that alpha-lipoic acid
can accelerate the recovery of smell.
Yeah.
And so that's something that,
it worked successfully for me.
I'm not saying that that's the only route.
You don't know if it worked successfully for you,
or if you would have recovered anyway.
I mean, you didn't do a control study.
But I was not willing to do the control experiment.
Exactly.
Let me say two things on this front.
First, the dean on the alpha-lipoic acid is,
yeah, it's not overwhelming.
But losing your sense of smell is overwhelming.
Yeah, no, no, I know.
And so I think people feel desperate.
One word about smelling the lemon,

and this is, I'll take that opportunity
to share more information.
When we smell things,
it's the result of more sensory subsystems
than the olfactory system alone.
So you have several chemo-sensory
sensitive nerves in your nose.
A primary one beyond the olfactory nerve
is the trigeminal nerve, the fifth cranial nerve.
So the trigeminal nerve has sensory endings
in your nose, in your throat, and in your eye.
It has three branches.
That's why an onion has smell
and burns your eyes and burns in your throat.
Is that why?
It's trigeminal, yeah.
The tearing of cutting an onion is trigeminal.
It's a trigeminal reflex.
Amazing.
We talked about trigeminal in the context of headache
during a headache episode.
It's a trigeminal reflex.
So the lemon you are smelling
may have been a trigeminal sensation.
So smelling the lemon with my eyes is what you're saying.
Well, no, with your nose,
but with your trigeminal receptors
and not your olfactory receptors.
Within olfaction researcher jargon,
there's what we refer to as pure olfactants.
These are odors that will stimulate
your olfactory nerve alone.
They won't influence your trigeminal nerve at all.
And an example just to get a sense of what that might be
would be the coffee right here is a pure olfactant.
Vanilla is a known pure olfactant.
These things have no trigeminal activation.
As long as we're on this topic
and we'll weave back and forth,
but I'm glad we are on this topic
because a tremendous number of people
wrote to me during the pandemic
and continue to about olfactory loss.

I've heard of this olfactory training
whereby if you have a partial
or even a complete loss of primary olfaction
that one is encouraged to smell
a number of different smells.
I grew up studying activity dependent wiring
of the nervous system.
It makes total sense to me why keeping neurons active
keeps them alive.
So this is not fire together, wire together type thing.
By the way, that's a quote from Carla Shatz,
not Donald Head folks or me.
But this is about keeping neurons electrically active.
In this case, olfactory neurons
in order to maintain their connections
because otherwise they will die.
Olfaction is a definite use it or lose it system.
And so that makes total sense.
And indeed there's very strong evidence for success
of the training programs,
more than the alphalopoic acid.
And so that's a real thing.
And what's cool about that is that you don't need
to go out and buy expensive things.
Although you can, of course there are people
who are capitalizing on this commercially already,
but you can just take things from your refrigerator
or your makeup cabinet or whatever and smell them
attentionally and constantly and sniff them.
And that exposure will help you recover.
There is good data on that by now.
You made that point in passing about regeneration
in the olfactory system.
Indeed, they're one of the cool things.
So in olfaction, you can study many things
through olfaction.
Indeed, one of them is neuro regeneration
because the olfactory neurons are really the only neurons
that do that systematically in the adult mammalian brain.
And whether the human olfactory system
shows the same level of regeneration
as it does in other mammals is
and was somewhat questionable.

And I'm just bringing that up to share a really cool study
that was published in neuron, I think somewhere
around 2014 where to address this question,
I just really liked the idea of doing that.
What the authors did was look at, in post-mortem,
they looked at levels of C14 in adults who were exposed
to atomic bomb experiments.
So you can actually look at these neurons
and time them based on exposure to radiation.
And that paper suggested that there's not as much turnover
in the human olfactory bulb as there is in other mammals.
Other lines of data suggest otherwise.
So this is kind of a debated question
as to what extent of neuro degeneration you have
in the human olfactory system as opposed to other mammals.
But that was just a really cool paper, I think, of doing that.
Fascinating.
Should I finish the path?
Just so we have the, so information then synapses
at the olfactory bulb from the olfactory epithelium.
And the pattern of that synapsing
follows what's referred to as the most extreme case
of convergence in the mammalian nervous system.
More specifically, what happens is that all the receptors
of a given subtype, and remember humans,
we said we have about 350,
in the mouse we have about 1,200 probably.
So all the receptors of one subtype converge
to one location in the bulb.
And this location is referred to as a glomerulus
or an imploroglomeruli.
And that may be a slight oversimplification.
It's in fact, two glomeruli.
There's a mirror, sort of a mirror cut line.
And so all the receptors of one subtype
will converge to two mirror glomeruli
on the olfactory bulb.
So you end up having two glomeruli
that reflect that one receptor subtype.
And so if, and this is as far as,
I'm giving you now the textbook view
of how the system works,
but then I can, I'll happily share with you things

that pose a problem for the textbook view
of how things work.
But the textbook view of how things work
is that every such receptor subtype
is responsive to a small subset
of different molecular shapes,
what sometimes referred to as ototopes,
the molecular aspects of the odorant.
So each receptor is responsive
to a different subset of ototopes, let's say 10.
And each ototope will activate
a different subset of receptors.
So potentially you have this insane
comet entorex of this potentially 350-dimensional space
in the human, potentially.
But then because of this convergence,
you end up having on the bulb in a way a map
reflecting receptor identity.
So let's say this coffee activates receptors
of type one, three, and seven.
So the glomeruli of receptors one, three, and seven
will light up, quote, unquote, when I smell a coffee.
And if you could take a snapshot of that,
theoretically you would have the map of coffee
and so on and so forth.
This is sort of the textbook view of how the system works.
And then information goes from the bulb
to several targets in the brain.
I mean, what is referred to as primary olfactory cortex
is piriform cortex and enthorinol cortex.
This is on the ventral surface of the brain,
the lower portion of our temporal lobe.
And information goes there directly,
but it also goes directly to the amygdala.
It probably goes directly to the hypothalamus.
It may go directly to the cerebellum.
It goes all over the brain.
So information projects widely from there.
And as far as people understand,
the map that may exist on the bulb
doesn't exist in the rest of the brain.
And the understanding of how coding occurs
in the rest of the brain is murky.

Commonly one hears that the memories that we have
of odors are somehow more robust
than the memories of other perceptual events in our life.
I don't know if this is true or not,
but people will say, for instance,
I can still remember the smell of my grandmother's hands
or the smell of cookies in her kitchen.
At a minimum, it points to the fact
that smell and memory are closely linked.
And you just mentioned a direct,
multi-station, but nonetheless,
somewhat direct path from the nostrils to the hippocampus,
one of the primary encoding centers
of memories in the brain.
Two synapses away.
Yeah, which is a remarkably short pathway,
considering that, for instance, just by example,
because some of our listeners
that won't be familiar with this,
but some will that sound waves that are transduced
into neural signals at the level of the inner ear
go through many stations before they arrive
at the location in the brain
where we make sense of those sound waves
as voices or music, et cetera.
Whereas olfaction is more of a direct route
to the memory centers.
Is there any just-so story or real objective truth
to the idea that olfactory memories are formed more easily
or maintained longer or more robustly
than other sorts of memories?
So, yes.
But first, I should say that I'm not an authority
on olfactory memory.
It's sort of, olfactory memory is a huge field of research
and somehow our lab has never really gone much into that.
Although, again, the same student I happened to talk about
before, Yair Ayusharun, who's again now a faculty
at Tel Aviv, ran a study, a paper,
we think we publish in current biology
called The Privilege Representation
of Early Olfactory Associations.
Basically, there's something about the first time

you experience a smell that generates
a particularly robust representation,
more than other sensory stimuli.
And that's what she, in fact, compared.
So there's something about the first exposure to a smell
in terms of the brain encoding that etches it into our being.
And this is an effect that has, you know,
it has echoes, of course, in literature.
I mean, you know, the biggest cliché
in this is to bring up the Proust effect, right?
So the Proust effect is when he ate the Madeleine
and then immediately the taste and smell
immediately reminded him of an event in his childhood
where the same Madeleine appeared.
But so that's something very real.
There's a lot of research on it,
not coming from our work.
So I'm not an authority.
But it does sound like there's something special
about olfaction.
And that doesn't mean that there isn't something special
about vision or audition.
Each one has its own unique.
I'm the last to argue that there's something special
about olfaction.
My students make fun of me because they say,
and there's some truth to that,
that I try to explain everything
through the olfactory system.
I mean, for me, everything is olfactory.
So, yes.
Through the lens of the nose.
I'd like to take a quick break
and acknowledge one of our sponsors, Athletic Greens.
Athletic Greens, now called AG1,
is a vitamin mineral probiotic drink
that covers all of your foundational nutritional needs.
I've been taking Athletic Greens since 2012,
so I'm delighted that they're sponsoring the podcast.
The reason I started taking Athletic Greens
and the reason I still take Athletic Greens
once or usually twice a day
is that it gets to be the probiotics

that I need for gut health.
Our gut is very important.
It's populated by gut microbiota
that communicate with the brain, the immune system,
and basically all the biological systems of our body
to strongly impact our immediate and long-term health.
And those probiotics and Athletic Greens
are optimal and vital for microbiotic health.
In addition, Athletic Greens contains a number
of adaptogens, vitamins, and minerals
that make sure that all of my foundational
nutritional needs are met.
And it tastes great.
If you'd like to try Athletic Greens,
you can go to athleticgreens.com slash huberman
and they'll give you five free travel packs
that make it really easy to mix up Athletic Greens
while you're on the road and the car on the plane, et cetera.
And they'll give you a year's supply of vitamin D3K2.
Again, that's athleticgreens.com slash huberman
to get the five free travel packs
and the year's supply of vitamin D3K2.
When I was at Berkeley,
I was walking across campus one day and I saw,
I think students, but I saw people on their hands and knees
with goggles on, gloves on.
And I think their mouths were covered too.
Everything was covered.
Was covered and they were walking,
they were crawling along the ground.
And I thought this was peculiar,
but then again, it's UC Berkeley.
And the joke is if it,
to get noticed on the UC Berkeley campus,
you have to be naked and on fire, right?
One or the other would not be sufficient.
Please don't run this experiment,
but it's that kind of place.
But nonetheless, a paper came out a few years later
describing the results of what turned out to be
your experiment that your laboratory was running,
which was having people follow an odor trail
with their nose.

And my understanding is that people can improve
their ability to track scents quite robustly,
especially if we deprive them of vision
and somatosensation that is touch and some other sensations.
Maybe you could just tell us a little bit about that study.
And for, I think in our audience,
I'm suspecting that many people
have a keen, keen sense of smell.
I have a family member who just like detect
any negative, you know,
putrid odor in the environment,
but also good odors exquisitely well.
And I have other family members
whose sense of smell is quite poor.
I'd love for all of those people to learn a bit
about what is possible in terms of training up
or improving our ability to smell.
And perhaps in the context of that study, if you will.
Yeah, so first,
before even talking about improving,
just off the bat,
humans have a remarkable sense of smell.
And this is something, again, in our lab,
we already said, you know, yeah, we know this,
this is all news, but to people
who come from different worlds,
we have to reiterate this.
Sometimes when I give public lectures
to non-alfaction audiences, I reiterate this.
Humans have an utterly remarkable sense of smell.
To put that a bit into sort of things
that are tangible.
So, for example, mercaptans,
which are added to cooking gas so that we smell it,
because otherwise it wouldn't have a smell,
so that the smell of gas,
it's not the smell of gas, of propane,
it's an additive.
Mercaptan?
Yeah, it's mercaptan.
The sulfur-like smell.
So, our detection threshold,
that is the level at which we can detect it,

is 0.2 parts per billion.
Okay, there's no machine
that can really do that that effectively.
No gas chromatograph, nothing.
Now, to give you another sense
of making this again really tangible,
we're working with an odorant in our lab
called Estra-Tetra-Enol,
that our participants can detect
when we have it mixed at 10 to the negative 12 molar
in the liquid phase.
To give you a real sense of that,
we did the math.
If you would take two Olympic-sized swimming pools,
and you would pipe it one ML, one drop,
into one pool versus the other,
you could smell the difference between the pools.
Incredible.
That's the detection threshold
that you have with your nose.
People have an utterly amazing nose, okay?
So, that's just in terms of its detection abilities,
which are just remarkable,
really up there in the mammalian world,
we're not a bad mammal in all factions.
And beyond that, we can improve, okay?
And the example you're talking about
actually started off as a lab bet, okay?
We were having a lab picnic.
So, I guess I should hear Flynn,
because I'm your guest
from the Weizmann Institute of Science in Israel,
but before going back to my home in Israel,
I was a faculty at UC Berkeley
in the Helen Wills Neuroscience Institute.
And this study was done during that time.
And we were on a lab picnic,
and we were having indeed
one of these sort of lab discussions arguments
on what humans can and can't do with their sense of smell.
And I said that humans could truly even track odor
like a dog, and people there said, no way.
And we ran this quick experiment,

which I have video of,
but I don't think we'll show it here.
But I actually have original,
the picnic video, we have it.
And a graduate student by the name of Cristina Zalano,
brilliant graduate student at that time,
who's now a professor at Northwestern.
And she's really leading the field
of all faction imaging today.
But she was the volunteer,
and we dragged a chocolate bar across the grass
and blindfolded her and checked if she could track
the track we made with the chocolate,
which she did very effectively, right?
And as far as-
Did you place her at the starting point of the line?
Or-
Yeah, I think we did.
I don't exactly remember what we did
on that sort of picnic tryout.
But I assume she never practiced that
in her life before, right?
And yet, she did it really, really well.
And then this went on as a lab bed in a way
that I said to my students,
okay, we have to make this into an experiment,
put it in an experimental setting
and quantify what's going on.
And they all said that it would be uninteresting.
That was the bet.
And I told them it would be in nature,
which is a bet I won in this case.
Nature, of course, being one of the three Apex journals
by itself.
It was nature neuroscience to prepare.
But so then we turned it into an experiment.
And what the experiment was,
is that we brought in participants,
naive participants, not graduate students from our lab,
completely deprived them of any other sensory input.
So we blocked their eyes, we blocked their ears,
we blocked everything.
We blocked, they were wearing heavy gloves.

You know, they can sense anything.
And we generated a consistent odor path in the grass,
which is what you saw.
We did that by burying twine under the grass
and odor impregnated twine.
So that way we could generate
a consistent odor trail every time.
Was it at the base of the grass or in the dirt?
It was buried.
It was buried under the grass.
Really?
Yeah, yeah.
Wow.
I did not know that.
It was buried under the grass.
And we conducted aerial photography.
And participants also had the sensor pack
that they were wearing,
where we measured nasal air flow
in each nostril in real time.
And we also used something called RTK GPS,
which is a way to lay radio frequency grid
over the GPS grid,
so that you have millimeter resolution in space, basically.
It's used by surveyors mostly,
so that we could track behavior.
And we found a few things doing this.
One is that people could just do this right off the bat.
The second thing we found that is when we train them up,
then within average of four days,
the rate limiting factor became the speed
at which they could crawl.
So as fast as you could crawl, you could send track.
Of course, you can't crawl as fast as a dog can run,
but as fast as you can crawl, you can send track.
And then to sort of add what made it really interesting
from a systemist neuroscience perspective
is that we asked whether having two nostrils
contributes to this.
So we built, we constructed a nasal prosthesis, if you will,
that had two versions.
One is that it combined both nostrils
into one big nostril centered,

and the other is that it maintained two separated nostrils.
And we compared performance under these two conditions,
and people performed better with two nostrils
over one centralized nostril,
although the flow remained the same.
So you're taking advantage of the information
that comes from your two separate,
totally separate nostrils.
By the way, the system I described before
of your epithelium and bulb and connection to cortex,
you have two of those, right?
It's completely unilateral,
well, almost completely unilateral system.
There's some very small exceptions to that, but-
So a representation on both sides of the brain,
much in the same way we have two eyes,
we're not a cyclops.
We can gain depth perception information.
We can perceive motion better as a consequence
and a number of a depth, especially stereopsis.
And we can locate sound
because of the difference between our ears
and how the head blocks them between and-
Amazing.
Another question about the mechanics and strategies
that you observed,
because I think there's information about the system,
the brain as a consequence.
Were you in a position to measure sniffing frequency?
And the specific question I have is,
were people doing something along the lines
of a quick sniffing or a-
Right.
A long draw in inhale.
You know, we didn't,
so yes, we were measuring sniffing and recording it
and we have all the data.
There was nothing very remarkable in that data,
in that study, although it may reflect
that we didn't analyze it carefully enough as well.
I mean, it wasn't a major component of our analysis.
Although we did look at it to some extent,
again, you're asking me about a paper

from quite a few years ago,
so I may be forgetting parts of it as well.
But-
I'm sure if it was a major component of it,
it would have risen to the top.
It definitely wasn't a major finding
of the sniffing behavior in the paper.
Although again, sniffing behavior is a huge portion
of our life and lab and it's taking us to places.
And it's reemerging now in our work.
We're doing tons of sniffing work.
You know, I can share with you something
that I think will interest your listeners
and viewers as well and we think
is really one of the most overlooked things
in neuroscience.
I'll invite you to do the following experiment.
So occlude one nostril by pressing on it from the side
and sniff in and then occlude the other and sniff in.
Do you sense a difference in flow?
Yes.
Do you know why that is?
No, and it was the next question on my list.
Don't feel badly about not knowing why that is.
Most people don't.
But that is a reflection of something referred to
as the nasal cycle.
So in fact, if you were to do that repeatedly,
you would find that your high flow nostril
and low flow nostril alternate
every two and a half hours on average.
In an absolute way or is it kind of like a sine wave,
like gradual shift to the one and then gradual shift back?
It can vary.
And we don't yet know the rules, all the rules,
but you have this constant shift from side to side.
The shift becomes incredibly pronounced in sleep.
So we can measure the power of the difference.
And in sleep, you have this phase shift of power.
You have a huge, like one closes and one opens totally.
And it turns out that this is linked to balance
in the autonomic nervous system.
So as you and your listeners know,

we have an autonomic nervous system
that has a sympathetic and parasympathetic component to it.
And they're in balance or imbalance in many diseases,
for example.
And this interplay between the auto,
between the sympathetic and parasympathetic nervous system
drives the switch from left to right nostril.
Just to remind people, sympathetic nervous system
has nothing to do with sympathy,
has everything to do with generating patterns of alertness.
It's sometimes called the fight or flight system,
any pattern of arousal, positive or negative.
And then it's balanced in a coordinated way,
or at least in parallel with the parasympathetic nervous system,
which is sometimes called the rest and digest system,
but is it associated with all sorts of things,
the sexual arousal response,
and a number of other aspects of our physiology.
So thinking of it like a seesaw of alertness and calm.
Perfect.
So now imagine, right?
Imagine you would walk around living your life, right?
Half of the time with one eye closed like this,
and the other half with one eye closed like this,
and you had this eye cycle, right?
And that was linked to autonomic arousal.
I assure you, you would go to PubMed,
there would be five million papers on the eye cycle, right?
And the eye cycle in every disease you can name,
and what it denotes, and what it tells us,
and what we can do with it.
You have exactly this marker.
You're walking around with a marker on balance
in your autonomic nervous system,
and we do nothing with it.
So we're in fact now doing a lot with it, okay?
So we built a wearable device
that is pasted to your body
and measures air flow in each nostril separately,
and logs it for 24 hours.
And we're collecting these 24-hour recordings.
We're calling it the nasal halter.
So we measure with the nasal halter,

and we're finding it as a disease marker.
I can give you a nasal halter measurement as an adult,
and I can say, this is work
by Tim Nasseroka, a graduate student in our lab now.
I can, so we can tell the difference between ADHD
and non-ADHD adults.
And we can tell just from the recording,
we can tell if the adults are on riddling or not.
So I can measure your nasal airflow
and say if you are or are not with ADHD,
and if you are or are not on riddling.
Incredible.
I have a couple of questions about this.
Is it the case that air flow through one nostril
is reflective of a sympathetic nervous system dominance
versus parasympathetic?
Or is it simply the case that this alternating
left-right nostril periodicity,
which you said I think is on the order
of about every two hours?
Two and a half.
Two and a half.
It switches to maximal on one side versus the other.
Is that simply reflective of an overall balancing?
Let's maybe, is it the hinge in the seesaw,
or is it the tilt of the seesaw?
So I don't have a good answer.
I don't have a good answer.
I mean, you know, I could give you sort of a,
you know, I could say that to some extent,
right nostril more open is more sympathetic
and the left nostril more open is more parasympathetic.
But that wouldn't be very correct.
I mean, you know, it is-
I'm sure that the yogis are gonna be all over this, right?
Cause I get this, my lab does do some stuff on breathing
and the yogis are always saying, okay, you know,
because there's this thing, I don't do yoga anymore,
not for any particular reason,
but where they'll have you breathe through one nostril
or the other.
And I've probably been asked this question
on social media 10,000 times.

Okay, wait, I'm gonna become public enemy number one
of the yogis right now.
So listen, we, so we-
They'll come at you with yoga mats,
which are not very dangerous.
We really, so since we're so interested in this mechanism,
one of the things we'd really like to know how to do is,
is to gain control of it somehow.
And there's this world out there of yoga
who claims to have control over this.
So we said, okay, let's bring like really serious
yoga practitioners and see if they can shift
their nasal cycle from left to right by will alone, right?
Not by manipulating themselves somehow.
And, and if yes, you know, we'll learn from them
how they do this and then we might, you know,
use this to cure ADHD or whatnot, right?
So, so we posted like on all the lists
of like the yoga teachers and had this parade
of yoga teachers walking into our lab.
This was one of the strangest-
A lot of sandalwood odors and bare feet.
White, white clothing and so on.
And, and so we, we studied, I actually know
we studied 14 yoga teachers, all 14 by, you know,
by the conditions of enlistment for this came in saying
that they, they can control shifting
from left to right nostril.
Without plugging in nostril.
Yeah, yeah, by the power of thought alone.
And you know how many of 14 succeeded?
Zero, including, including one, you know,
there was extreme one was we had this guy who, you know,
and we're recording and we know how to record
this really well, right?
And, and he's sitting there saying, yeah,
I'm switching now and I'm, it's switching.
And, you know, you're looking at the monitor
and no, it's not switching.
And, and so no, no yoga teacher that we found
could willfully switch between left and right nostril flow.
And yet they're, they are convinced that they are,
and I have to imagine they're not trying to, you know,

there's no incentive for them to lie, right?
Yeah, no, I, even the opposite, I mean, you know,
this puts them in an awkward position once.
Yeah, I don't know what the deal is,
but, but none of them can do it.
Given that the alternating flow through one
or the other nostrils reflective of the autonomic nervous
system has this two and a half hour of periodicity,
if I suddenly enter a bout of stress, for instance,
does it switch because that's reflective
of the autonomic nervous system?
The reason I'm asking this question is not because
I think that's necessarily important as it relates to stress,
but I'm trying to understand the direction of causality.
In other words, is the unilateral smelling through
or unilateral nostril smelling periodicity,
there when we named it something,
I get the wrong thing, I'm sure,
is that driving the shift in the autonomic nervous system
or is it merely reflective of the shift?
So you've very concisely now worded aim too of a grant
that was probably just rejected,
but basically we're trying to answer exactly that question
and we're currently running experiments on that line.
So we have one experiment where we're looking,
so we're exposing participants to pain.
We're using cold water hand exposure.
It's a really cool paradigm
because there's huge individual differences.
We just started this, we built the setup just now
and you have a lot of meat to work with there
because there's a lot of individual differences.
It's capped at three minutes for safety reasons
because you have participants putting their hand
in two degrees Celsius water,
but there'll be participants who'll pull it out
at like 10 seconds, nine seconds,
and then you'll have three minutes as well.
So there's lots of, lots of, and already,
so now I'm sharing pilot data with the USO to this might,
when this ends up being published, it might be the opposite,
but so far it seems that the exposure to cold
generates a shift in nasal flow and nasal balance.

So autonomic arousal can drive the shift potentially.
Earlier you were describing the architecture
of these smelling systems,
and you mentioned these glomeruli
where the olfactory receptors converge in the bulb.
And then later you mentioned that the system is unilateral,
but with a mirror representation on both sides of the brain.
So for those who don't think in terms of neuroanatomy,
what Noam was describing is the fact that,
of course there are two nostrils
and then a bunch of receptors,
they converge in these glomeruli,
but you have a mirror representation of that
on both sides of the brain
and that most of that information
is kept on one side of the brain or the other.
There isn't a lot of extensive intermixing
at the first order of processing.
So the question I have is whether or not you believe,
I'm not asking for data,
first I just want to know what you believe,
that this alternating nostril airflow phenomenon
has anything to do with preferential processing
of olfactory information
in terms of right brain, left brain with the caveat
that anytime we hear right brain, left brain,
we've covered this in a previous episode.
Most of what people hear out there
about right brain, left brain,
emotionality, logical stuff is completely wrong,
doesn't exist is a total fabrication
and we'd like to abolish that myth,
but with that aside or set aside rather,
what are your thoughts on why the information
would switch from one side of the brain
to the other at all?
Yeah, I don't think that the nasal cycle
is an olfaction story.
So I don't think that this was shaped
by the olfactory system,
nor do I think this has major impact on olfaction.
I think the nasal cycle story is a different story
about brain function.

So we have this sort of pet theory
where calling now the snipping brain approach
where basically we think that nasal inhalation
is timing and driving a lot of aspects
and patterns of neural activity and cognitive processing.
And this theory is olfaction inspired in its beginning.
That is, I mean, if you think of the mammalian brain,
it's which evolved from olfaction,
it's sitting there and in olfaction
because olfaction depends on sniffing.
You have this situation where you have a sniff,
you have information and then flat, nothing, right?
And then you have information and then nothing.
So information processing is one to one linked
to nasal inhalation.
And we think that this property evolved
to be meaningful in brain processing in general,
not only of olfactory information,
but of any type of information
because the brain evolved in this way,
in this way that it processes information
on inhalation onset.
So a study led by Ofer Perl from our lab
two, three years ago,
we looked at something completely non-olfactory.
We looked at visual spatial processing
and we compared visual spatial processing
on inhalation versus exhalation.
And the brain does this completely different
on inhalation versus exhalation.
In that particular task,
people performed significantly better
on inhalation versus exhalation.
What was the task?
Was it an olfactory task?
No, no, it's a visual spatial task.
So this is a task where the specifics of the task
where that you see a shape
and you have to determine if it's a shape
that can or cannot exist in the real world.
So some of them are these like usher shapes,
like where one facet doesn't reach the other facet.
The impossible figure type stuff.

Yeah, but structural shapes, not,
and so a pure visual spatial task,
we intentionally went for a task
that is not considered a ventral temporal task,
an olfactory cortex task in any way.
And people performed much better
on inhalation versus exhalation at doing this task.
Was there a both nostrils occluded version
where people were forced to mouth breathe?
Yes.
And in this particular task,
they also did better on mouth inhalation
versus mouth exhalation,
but the difference wasn't as pronounced
as it was with nasal inhalation versus exhalation.
So I'm a big proponent of nasal, not mouth,
breathing whenever possible
for many health related reasons.
I'm a big fan of the book, JAWS,
a Hidden Epidemic written by colleagues of mine
at Stanford.
It's familiar with it.
Yeah, and this idea that people who mouth breathe
experience more colds, more infections of various kinds.
It's not good aesthetically or for the denture.
I never know.
The teeth, the gums, it's stuff.
Folks, sorry, my dentist is gonna come after me.
Need to go to the dentist anyway.
That nose breathing is great
for your health relative to mouth breathing.
So I think it's also good for your cognition,
not only for your dental health.
I think that nose breathing shapes cognition.
And there are other labs who are finding the same.
Again, Cristina Zellano is doing work on this line.
She had major contributions here
and Joanne Leunstrom is doing work on this line.
There's lots of studies suggesting
that nasal inhalation is timing,
cognitive processing and modulating it.
Incredible, perhaps not surprising,
given what you've taught us about the olfactory system.

I mean, these two holes in the front of our face,
these nostrils, I mean, are a pathway to the brain, right?
I love to tell people,
because I work on the visual system in my lab
that your eyes are two pieces of brain extruded
from the cranial vault, which they are,
the retinas anyhow.
And then you never look at anyone the same way again.
But the olfactory sensory neurons are right there
at the top, so those caverns that we call nostrils,
and they are brain.
Yeah, definitely.
It's the only place where your brain meets the outside world
because in your retina they're protected by a lens.
And here you have neurons in contact with the world.
This actually has been the source for some theories
on a potential route for neurodegenerative mechanisms.
So as you may know, loss of the sense of smell
is one of the, if not the earliest sign
of neurodegenerative disease.
So for example, in Parkinson's disease,
there's loss in the sense of smell,
probably 10 years before any other symptom.
But people have failed to make this a diagnostic tool
because it's nonspecific.
So it's not as if you could come to your doctor
and say, I'm losing my sense of smell,
and they'll say, oh, early sign of Parkinson's
because you can have many reasons
to lose your sense of smell and so on.
But olfactory loss, again, is an early sign
of neurodegeneration, and there's at least one theory,
particularly about Alzheimer's disease,
suggesting that Alzheimer's may be the result
of a pathogen that enters the brain
through the olfactory system.
How interesting.
It's not, of course, a mainstream
or a widely accepted theory of any type,
but it just highlights this notion
that the nose is a path to our brain.
I think these non-invasive readouts
of potential neurodegeneration,

such as visual tests because of the fact
that the retinas are part of the brain
and loss of neurons in the retina is often associated
with other forms of central degeneration,
Alzheimer's, Parkinson's, et cetera,
as it's a little more invasive than what you're describing.
I'm beginning to wonder why we don't have
a olfactory task every time we go to the doctor
that would allow tracking over time,
because, of course, as you mentioned,
someone can lose their sense of smell.
Does that mean they're getting Alzheimer's?
Not necessarily, but if their sense of smell
was terrific the year before
and it's 50% worse the next year.
That's a really bad sign.
Yeah, that's a bad sign.
And so what we're talking about
is something completely non-invasive
and could be relatively pleasant to innocuous,
depending on the odors used.
So, yeah, so first I can answer that,
and the reason that that's not happened,
and that may be changing right now,
but the reason that has not happened
is because olfaction has not been effectively digitized.
So if you need to generate really precise visual information,
you can buy a monitor for 100 bucks
that is at the resolution of the visual system, basically.
And if you want to generate auditory stimuli
really precisely, then you can buy an amplifier
for maybe a bit more than 100 bucks, but not that much more,
and you'll be at the resolution of the auditory system.
In our lab, we build devices that generate odors.
We call them olfactometers, which is a misnomer
because they don't measure anything,
but that's what they've always been called.
So we call them olfactometers as well.
And we've already built at least one olfactometer
that costs a quarter of a million euro,
and it's pathetic, right?
So it's pathetic, it's slow, it's contaminated,
it's nowhere near the resolution of your system.

So one of the reasons that's not happened
is just the utterly poor control of the stimulus.
Mind you, to some extent, it has happened
in that there are standard clinical tests of olfaction,
basically two that sort of control the world in this respect.
The older one is a test called the UPSIT,
which stands for the University of Pennsylvania
Smell Identification Test.
It was developed by Richard Doty in Penn,
and it's a test where you scratch and sniff,
and it's a four alternative force choice test
with 40 odorants.
So you have these 40 pages that you page through,
and you sniff and smell,
and it's been normed on gazillions of tests.
I'm always amused by it because,
so Richard Doty made a ton of money on the UPSIT,
but he needed it because he has a habit.
He has a NASCAR.
So this, every time we buy UPSITs in the lab,
I say there's another gallon of gas into Richard Doty.
He raises NASCAR?
Not NASCAR, but one lower than that.
I don't know, some sort of formula A or formula Ford,
or some, he raises a car.
And so that's where all the UPSITs went.
So I always feel good about buying UPSITs
because I know they're going to that good cause.
Keeping him in the fast lane.
But so that's one test that's out there,
and indeed has been shown as a,
so there's reduced UPSIT in Alzheimer's, in Parkinson's,
and in a host of other diseases.
And there's a European version called sniffing sticks
that Thomas Hume has developed.
And it's basically the same sort of concept of,
that one isn't scratch and sniff.
It's like these pens that you open up and sniff.
But those exist, but they're not as convenient
as delivering stimuli and vision and audition.
And that's why you don't have what you've just suggested.
Another thing, another place where you don't have it,
which I think is even more,

would have been even more meaningful,
is you don't, of actually it's not tested in newborns, right?
Where vision and audition is.
You know, there's this thing called congenital anosmia, right?
Which is being without the sense of smell from birth,
supposedly congenital,
which is a half a percent of the population.
It's not a trivial number.
Not totally, yeah.
But nobody knows if that really is true.
Because here's an amazing factoid.
Guess the average age at which congenital anosmia
is diagnosed.
And this is a horrible statistic for me,
for the way I see the world.
But what do you think the average age of diagnosis is
for congenital anosmia?
Five years of age.
14.
Incredible.
14.
So most people who are one half of a 1%
of the human population, presumably,
is without the sense of smell
and doesn't realize that until they're 14 years old.
Well, I don't know when they realized it first,
but it's formally diagnosed at 14 on average.
Which means some of them even later, right?
And, right, it's a distribution.
Well, what do they suffer?
Yes, so first of all, they suffer socially.
And there's a host of deleterious life events,
associated with congenital anosmia.
They die younger.
So this is work out of Ilona Kroy in Germany.
And amongst the various things that are predicted
by anosmia is shorter lifespan.
But things like reduced social contacts,
reduced romantic social contacts,
it's not a good thing.
And do they lack olfactory bulbs?
I'm presuming they have noses and nostrils.
There is a condition I'm aware of

where children are born without noses or nostrils.
Very rare, very rare, we won't focus on that
because it's exceedingly rare.
But they're born with noses and nostrils.
And here's the thing, right?
We don't know if they're born with olfactory bulbs.
Most of them, although not all of them,
but most of them don't have olfactory bulbs
in adulthood, or I should rephrase that,
have remnants olfactory bulbs,
really shriveled olfactory bulbs.
But nobody can say the cause and effect here.
Before we talk about the role of the requirement
for olfactory bulbs for olfaction,
a very interesting topic in its own right,
I'm curious as to whether or not
their endocrine system is altered.
Because as we'll soon talk about,
there's a lot of signaling through the nose
from between individuals that triggers things,
everything from the onset of puberty
to feelings of romantic attraction, attachment,
these sorts of things, is it known whether or not,
and I should say, excuse me for interrupting myself,
but as long as I'm interrupting you every five minutes,
I might as well interrupt myself too,
that we are well aware of the proximity
of the olfactory system to some of the hypothalamic systems
that regulate the release of gonadotropins,
which control testosterone and estrogen production,
so are they hormonally normal?
So some aren't, some aren't, and I'll be specific.
So there's a condition known as Kalman's syndrome,
which is hypogonadic development in men.
And in Kalman's syndrome, they're practically all-anosmic.
So to answer your question, yes, there's a direct link,
and it materializes in Kalman's syndrome.
That said, not all congenital anosmic individuals
have Kalman's syndrome, and not all,
but almost all people who have Kalman's syndrome are anosmic.
So Kalman's syndrome goes with anosmia.
I think, so there's a female equivalent of Kalman's,
or I don't remember its name.

It's not in the Turner syndrome family.
I'm not sure.
And I think it's also associated with anosmia,
but I'm not confident of that.
But Kalman's is associated with anosmia.
So the answer is yes.
And we can maybe, all-faction and reproduction
are tightly linked, and they're tightly linked
in all mammals, and we are big terrestrial mammals,
and all-faction and reproduction
are linked in humans as well.
Yeah, we will definitely get into that.
I'd like to just take a brief moment
and thank one of our podcast sponsors,
which is Inside Tracker.
Inside Tracker is a personalized nutrition platform
that analyzes data from your blood and DNA
to help you better understand your body
and help you reach your health goals.
I've long been a believer in getting regular blood work done
for the simple reason that blood work is the only way
that you can monitor the markers,
such as hormone markers, lipids,
metabolic factors, et cetera,
that impact your immediate and long-term health.
One major challenge with blood work, however,
is that most of the time it does not come back
with any information about what to do
in order to move the values
for hormones, metabolic factors, lipids, et cetera,
into the ranges that you want.
With Inside Tracker, changing those values
becomes very straightforward
because it has a personalized dashboard that you can use
to address the nutrition-based, behavior-based,
supplement-based approaches that you can use
in order to move those values into the ranges
that are optimal for you, your vitality,
and your longevity.
Inside Tracker now includes a measurement
of apolipoprotein B, so-called APOB,
in their ultimate plan.
APOB is a key marker of cardiovascular health,

and therefore there's extreme value
to knowing your APOB levels.
If you'd like to try Inside Tracker,
you can go to insidetracker.com slash huberman
to get 20% off any of Inside Tracker's plans.
Again, that's insidetracker.com slash huberman
to get 20% off.
I have a story slash question
that I'd like to tell you, ask you as a segue to that.
Noting, of course, that we'll get back
to the requirement for olfactory bulbs,
yes or no, for olfaction.
And this relates to when I was growing up,
I grew up at the end of a street
with a lot of boys of my age
who, just by coincidence, had a lot of older sisters.
They were my older sister's age.
It was fortunate, so I had a lot of kids to play with.
We would hang out at each other's houses,
bike, build jumps and do all those things,
like kid stuff, fort stuff, get into trouble or whatnot.
And oftentimes we would end up leaving our articles
of clothing at each other's houses all the time,
like t-shirts and jackets.
And so my mom was constantly coming in and saying,
there's all, there's this clothes,
like someone left this here, I don't know who it was.
We were all more or less the same size.
And from as far back as I could remember,
six, seven years old and onward,
I could pick up a shirt or a jacket,
smell it and say, oh, well that's Eric Eisenhart's shirt,
a friend of mine there, I just gave his name.
Or, oh, that's Scott Madsen's shirt.
I could just smell the shirt
and in a conscious way know who it belonged to.
Having never, I promise,
not that I would pretend if I had,
pretend I hadn't if I had,
but having never actually done the exercise
of going and smelling my friend intentionally.
Right.
In fact, if anything, I had all the reasons in the world

to avoid smelling the other young boys in my neighborhood.
Okay, so that raises a question of whether or not
we are consciously and or subconsciously
coding identification of people that we interact with
frequently or infrequently in terms of their smell
or some other aspect of their chemistry.
Yeah, so, yes.
We're doing that all the time in my view
and a lot of this processing,
almost all of it is subconscious
and I don't know why already,
already put that out there, right?
I have no idea why human nature has,
or nature or culture or whatnot has pushed this
into the realm of subconscious
and something we're unaware of,
but we do it all the time
and our lab has lots of studies on this front.
One of them you may be familiar with
that had gained some notoriety because it's amusing.
So we look at human behavior a lot.
We try to look at it through our nose
and in the way we look at what people are doing.
We try to think, if I was a dog,
what would I think of this?
And if you look at dogs,
when they interact, they visibly sniff each other.
It's very obvious, they walk up to each other
and they sniff each other.
And yet humans don't typically walk up to a stranger
and carefully sniff them, right?
I mean, we're sort of obliged to sniff our babies.
That's considered almost something you're supposed to do.
And it's not culturally taboo to sniff our loved ones.
It sort of doesn't seem like an odd thing to do,
but we don't sniff strangers, right?
Well, or do we?
So we're finding more and more mechanisms
where we do this and the one I'm referring to now
for one example is we started looking at hand shaking.
Hand shaking is this really odd behavior.
And it's not only in the West, by the way,
as some people think it's only a Western thing.

It's almost everywhere.
And there's really poor understanding
of how this behavior evolved.
Like where did this thing come from?
So if you look for the Wikipedia version, right?
Then they'll tell you that it's to show
that you're not holding a weapon in your hand.
But there's really no good evidence for that.
It's a bit like the trillion bloodhound receptor story, right?
I mean, we tried to find it.
Why do people say that?
They just do.
And we started looking at people hand shaking
and we noticed, or it seemed to us that we're noticing
that people will shake hands and then we'll go like this
and like this.
For those of you listening not watching,
Noam is taking his hand and wiping it on his face.
Grabbing his nose or touching his side of his cheek.
Yeah, these things that we do all the time
after a hand shake.
Well, so first of all,
we do them all the time just period, right?
The baseline here is really high
and we'll get to that in a second.
But these behaviors that you could easily not notice, right?
And so we asked whether that's a real thing.
And this was a study led by Dan Frouming
in our lab at the time.
And what we did first, and if you want, we can link.
So this was published in E-Life
and one of the nice things about E-Life
is that it has a very effective way
to embed videos in the publication.
So if you want, we can link this to your system later on.
Put it in the show note captions as a link on YouTube
and the other four platforms, Spotify, Apple.
So what we did is we brought in participants to our lab
and we sat them in the room, experiment room
and told them the experiment would start soon
and they should wait for us there.
They didn't know what they were coming from.
Unbeknownst to them, they were already being videoed.

Of course, later on, they had the opportunity
to not agree to saving the video
in which case we would delete it immediately
or letting us use it for science
or some letting us use it for more than science
for the video that's now on E-Life.
And we would walk into the room and say,
okay, just wait here.
We'll be right back with you to set up our experiment.
And they would sit there for three minutes.
And during those three minutes, we could later quantify
how much indeed they just by baseline,
how much they touched their nose or their forehead
or their chin or how many times their hand reaches their face.
And by the way, that baseline is not low, okay?
And then three minutes later,
an experimenter would walk into the room
and would share a consistent text.
It would be, you know, we're still setting up
our equipment in the other room and so just wait here
and we'll be right back with you.
But in the meantime, just wait here.
And the experimenter went through this like 20 second
fixed text and in half of the cases it included a handshake.
This was a new experimenter,
not the one who put them in the room.
So that's the first time they met.
So it'd be, hello, I'm, you know, so and so
they would put out their hand and shake their hand or not.
Okay, and we did all possible interactions
in terms of gender.
So we matched male participants with male and female
experimenters and female participants
with female and male experimenters.
And so you had handshake and no handshake conditions.
And then you can quantify that behavior
of the hand going to the nose after handshake.
And there was a remarkable increase
in the hand going to the nose after handshake.
And this is one of the nice cases we,
the paper includes statistics,
but you don't need statistics here.
Just look at the video, it's unreal.

The video is unreal.
So interesting.
So the hand goes to the nose.
Now we did a few controls here to verify
that this is an olfactory behavior.
One is unbeknownst to the participants
we measured nasal airflow and people not only bring
their hand to their nose, they sniff it.
So in this is perfectly timed.
They go like this.
Okay, so they're sniffing their hand.
And in an additional control study, we manipulated it.
So we built this little James Bond thing
of a watch on the experimenter's hand.
They could emit an odor.
And the experimenter didn't know what odor
they were emitting and they could emit either a pleasant
or an unpleasant odor.
And we could drive the self sampling afterwards up or down.
So this was an olfactory behavior.
No doubt about it.
I mean, we're quite confident.
So people in that case,
people must have been sensing the odor on their own hand
because they shook the hand of the experimenter,
pleasant odor, and they're more frequently bringing
that hand to their nose versus unpleasant odor
that had been introduced to their own hand
by the experimenter.
Yeah, but no, I think they were sensing the ambient odor
that came in with the hand that choked
and then that either drove them to sniff their hand
more or less.
The odor cloud of the experimenter.
And there's an interesting thing going on here too
because people didn't only smell the hand that choked.
They also smelled the other hand.
And we think that there's something going on here
comparing self to other.
And we think a lot of self sampling might reflect that.
There's on the same line and again to link
to your childhood story of identifying your friends
by smell.

A study we published just last year
by Nimbara Vrabi in our lab
where Nimbara came with this basic interest
in this phenomenon that's loosely referred to
as click friendships.
So people you meet and you click right away, right?
You immediately become close friends.
And this is a phenomenon that is poorly described
or is poorly described in literature as an entity.
And yet anybody will tell you
they know what you're talking about, right?
I mean, if you tell somebody you click with right away,
you become intimate within five minutes, right?
Everybody experienced this in their life to some extent.
And the question is what was there, right?
What was it?
Was it because you looked the same?
Could it be was it because you had the same sports team
that you liked?
Or is there something deeper here?
And in buzz theory was that similarity in body order
may contribute to this.
That people who smell the same will click in some way.
And so to address that,
she actually recruited click friends from all over Israel.
She posted all over social media
to identify pairs of friends.
So these are same-sex, non-romantic dyads.
So these are friends, men and women,
whose friendship started as a click
where here this becomes sensitive
because it has to be a mutual click, right?
Later on, we discovered there could be one-sided clicks.
So if somebody is sure they clicked with somebody else,
but the other person...
There's a name for that in neurology
that our common friend, the late Ben Beres taught me,
which is there's a phrase that neurologists use
called sticky.
These are people that come up to you
and start asking you questions
and then won't leave you alone.
They're so-called sticky people.

And if you ask these sticky people,
sticky in air quotes,
because they're not physically sticky.
They may be.
They could be.
What do you think of this person?
They'll say, oh, they're great.
We're really good friends.
And so they've made a unilateral click friendship.
And yes, neurologists are talking about you.
If you're one of these people,
neurologists are talking about you.
There's an informal diagnostic code, sticky.
So she recruited click friends,
and then she sampled their body order.
And we have a protocol for this.
They're given, you know,
odorless shampoo and soap to use for three weeks
or something.
And then they sleep two nights in this t-shirt
where they have to sleep alone.
And then we extract the body order from the t-shirt.
And so we have a way to extract,
a method to extract body order.
And then she first asked whether indeed
click friends are more similar in their body order
than you would expect by chance.
And she first tested this with a device,
a machine we call an electronic nose.
So an electronic nose is sort of a very poor effort
to mimic what the mammalian nose does.
Basically, it's a bunch of sensors
that respond to airborne molecules.
In this case, sensors referred to as moxers
as metal oxide covered sensors.
And so she used an electronic nose
to sample these body orders.
And she found that click friends are indeed
more similar to each other
than you would expect by chance, by random dyads.
And this was a significant difference.
And after she found that a device could do this,
she had other participants do this.

So she had people smelling the click friends
versus non-click friends.
And they judge them as being more similar to each other
than not.
Now, again, you might wonder is this causal or not, right?
Because maybe click friends go to the same restaurant
together all the time or whatever,
live in the same neighborhood.
And that's why they smell the same.
So to address causality,
she recruited total strangers
and first smell them with the electronic nose
and then engage them in a social interaction,
something called the mirror game.
So in the mirror game, one person moves their hands
and the other person is really close to them,
like right here, so they can smell each other
and has to move their hands with the other person.
And one prediction, they're panned out,
but another didn't, the one that didn't.
So she predicted that people who would smell more
similar to each other would be better at the mirror game.
That is, they would follow each other better.
That did not pan out.
However, she then also had,
the interaction was completely non-verbal.
They were not allowed to speak with each other
and she did an entire round robin.
So everybody played with everybody else.
This was an insane experiment to run.
And she then, at the end of the experiment,
each person rated each other person
as to how much they think they would want to be their friends
and also on a bunch of ratings, how nice they think they are,
how affectionate they think, a bunch of ratings, okay?
All of this was predicted by the electronic nose.
So people who smell more similar to each other
think that the other person is more likely to be their friend,
is more likely to be a nice person, et cetera, et cetera.
So we could actually predict friendship
using the electronic nose.
So this is not a result of friendship.
It plays into the causal elements of building friendship.

So this is to relate to your childhood story.
There's something going on here.
We're constantly smelling ourselves, constantly.
This constantly, I mean, if you want to,
the reason I'm smiling, I mean,
and your viewers or listeners will understand why I'm smiling,
I'll send you a video to link into your podcast here.
We thought of calling,
the fact that people constantly sniff themselves,
we thought of calling this the low effect.
And low, so in America, this won't pass that effectively,
but in the rest of the normal world,
Joachim Low is the soccer, the national soccer coach
of the German soccer team.
So, I mean, I don't know who would be a very famous coach
here, but Steve Kerr, I mean, this is the, you know,
this is a super, super famous name all around the world
where soccer is the primary sport that people watch.
And once people will see this video,
they'll understand why we thought of calling this
the low effect.
It's very graphic, but people are constantly smelling
themselves, they're smelling themselves with their hands,
they're smelling themselves explicitly.
People are constantly smelling themselves,
they're constantly smelling others.
I find this topic so interesting.
And first of all, confession,
I definitely smell myself multiple times per day and-
Everybody does.
Okay, good.
And I would do it anyway.
I think I, like most people,
I either find my own smell to be neutral, to pleasant, right?
Occasionally I'll be like, whoa, I need to take a shower.
As long as we're talking about smelling oneself
and friendship, kinship, and its relationship to smell,
we have to talk about the relationship between smell
and romantic attraction and bond.
So my understanding is that if, for instance,
a mouse is given the option to mate with any number
of other different mice,
they will bias their choice toward the mouse

that has the immune composition, the so-called MHC,
major histocompatibility complex,
which reflects immune diversity.
The immune system that is most distant from theirs,
and the evolutionary argument being that were they to
produce offspring, that the array of immune genes
would be much broader than if they were to select
an animal very close to them.
And in addition to that,
that one of the most strongly selected against behaviors,
not just culturally,
but at the level of eliciting a sense of disgust,
maybe even from the activity of the hypothalamus,
is mating with very close kin, aka incest,
because that can potentially, we know,
produce as a higher rate of mutations.
In other words, whereas you've described the relationship
between smell and choice of friends,
as you choose people who smell more like you,
my understanding is that in the context of choosing
romantic partners or sexual partners or both,
that you choose the person whose odor
and therefore immune composition is most different.
Right.
So the way you describe the animal literature is correct.
And there's evidence to similar mechanisms in humans.
Our lab has not worked directly on this issue
of romantic selection based on odor.
There's a bunch of papers,
wedkind et al and the wedkin lab,
and also Porter, I'll email these to you later on,
that have done a lot of this work
and find exactly, as you say,
that romantic odor preferences in humans
are influenced by body odor,
and that this is linked to MHC,
is the compatibility complex makeup
of the portion of our genome
that shapes our immune system to some extent.
So this effect has been studied and reported on,
again, extensively in mice,
and also in humans,
not work that we've done.

The one sort of tangent work we've done,
and I'd like to maybe tell you about,
it relates to an effect that is one of the most remarkable
effects in mammalian social chemo signaling.
And also related to,
so it's not related to romanticism in any way,
but it's related to reproduction.
And indeed, in our lab,
we've not looked at romanticism,
we have looked at or are looking at reproduction.
They're not always the same.
Certainly.
Oh, they can't.
Animal mammalian or terrestrial mammalian
reproductive behavior is dominated by the sense of smell
in mammals.
And here, remember, initially, when you started off,
I noted that there are several subsystems in our nose
that transduce odorants,
and so primarily the main olfactory system,
which is cranial nerve number one,
and the trigeminal nerve,
which is cranial number five.
Most terrestrial mammals have another subsystem,
referred to as the secondary olfactory system,
that has a separate sense organ in the nose.
This organ is known as the vomeronasal organ.
It's a small pit in the nasal passage
of most terrestrial mammals.
Sometimes it's described as a communicating pit,
because sometimes it connects the nasal passage
to the roof of the mouth.
Sometimes it connects both.
And so there's the sense organ
with its specific receptor subtypes,
VNRs, vomeronasal receptors.
And this,
is linked to a sort of separate portion
of the olfactory bulb,
not really the main olfactory bulb,
but what's referred to as the accessory olfactory bulb.
And from there directly to the limbic system,
to the portions of the brain

that control reproductive behavior,
and aggressive behavior.
And in most terrestrial mammals,
this subsystem processes odorants
that are sometimes referred to as pheromones.
Although that's in many ways a problematic term,
but odorants that are referred to as pheromones,
namely odorants that are emitted
by another member of the species
to influence that member of the species
and alter behavior or hormonal state.
And some of these hormonal effects
are utterly remarkable.
And in my view, the most remarkable of all
is an effect known as the Bruce effect.
This was an effect discovered by Margaret Bruce in 1959.
She was a British scientist.
And in the Bruce effect,
when you expose a pregnant mouse
at an early critical stage of the pregnancy,
I think up to about day three,
if you expose the pregnant mouse
to the odor of what is referred to in technical terms
as the non-stud male,
that is a male who did not father the pregnancy,
she will miscarry the pregnancy, she will abort it.
That's an insane decision made by the female here,
because she's invested quite a lot in this,
in biological terms and in forming this pregnancy
and maintaining it.
And yet she drops it on the basis of an odor.
And this effect is remarkably robust.
And what do I mean by remarkably robust?
So this will occur on about 80% of exposures.
Now, as you know, 80% is 100% in biology.
I mean, there's nothing that happens at more than 80%.
So it's a remarkably robust effect,
this dropping of the pregnancy.
And we know it's mediated by chemo sensation,
through the nose.
We know for sure, and we know in the following way.
So first, it's enough to just bring the odor
of the non-stud male.

You don't have to bring the male himself, right?
So you just can bring bedding from a non-stud male
and that will induce the Bruce effect.
But of course, the most telling set of experiments
is that if in the female mouse,
you ablate the vomeronasal organ,
you just burn this tiny structure in the nose,
and the effect disappears.
So the effect is completely dependent
on the vomeronasal organ.
And I find this odor a remarkable effect, right?
I mean, again, because of the extent of cost
that the female takes on here,
based on this information and smell.
Now, humans, the sort of the going notion
in all factions is that humans don't have
a functional vomeronasal organ.
So we don't have that functional organ in our nose.
Now, I'll point out, we actually do have the pit.
So the structure, or the outlining structure is there.
But the pit that we have is considered vestigial
and non-functional.
And what about this thing I learned about at Berkeley
in integrative biology class
that we have something called Jacobson's organ?
This is the same organ.
So Jacobson's organ is the vomeronasal organ.
It's also called Jacobson because I think Jacobson
was a military physician in like the 1800s in Holland
or something, and he found it in a soldier
who was operating on or something like that.
The story comes from something like that,
but Jacobson's organ is another name
for the vomeronasal organ.
These are one and the same,
the sensory organ of the accessory olfactory system.
And again, the going notion is that the human Jacobson organ
or vomeronasal organ is vestigial.
It's non-functional.
Does that necessarily mean
that we don't have these pheromone effects?
No, it does not.
So first of all, we know that lots

of what are considered pheromonal effects,
namely social chemo-signal and rodents
are mediated by the main olfactory system.
We know that for sure.
There are several examples for this
in mice and rats and rabbits and so on and so forth.
So A, these can be mediated by the main olfactory system.
And I'll come back to that in a second,
but first to finish the Bruce effect.
And second, and I'm going out on a limb here,
but I'm willing to take that risk.
I'm, for me, the jury is still out
on human vomeronasal organ.
The decision or the notion that it's non-functional
relies on about one and a half papers, postmortem,
looking for the nerve that connects this thing
to the brain and failing to find it,
using staining and so on and so forth.
But staining postmortem studies in humans
are notoriously complicated.
Basically, for many reasons,
one of them is that the material
has just always has gone through.
It's not ideally set as it is
when you sacrifice an animal and study its tissue.
So based on really, really a paucity of studies
that fail to find this nerve,
the notion is that the structure is vestigial in humans.
I don't have any evidence that it's functional, mind you,
but I'm just not sure that it's not.
But what we do have a suspicion
is that humans may experience something
similar to a Bruce effect.
So first of all, humans have an enormous number
or ratio of spontaneous miscarriage.
Are they occurring more often in the first trimester?
Because you mentioned that in the Bruce effect,
in the mice is in the first three days
or so falling pregnancy, which in the mouse gestation,
as I recall, is about 21 days in the mouse.
You're talking about one seventh of total gestation.
So I'm not quick enough to,
nor is it important to translate,

but this would be first trimester in humans.
Which is indeed early first when most miscarriage occurs.
Now humans have, again, a huge number of miscarriages
and the numbers I'll soon share them with you,
they sound odd.
And the reason they sound odd is because if you have
what's sometimes simply referred to as failed implantation,
this can occur in days one, two, nobody ever knows.
So some papers talk about 90%
of all human pregnancies end in miscarriage.
This is counting a failed implantation in day one, two, et cetera.
More conservative studies talk about 50%.
Nobody will argue 30%.
So a huge number, a huge number
of human pregnancies end in miscarriage.
Now out of these, there's a portion
that are unexplained, right?
So nobody knows why.
I mean, there are a portion that are explained
by all sorts of genetic factors, developmental factors
and so on and so forth.
But there's also a proportion that are unexplained.
And so all I'm saying is that there's a statistical backdrop
or setting, if you will,
for something like a remnant bruce effect in humans.
Now with that in mind, we approached a group
of, we enlisted a group of,
they're not really patients and participants in a study
of people who, couples who are experiencing
what is referred to as unexplained repeated pregnancy loss.
So formally, if you have two consecutive
unexplained miscarriages,
then that is sufficient for the diagnosis
of unexplained repeated pregnancy loss.
However, in our cohort of 30,
we had couples who experienced 12 consecutive
unexplained repeated pregnancy losses.
So the two is just the formal,
all of our cohort was like 12, five.
So this is an emotional difficult place to be.
And these are couples who are losing their pregnancy
for no apparent reason.
So they've gone through all the tests

that you can imagine of genetic incompatibilities
and all sorts of issues, clotting,
all the known suspects for pregnancy loss.
And the medical establishment remains totally at a loss
as to why these pregnancies aren't holding.
And so we hypothesized that perhaps here
there's something akin to a bruce type effect.
Obviously it's not gonna be the same as in mice,
but something like a bruce effect.
Now, of course, at that stage,
we could not do anything causal to test this, right?
But what we could do is to seek circumstantial evidence
to see if where there's fire, maybe there's smoke.
And what we did was we tested all faction
and more specifically the response to male body odor
in the couples experiencing repeated pregnancy loss.
And we found a few things.
First of all, if you think of the mechanisms behind
the bruce effect, the bruce effect implies
that the female has to have a very clear memory
of the fathering male,
because if she's gonna miscarry
in response to the non-father,
she has to know father, non-father.
I mean, that means that there's a pronounced
or factory memory at the moment of mating, okay?
And in mice, this has been very well characterized
and attributed to the Ontario factory nucleus,
a structure in the brain.
But you'd have to have this memory
in order to make that decision.
Now, so to address that,
and here you're gonna see that you and your childhood story
from before stand out a bit as skillful,
is that the first thing we did was just behaviorally test
whether these women and control women
could identify the smell of their spouse.
And you might be disappointed or we would all
are probably a bit disappointed to learn
that control women are very poor at this.
So you would think that women would be good
at identifying the body odor of their spouse.
They're not, they're not far from chance.

However, the women who experience repeated pregnancy loss
are more, they're double at their performance level.
So this is not a nuance effect.
Women who experience repeated pregnancy loss
can identify their husbands or their spouses
by their body odor.
With much greater acuity than the typical person.
Double, a bit more than double and way above chance.
Yeah, no, sorry, I posed it as a question,
but I meant, yes, with much greater acuity
and double is a significant improvement.
Are they much better at detecting any odor?
No, they're not.
We did the controls and they're not.
And then we also measured using fMRI,
we measured their brain response
to a stranger male body odor.
And this was quite remarkable because we approached,
so this was a full brain analysis,
without a region of interest analysis.
So it's not as if you're tweaking your statistics
to look at one part of the brain,
you're just looking at the entire brain
in the response to male body odor and asking,
De Novo, is there a difference between
these two groups of participants?
And there was one huge difference
and it was in the hypothalamus.
And so there was a difference in response
to stranger male body odor between the two groups.
So olfaction is altered in spontaneous,
repeated spontaneous pregnancy loss.
We don't know this is causal, right?
But that was enough for us to approach the ethics committee
to run a causal experiment.
And we're at the beginning of that now.
Incredible, I can't wait to hear the results of that.
It's gonna take, it'll probably take years, a few.
Because these are slow experiments to run.
Recruitment is complicated,
but basically we're blocking smell
in couples who are trying to maintain a pregnancy.
I want to touch on some other so-called pheromone effects.

And one thing I heard you say during a talk,
which I think really captures this whole issue of,
are there pheromone effects in humans?
Very nicely as you said,
whether or not it's a classic pheromone effect
or whether or not it's olfaction or something else,
this is chemo sensory signaling between individuals.
The reason this is important to me is a few years ago,
I did a social media post about pheromone effects in animals
and some potential pheromone effects in humans.
A couple of the human olfaction estas,
more from the, actually who work on animal models,
really came after me with intense sniffing,
saying there is no evidence for human pheromone effects,
human pheromone organs.
And I think today you've beautifully illustrated how,
regardless of the answer to that,
humans are contained and are emitting chemical signals
that influence each other's physiology and behavior.
For sure, for sure.
And the term pheromone is a problematic term in any case.
I mean, the term was put forth to describe insect behavior.
So if you were given a hard time by the mouse people,
you could have given them an equally hard time
if you were an insect person,
because really the place the term is accurate is,
so the first pheromone that was discovered was bambicol,
which is the pheromone that has the male moth
followed the scent trail of the female moth.
Bambicol is a pheromone.
Insect pheromone people will argue that this stuff
that people talk about in mice and rats is not pheromones.
And it all becomes semantics.
It's sort of like nerdy inside ball.
It's all semantics.
So I don't, in our publications,
we don't use the term pheromone,
because it would not help me
and it would probably only hurt us.
And so we talk about chemo signals
and humans definitely emit chemo signals from their body
and these chemo signals influence other humans
and influence their behavior.

There are several examples of this.
One of them I'll point out first,
which is sort of the most widely studied
and not mostly from our lab actually.
I mean, the flavor of the month
for the past 10 years in this field
is what's referred to as the smell of fear, right?
So this is probably true of many mammals and humans.
It's true of we emit a specific body odor
when we're in the state of fear.
This was first discovered in humans by Denise Chen
out of, I think, brown, I'm not sure.
I think that's right, yep.
Humans emit a particular body odor
when they're in a state of fear
and this body odor influences other humans,
in effect, increasing their autonomic arousal,
their sympathetic state.
So in effect, you could say that fear is contagious a bit.
So the smell of fear is contagious.
By the way, culturally, we know for ages
that dogs can smell fear in humans,
but actually that was only really shown
about a year and a half ago in a study.
So it was always said,
but it wasn't really shown effectively.
It was shown about a year and a half ago in a study
that dogs indeed can smell human fear
and humans can smell human fear.
So several labs starting from Denise Chen
and Haviland Jones and then in our lab and in other labs,
if you collect body odor from people in a state of fear
and collect body odor from the same people
when they're not in a state of fear,
other people can determine which is the state of fear or not
and this influences their behavior.
What about the smell of safety
or is that simply the absence of the odor
corresponding to fear?
And the reason I asked this is somewhat woven
into our prior discussion about mate choice.
Again, I'll ask the question in a form of brief anecdotes.
I'll use the I had a friend who approached here,

but one phenomenon that has nothing to do with me
in particular, I think this is a common phenomenon
is romantic partners leaving articles of clothing
at each other's homes.
Now this could have other purposes to mark territory,
but visually marking territory,
but also scent marking territory is very common
in the animal kingdom.
It's not uncommon for romantic partners
when one is traveling or away for the other partner
to smell their article of clothing
in order to bring about positive connotations
of the other partner, very common behavior.
If you're doing this folks,
other people are doing this too.
It raises questions, for instance,
about whether or not the morning period post breakup,
whether by decision, by death,
or by some other phenomenon that's forced the breakup,
whether or not that morning period has something to do
with an olfactory unlearning of and mate slush
and on and on and on.
With all these insights,
I would offer you to be a postdoc.
Well, I was gonna say,
listen, I have a sabbatical coming up.
So I would love to do a sabbatical.
But it's gonna kill me.
No, exactly.
You don't want me to work for you.
We talked about this earlier.
That's what I'm saying.
For other reasons, exactly.
There's a story there,
what Noam is referring to.
I'll just tell people
because the Inside Jokes on a podcast don't really work.
Earlier I was referring to the fact
that I've had three incredible scientific mentors,
undergraduate, graduate and postdoc.
But for reasons that are unclear to me,
the first one died of suicide.
The second one, cancer at 50.

And the third one, pancreatic cancer in its early 60s.
And the last one before he died,
who was an MD and a common friend of Noam's
and I turned to me and said,
Andrew, you're the common denominator.
So the joke that you don't want me to work for you.
So nonetheless,
I would love to do a sabbatical in your lab.
So what I was trying to say in that roundabout way
is that those are all really keen observations
and good ideas for sure.
And they just highlight again,
you know, that we're incredibly olfactory animals.
You know, and you're even talking about the nuance.
We're very olfactory even not in the nuance.
I mean, I have this,
when people tell me that, you know,
that we don't use our sense of smell
and we don't need it and all that.
And I have to deal with this a lot, right?
I have to deal a lot.
You study vision.
Nobody will tell you that vision is unimportant, right?
I have to visually dependent.
I don't need a dog to take over my olfactory system
if I lose olfaction.
But I'll tell you from having lost my sense of smell
for one day, I was in intense fear.
I bit into blue, I love blueberries.
I'm like a drive by blueberry eater.
If they're there, I just kind of pick them up
like a grizzly bear and cram them in my mouth.
So keep them away from me if you don't want them eaten.
But I can't, I almost can't help myself.
I bit into a blueberry or a handful of blueberries
and they just, it was the sensation of little bags of water
and I immediately felt like tremendous grief.
I'll tell you a sort of a throwaway line
that I use in this when I talk with people.
You know, I mean, you know,
take the two most basic behaviors that sustain us, right?
Let's say I give you a choice
between a beautiful looking layer cake

with strawberries and blueberries and whipped cream,
but that smells of sewage
versus some gray brown mix that smells of cinnamon.
Which do you eat?
Simple, the latter.
Right, you eat the latter, right?
Now imagine I offer you a mate.
Choose the gender of your liking, right?
It looks like a Greek god or goddess, right?
But smells of sewage
or an ordinary looking individual that smells of sin itself.
Who do you choose?
The latter.
So in the two most basic behaviors we have,
we follow our nose, not our eyes, right?
Definitely not always in predictable ways
because you offered an extreme example,
which is the best example,
but I for instance, for reasons I don't know,
I've never liked the smell of perfume ever.
In fact, I find it aversive,
but I do, I confess,
I do like the smell of certain body odors very much.
And I'm very particular about that.
And I know within an instant.
And so this is a problem for any romantic partner
who likes perfume for me,
but I know many people like perfumes and colognes
and things of that sort.
I like perfumes.
I've also been told that by someone
that they couldn't spend time with me
because they do not like my smell.
In fact, they dislike it.
And fortunately for me,
there's at least one person on the planet who said the opposite.
So I completely agree with what you're saying.
I can also say that I imprinted on the smell of,
I had a Bulldog Mastiff
when I raised from the time he was a puppy.
And I imprinted on,
I imprinted on his smell immediately.
And even though to other people,

it was a Bulldog Mastiff after all,
his smell was rather aversive.
To me, he smelled delicious, right?
And maybe it smelled like home
and he was my best animal friend for a long time.
So and on and on and on, right?
The smell of children, as you said, the backs.
We had a guest on this podcast
who I'm sure you're familiar with, Charles Zooker,
a professor at Columbia has done incredible work
in vision and olfactory, thirst sensing.
And I talked a little bit about this,
that there's something in the breath of romantic partners
that's hopefully a petitive, not aversive,
as well as in children,
he was talking about the smell of his grandchild,
the nape of their, the back of their neck
and how he misses that smell.
Because when he thinks about missing his grandchild
or children, it's that smell that's associated
with that feeling.
Hexadecanal.
Yes.
Charles, your grandchildren smell like hexadecanal.
Yes, they do.
He's gonna come after me now.
And so this is a study ran by Eva Mishor,
who was a graduate student in our lab.
And Eva was interested in aggression.
She was really into aggression.
And actually when she started and so when she started off,
we said, okay, let's do chemo signaling of aggression.
She actually was going to like MMA clubs
and collecting body odors.
And we had all sorts of ideas going
and she worked on that for quite a bit.
It never went anywhere really.
And then at the same time,
we had a colleague of ours from Germany.
I mean, when I say colleague,
primarily a friend or acquaintance,
I met at conferences, Heinz Brier,
and he was studying in his lab,

a molecule, hexadecanal,
that was a chemo signal in mice.
Where in mice, it was described as a chemo signal
that promotes social buffering.
Where social buffering, as far as I understand,
it's not my field, but as far as I understand,
it's basically a feel good together thing.
So when lots of mice are together,
they feel good about being in a group
and that's social buffering.
And it's promoted by hexadecanal,
which they emit in their feces, mice.
And in his work on hexadecanal,
and so Brier and his colleague, Stortzman,
they discovered the receptor for this
and then they went and discovered
that the receptor is very highly conserved
throughout mammalian evolution,
and therefore they hypothesized
that maybe this is a universal mammalian signal.
Now, which is unusual because in chemo signaling,
typically you tend to think of things
as being very species specific,
but here they hypothesized that maybe hexadecanal,
which promotes social buffering in mice,
may do something in all mammals.
Again, because this receptor is very highly conserved
or 37B, I think.
So they, so he approached us and said,
look, you got to study this stuff in humans, right?
Because he knows us as the human people, right?
I mean, we go to these olfaction conferences
where lots of people study mice and zebrafish and whatnot
and we're the human group.
So, and eventually he just FedExed us hexadecanal.
And so we had this thing sitting around
and Eva was not going anywhere with her aggression studies
with sweat from human participants.
And yet she built the entire paradigm
to study human aggression.
So they're standard paradigms.
This is a paradigm known as the TAP,
the Tyler aggression paradigm.

I'll soon describe it.
And so we said, okay, we have this hexadecanal stuff here
and it promotes social buffering.
Social buffering sounds like it would make you less aggressive.
Why don't you run your TAP experiment using hexadecanal?
What's the TAP experiment?
So basically what you do is you bring in a participant to lab
and you have them thinking that they're gonna be playing
against another person in this game.
And you can do something like have another person walk
into the other room playing online, so connected.
So you can fool them into being quite convinced
that this is what's happening.
And they go into their own room
and in the initial game they play,
on each round, they're provided with a sum of money.
And this is real money that they'll receive
at the end of the experiment.
And by turn, each one of them decides
how to divide the money up between the two, right?
So they're playing against another person, they think,
but that's actually a computer algorithm
that they're playing against.
And the computer algorithm is programmed
to be in scientific terminology, a jerk, right?
So like let's say they have to divvy up 100 chequil,
which is the Israeli currency.
So the other player would say, okay, I'll keep 96
and you get four, right?
And then if you can either accept it
or not accept it and then neither of you get anything, right?
So basically you're being shafted
by the other side all the time.
And this is called the provocation phase.
You're really getting angry at this person
because they're really not nice, right?
They're shafting you on every trial or almost.
And you play this game and it goes to its end
and then you play a second game
as far as you know against the same participant.
And the second game is a reaction time game.
So a target shows up and the first to press it wins.
And on every trial where you win, if you want,

you can blast the other participant with a loud noise.
And it's a really loud noise.
So you're also wearing earphones, it's 90 dB
and it's a screeching horrible sound.
It's the most punishment that an IRB committee
will let you endure on a participant in the experiment
unless you're in stand for 70 years ago or whatever that was.
No, I was referring to the classic prisoner experiment
which took place in the building next door
to where I work by the way.
So you can blast the other participant
with varying levels of sound
and you have a selection box from something very low
to something very high.
And what's nice about this is that then allows you
to quantify aggression
because the more volume you're blasting the opponent
with the more aggressive you are towards your opponent.
And so you have a measure of aggression.
Again, the Tyler aggression paradigm obviously invented
by Tyler, very well validated studied
all over a very standard protocol.
So we brought in participants
and had them play the Tyler of the Tap
either under exposure to hexadecanal or control.
Now, hexadecanal doesn't,
it's incredibly difficult to even detect hexadecanal
but just in case, because it's not very,
it's considered a semi-volatile,
it doesn't have a strong smell.
But we buried it both the control and the hexadecanal
in a control order that hid them in a mask.
And she ran lots and lots and lots and lots
of participants, men and women.
And I'll first tell you the result with men
which is that hexadecanal consistently reduced aggression.
People were less aggressive under hexadecanal.
The effect size was quite meaningful.
And later on we learned because I'm no specialist
in the world of aggression
but compared to the effects seen in the aggression world
in research, really, really strong effects.
So unusually strong.

So hexadecanal lowered aggression in men
and we were like, cool,
this is sort of what we were hoping to see
consistent with the hypothesis
and consistent with it seems to do in mice.
But then we looked at data from women
and hexadecanal increased aggression equally significantly.
Is this thought to be something related
to maternal protectiveness?
We're getting there.
So you got there really fast.
It took me a year but, and Eva got to it really.
I'll tell you, because remember
we're reaching the back of the head of your,
of who's was it?
Grandchildren?
Charles Laker.
Charles Laker.
Charles Laker, one of the kingpins
of the New York neuroscience mafia.
Yes.
So this was really odd to me at that time.
And so I didn't have the intuition you just had.
And I was like, Eva, there was some bug here.
I mean, this, this, it makes no sense to me.
You know, why would something increase aggression
in women and decrease aggression in men?
This is really, really strange.
And, and I said, okay, I want to see this happen again
before, you know, we go ahead with this.
So she went and did the entire experiment again.
And this time she did it within the fMRI magnet
so that we can also track brain activity
while this was happening.
And first of all, it replicated again.
So once again, hexadecanal made men less aggressive
and women more aggressive.
And the extent of more than the effect alone,
the dissociation was remarkable.
This has, it's almost like a chromosomal test.
I mean, you look at the data on the unit slope line
and all the men are below and all the women are above.
There's this figure in the paper.

Then she also looked at the brain data and this is,
you know, although our lab does a ton of fMRI,
it's one of the major tools we use to measure brain activity.
I'm quite cognizant of the limitations of fMRI.
And this is, I think, sadly, I think the only study
in my career at least where I actually managed
to also get a mechanism out of fMRI,
not only an area that's involved in activity.
And so here's what we saw that hexadecanal alone
increased activity, quite pronounced in an area
of the brain known as the left angular gyrus.
Now this is an area involved in what's referred
to as social appraisal.
So that was kind of cool in that a social order activated
the social brain, not the olfactory system per se,
and very pronounced.
So on one hand that was cool, but then what was uncool
was that it did the same in men and women.
And this was in contrast to behavior,
which you don't like seeing, right?
I mean, because you would expect brain activity
to reflect behavior and it increased activity
in the left angular gyrus in both men and women.
But then she did a follow-up analysis,
which was look at what's referred to as functional
connectivity, that is how does this region of the brain
talk with the entire brain as it were
under hexadecanal versus control?
And here the dissociation reemerged powerfully,
whereby the connectivity from the angular gyrus
was mostly to the classic neural substrates of aggression,
so the amygdala and the temporal pole,
and the connectivity went in opposite directions
in men and women.
So hexadecanal increased functional connectivity in men
and decreased it in women.
So in a way, this is almost saying
that the default brain reaction is aggression, right?
The default is to aggress.
And in men, hexadecanal increases the control
that the left angular gyrus is holding over your aggression
and keeping you back.
And in women, it let it roam free

and they became more aggressive.
But I was still puzzled.
So I was convinced this happened twice.
The MRO data provided not only a pattern,
but a mechanism, which is unusual.
And yet I was telling Eva, you know,
but this makes no sense to me.
And then her insight, which of course afterwards is like,
is no, there's a place where this makes perfect sense.
And that is if you are a mammalian offspring
because paternal aggression is often directed at you.
There's infanticide all over,
and sadly there's male aggression
towards human children as well.
And maternal aggression is often protective.
So if you are an offspring,
if you have a molecule that will make your mother more aggressive
and your daddy less aggressive,
both of those are good for you.
So you're winning.
So we remembered a recently published paper
from a group in Japan
that looked at the odors emanating from baby heads.
We now come full circle to circus grandchildren.
They used a method known as GCMS,
gas chromatography mass spectrometry
to measure the volatiles from baby heads
because baby head odor is a cultural thing
across cultures, even in Japan.
And so we quickly went to that paper
and to see if one of the molecules that report is hexadecanal
and we were very disappointed
that it wasn't one of the molecules
that reported in the paper.
And so we wrote to the authors
who are since then our co-authors.
And we said, look, you know,
we're studying this molecule hexadecanal
and we don't see any results.
And we were wondering maybe you had some results
that you didn't publish
or some supplementary materials or whatever.
And this lab, which is a hardcore GC lab said,

no, no, hexadecanal is a semi-volatile, which we knew.
And our previous paper was not directed
to the semi-volatile range,
but we can now do use what's called GCXGC,
double GC that is directed at semi-volatiles.
And we can do this again.
We just studied 11 babies
and we can see if this is an issue.
So he said, yeah, please do.
The bottom line of all this is that hexadecanal
is the most abundant semi-volatile in baby hits.
It's tons of it coming out of baby hits.
So babies, again, speaking about
if humans do or don't chemo-signal,
babies are conducting chemical warfare, right?
They're, you know, reducing aggression
in their fathers or males around them
and increasing aggression in their mothers
or females around them.
And both of those things are good for them.
Incredible.
This is somewhat different than what we're talking about
and yet similar in other ways
because it's built off of anecdotal evidence,
but it's anecdotal evidence that you hear all the time.
And yet when you look in the scientific literature,
at least by my read, the data are not clear,
maybe even contradictory.
And that relates to the coordination of menstrual cycles
among co-housed women or women who are friends.
The, you know, many women listening to this
and maybe some men who are aware of this effect
will say, oh yeah, absolutely.
When I spend time with my friends or go away camping
or even spend a day with them,
our menstrual cycles become coordinated.
However, my understanding is that the early literature,
Barbara McClintock.
Correct.
Discovered this phenomenon, published a paper in science
as an undergraduate.
1971 Nature.
Amazing, Nature paper.

Again, one of the three Apex journals
and as an undergrad, fantastic.
So discover this, describe this,
and probably women all over the world
who became aware of this one way or another,
probably said, yes, absolutely.
This gives validation to what we've observed over and over.
And yet as subsequent papers have been published,
this result has been called into question.
Is there any final word on whether or not menstrual cycles
become coordinated among women who spend time together?
And if so, is there any role of olfaction in this?
Or chemo sensing through the nostrils and or mouth
to support this idea?
So, yeah, so I'll start off indeed to echo the background.
Is that this study was conducted by Martha McClintock
when she was an undergraduate at Wesleyan College.
And she noticed that she thought her menstrual cycle
and her co-inhabitants in her dorm room
were coordinated in time.
And I should say that this comes on the basis
of similar or related type effects in rodents.
Now, rodents don't have a menstrual cycle like humans do,
but there's an effect in rodents,
which is the Witten effect,
which resembles this type of effect.
And she published indeed that papers
on undergraduate in nature in 1971.
And to answer your question,
she published a follow-up in 1998, also in nature,
with then her graduate student, Chicago Stern.
So this is Stern and McClintock, 1998.
And here's what they did.
They collected sweat from donor women
and deposited it on the upper lip of recipient women.
So this would be a fun experiment for you,
at least because you said you like body orders,
but for many others, perhaps it would be daunting.
Well, I like certain body orders from certain individuals.
Okay.
I don't think I uniformly like all body orders,
although I do send a uniformly,
not like the smell of perfume,

although I should just to clarify
because I put this out there
and I've learned the hard way
in the comments section on YouTube.
Some of those perfumes I find downright aversive.
Like it's, I think the great Marcus Meister,
who a great neurobiologist once said,
there's basically three responses
to either yum, yuck, or meh.
So some are truly yuck.
I've never heard that one.
I don't like that one, right?
In terms of the animal behavior, human behavior,
we either move forward and back or stop or pause.
So some are truly a yuck.
Some many are meh.
Zero to date are yum for me.
Now body orders, the distribution is shifted.
It could be any one of those three, yum, yuck, or meh.
So just to be clear,
but the yum category is definitely included.
Thank you for allowing me to do that.
Yeah, yeah, yeah, yeah.
So she did this study.
So because right in the original McLintock study,
you might suspect other drivers of the effect.
Let's say you accept the effect,
but still there might be other social drivers
of the effect that are not body order, right?
There might be some dominant woman
who's dominant in some other way
and this might be driving the coordination, right?
So here there was no direct link
between these women other than body order.
So if the effect reemerged,
it would definitely be an olfactory effect.
And what she found is that if she took a switch
from the follicular or the ovulatory phase of the donors,
one extended the cycle in recipients
and one shortened the cycle in recipients.
I don't remember which was which,
but basically definitely denoting
a chemosignaling effect with opposing effects

on duration based on the time it was collected from.
Again, published in Nature in 1998.
That said, there's a quotation.
I think this is from,
I'm not sure, but that if something's published
in Nature or Science,
that doesn't necessarily mean it's not true.
So with that in mind,
the findings were since called into question, widely.
One reason is just statistics of cyclic events
are surprisingly complicated.
So it's tricky.
Once you have a cyclic event, statistics become tricky.
And so Martha took a lot of heat on the statistics
of claiming an effect.
And I think there was at least one effort
of replication that didn't really work out.
If you ask me, I'm on the fence.
So, but I may be in a minority in my field.
I think a majority in the field is currently negative.
I'm not.
And we've said in the lab
that we should do a planned replication.
We will.
Again, it's a horrible study to run.
It's tons of work and you have to run it
for a really long time.
And so it's just completely non-trivial.
But we have a graduate student now in lab
interested in these exact things,
Ruth Weissgross, and she's doing similar stuff.
And I hope we'll do that.
I hope we'll try to replicate this.
Very interesting result.
And I think interesting because of its real world,
meaning outside the laboratory, of course,
our experiment analog,
but also because pheromone effects
and all factory effects in humans
seem unique among neurobiological slash endocrine phenomena
because there seems to be so many stories
that we all have of the smell of our grandmother's hands
or the recognizing the scent of somebody.

Or I knew from the moment that I smelled their breath
or I just liked their smell kind of thing.
These kinds of things that inform the deep potential
for a real biological phenomenon,
as opposed to the kind of thing like,
oh, you just throw something out there,
oxytocin is bonding.
And all of a sudden, the general public,
not to no fault of their own,
comes to think that every aspect of bonding is oxytocin
and every defect in bonding is lack of oxytocin.
But the general public provides a sort of a rich,
it's fodder for exploring all these things.
And a lot of times they turn out to be true.
When in the context of old action.
Yeah, no, it's a very primal system.
So it's linked to the most limbic primal mechanisms
in our brain and it drives primal behavior.
It's an incredible system.
I have a question about a particular study,
but I'm just gonna cue it up
and you'll know immediately what I'm queuing up.
And that is, what is the relationship between odors
and hormones and in particular, crying?
As I pointed out previously,
the sort of flavor of the month
in human social chemo signaling research
is the smell of fear.
And the media of the month is sweat, right?
So the few, maybe tens of labs in the world
that study human social chemo signaling,
all collect sweat and that's the media they look at.
Is it always from the armpit,
or are there meaningful differences
in terms of the sweat emitted
from different locations on the body?
I already know the answer to that as I ask it,
but let's just stay above the waistline and...
Oh, no, no, yeah, yeah.
Or below the waistline.
We're biologists after all.
We just...
Yeah, so it's funny, we're working on a paper on that right now

on the smell of fear.
So we have a nice paradigm for generating fear.
We throw people out of airplanes.
It's a very effective way to generate fear.
I have to come to your lab.
It sounds like the greatest lab in the world.
We didn't invent that, by the way.
The first to do that was,
and I hope I'm pronouncing her name correctly, I think.
It's Mujica Perudi.
But that's our paradigm for generating fear.
And we started that on our own,
but we've since entered into collaboration
with the Israeli Paratroopers Brigade,
and we now collect body odor from every first time jumper.
So we went that path
because we, like everybody else in this field,
the holy grail there is finding the molecules, right?
I mean, if you'll have the fear molecules,
that's bonanza, right?
Because, I mean, you could think of many reasons
why it would be a bonanza, but for me,
if you find the molecules,
you can then try and find the receptors.
And when you find the cognate receptors,
you can then develop blockers.
And you can imagine,
you know, what's the term I'm looking for?
I'm switching into Hebrew.
It's about midnight now, right?
I'm sorry, it's two in the morning.
You're doing it incredibly well,
considering the inversion of the circadian thought.
We would never know.
No one traveled in today from Israel.
So he's a circadian inverted, as we say.
Anxiety, so you can imagine developing
like a nasal spray against anxiety, right?
Where you would quell those receptors
and kill the fear response, right?
Which rather than going the current path,
which is through neurotransmitters
that then have effects all over the place,

you would be getting fear at its source, right?
So that would be why I would want that.
And we figure out that doing that,
you know, collecting fear from like three,
four or five people in an experiment,
you'll never be able to do analytical chemistry on that.
So we now have a setting we call Fear Bank,
which now has more than a thousand samples in it.
So we're trying to do analytics on that.
But in doing that, we've joined the crowd,
everybody's doing fear and everybody's doing sweat.
And in one of our discussions in the lab,
we were saying, well, there's gotta be,
or there potentially definitely could be additional
bodily media that are playing into social chemo signaling.
Now, many of these, you know, you can't really study, right?
I mean, so, you know, just to throw it right,
most terrestrial mammals communicate
social information through urine.
But, you know, starting doing experiments
with humans with smelling urine,
it would be difficult, you know,
both in IRB and in agreement and, you know,
and then we, you know, this is a rare case
where we actually hypothesized what we saw to do.
And, you know, the only claim in retrospect
that it was hypothesis is tears.
We started thinking about tears and looking into tears
because tears are a bodily liquid emotional tears
that we emit in emotional situations
where these are situations
where non-verbal communication is critical and key.
And tears are a liquid that is puzzling
beyond ocular maintenance, right?
And so, you know, the most influential text,
I think till this day in emotion research is Darwin's book,
The Showing of the Emotions in Man and Animals,
I think is the full name of the book.
And an entire chapter, chapter six is devoted to tears,
an entire chapter of this book.
Why?
With no conclusion.
Why?

Because the book revolves around
describing the functional antecedents
of emotional expression.
So for example, showing of the teeth
as a sign of aggression, right?
So animals first bit with their teeth
and Darwin argued that through evolution,
just showing the teeth alone became an aggressive sign
because it started from biting.
Or what I find is a beautiful example,
and this is work partly done by Adam Anderson,
now at Cornell, is the emotional expression of disgust.
So disgust, which comes from one disgusia, distaste, right?
Is spitting something out of your mouth.
Now, what Adam showed is that
the musculature patterns of activation
and the temporal sequence of activation
when you experience moral disgust
are the same as when you spit a bitter taste
out of your mouth, right?
So again, so there's a functional antecedent
spitting something out and through evolution,
the argument was that it became an expression of emotion
and you express disgust just as if you're spitting
something out of your mouth,
even though they're, you know, in the case of moral disgust,
there's nothing you're spitting out of your mouth.
So Darn systematically went through
the expressions of emotions
and for each one went to their functional antecedent
and explained everything very nicely.
And then he got stuck with tears, right?
Because tears are an obviously emotional expression
and he could not find a functional antecedent.
So he ended up saying,
this is an epic phenomenon, basically.
Right, I don't know why.
What all scientists do when they don't have
a good explanation and blame it on nature.
Right, right.
But he bothered to write this entire chapter
on the ocular sort of maintenance function of tears
and so on and so forth, but nothing emotional.

So we thought, well, maybe the function is a chemical signal.
And, you know, so with that in mind,
we harvested emotional tears,
which was also an amusing event on its own, right?
Because we posted messages on all sorts of boards
that we're seeking experiment participants
who cry with ease.
Now this generated an unfortunate gender bias
in our study, right?
Because we received about a hundred women volunteers
and about one man.
And, you know, I think this is not a problem
only in macho Israel, right?
Probably anywhere in the West.
I mean, definitely in America would be the same, I think.
My guess is that there are probably men out there
who cry easily, emotional tears.
Oh, I'm sure.
But they're not gonna show up.
Yeah, yeah, that's what I'm saying.
It's a cultural thing.
It's not, you know, you're not gonna come to a lab
and say, you know, I cry all the time.
It's just not gonna happen.
And then what we did is,
for each one of these participants,
you know, we would ask them, you know,
is there a particular film event that you know of
that, you know, a scene that makes you cry?
And interestingly, in these effective criers,
there's always, oh, yes, you know, the scene and so and so,
I always cry profusely from that, you know, they have their-
Can you give me an example of one of the more
commonly needed scenes?
Yeah, yeah, with these.
The movie, The Champ.
The Champ dies.
He's a boxer.
And he dies and literally in the hands of his
about eight year old son.
And his son is standing next to his bed
and, you know, saying, champ, champ.
And he dies.

Right?
It's a winner.
Okay.
Waterfalls.
Yeah, yeah.
Got it.
So, you know, we're probably the neurobiology lab
with most sad movie films on those shelves in the world,
right?
We have a whole huge collection.
There is such a thing as tears of joy, by the way.
So no.
No?
We're going ahead of ourselves.
Let's say we tried to collect them and failed.
Even people who think they shed tears of joy and laughter,
their eyes water a bit, but it's not the same thing.
In the effective criers, we end up screening.
So, you know, we collect a full ML of tears,
a full ML of tears in about 15 minutes.
So that's pouring, right?
And that doesn't happen from laughter.
That we, or we've never seen that.
We've never seen that happen from laughter.
We tried.
So, we have all these sad films.
And by the way, one of the amusing things is,
when we ultimately published this paper in Science,
we were forced, in retrospect,
to go out and actually buy the films.
Right?
I mean, originally, we like downloaded the rear there,
but you can't because you'd be violating copyright laws.
Right, so we had to buy, like,
purchase all these films, let the participants watch them.
So, we actually have these in lab, like DVDs,
you know, that we actually purchased, but, so...
Nice coverage of potential legal fallout there, no.
No, we did.
No, I believe it.
No, I believe it.
Yeah, it was that, I believe it.
So, yeah, and, well, we can touch on that later.

But, so, most of these volunteers who come saying
they can cry with ease actually don't meet the bill.
And so, out of the about 100, at least,
more women that we screened,
we ended up with about six who could really come to lab
week after week and pour tears.
There's a name for this in psychiatry.
They call it a narrative distancing.
Some people, when they watch a film
where someone's getting hit,
they flinch quite a lot.
It's almost as if they're experiencing it,
but it works in the opposite direction, too.
I know someone like this,
where if they watch a film that someone's experiencing
something even mildly positive, they're mood elevates.
So, they can quickly bridge,
and it's not always adaptive, as you can imagine.
So, there's lack of narrative distancing.
Right, yeah.
What one issue you can bring up
with this entire line of studies in our lab is,
I don't know if there's something very unique
about the donors, right?
I mean, we're assuming these are tears.
No, this is pretty common.
I think that the numbers I saw out there
about five to 8% of people.
That's exactly what we got about, right?
Interesting.
About 600.
So, we collected tears,
and we exposed participants to these tears.
And we found a few things.
First of all, the tears are completely odorless.
You cannot detect them at all.
Completely odorless.
And yet, when you sniff them,
you have a pronounced reduction in testosterone
within about 20 minutes, half an hour.
This is men and women smelling women's tears.
Men smelling women's tears, but not perceiving any odor.
Nothing, just sniffing them.

And you have about a 14% drop in free testosterone.
Free.
Okay, so this is testosterone
that's already been liberated from the testes.
Free testosterone.
And so we've done a few hormone that's either bound
or unbound, is unbound, excuse me,
from sex hormone binding, globulin, et cetera.
And it's the active form.
So, it's subject to very short time scale changes.
Yeah.
And this is, people who studied testosterone,
which is not me, but they tell me
this is a really strong effect.
Like it's hard to even pharmacologically get
an effect like that, that fast.
I mean, no in pharmacology.
Yeah, years ago I spent time studying endocrine effects
of this sort, and that's a tremendous resized effect.
So, and so here I'll point out in passing
that one of the concerns we had because of the effort
to run this study is that nobody would ever try
to replicate it.
And to our joy, about two years later,
an independent group from South Korea, Oed Al,
I don't know at all, replicated the testosterone effect
to a T, I mean, like same numbers.
So, it lowers testosterone and we then also looked
using MR at the effect on brain activity
and saw pronounced effect on activity,
a dampening, a lowering of activity under an arousing state,
a lowering of activity, both in the hypothalamus
and in the fusiform gyrus for whatever reason,
I don't know.
Face recognition area.
Other things, yes.
And we don't know why, but pronounced.
And currently, Shania grown in our lab
is replicating this again.
And this time with a stronger behavioral component,
and I can share with you unpublished data now under review
that's, as you would expect,
given the effect on testosterone perhaps,

sniffing tears lowers aggression in men.
Using again, the TAP, the same experiment used by Yvonne
in the hexadecanal experiment.
The TAP, I'm gonna think of that as the sadist,
the titration, the sadist titration.
Yeah, yeah, Tyler aggression paradigm.
So not only the Milgram experiments of the 1950s,
which post, this was looking at sort of post Holocaust behavior,
people basically in American laboratories
thinking they were torturing other people.
Simply because they were told to,
and a lot of people did that,
even though most people would report
that they would never torture somebody else.
Yeah, yeah, humans are not a wonderful species.
Or as we could say, I think it was the great Carl Jung
that said, we have all things inside of us,
but the goal is not to experience them all, certainly.
It's an incredible study, and it points again
to the power of these chemo sensory systems and pathways.
And obviously, there's so much here.
I don't know if you want me to tell about this or not,
and I guess you can edit it out if you don't,
but this is just sharing stories
about the politics of science.
So whereas the effect on testosterone
was replicated by an independent group,
in the original study in science where we had,
it had three components.
One was the effect on testosterone, which was robust.
The second, which was brain activity, which was robust.
And there was a significant but weaker effect on behavior,
and I don't think we studied the right behavior
in retrospect.
What we looked at then was ratings of arousal
associated with pictures.
And there was an effect, it was significant,
but it was not what carried the story.
Now, there's a lab in Holland of a guy by the name of,
I'm probably mispronouncing this,
but I think it's Vinger Hoots.
For the non-Dutch.
Yeah.

Dutch names are always a little bit of a challenge, but.
And I shouldn't say that, being in Israeli,
I shouldn't go too much on that line,
but that lab really didn't like our original tier story.
And the reason they didn't like it
is because they've built a career on this notion,
including a book with this title,
that emotional tears are uniquely human.
Now, here I should, well, I should share.
So one of the things we really liked about the tier result
is that partially before we did our work,
but more afterwards, and we liked that because usually things,
so usually in our chemo signaling work,
like what I told you before about the Bruce effect,
we look at what happens in rodents
and we see if the same thing is happening in humans.
This was a rare case where after we did this work,
more or less identical effects were discovered in rodents.
So a paper published in Nature two years later
found that mouse tears, mouse pup tears,
lower aggression in male adult mice towards them.
In a smell dependent way.
Yeah, yeah.
And they also actually found the actual component in tears
that, so the tear pheromone that lowers aggression, right?
So this has us thinking of tears as you can think of tears
as like a chemical blanket in a way
that you're covering yourself up again
with to protect against aggression, right?
And so our finding, which to me,
I mean, this is consistent with how I think
about behavior in general,
I don't think beyond language,
there are very few things,
definitely sensory things that are uniquely human.
I'd be hard pressed.
But so our finding against their story, right?
Because here we're saying, no,
tears are this chemo signaling mechanism like all animals.
And by the way, just after this entire debate,
about six months ago, there was a paper in current biology
that dogs emit emotional tears.
And it was the dogs emit emotional tears

when they reunite with their owners.
And you were talking before about oxytocin.
So I think what they showed there is that not only that,
but that the view as seeing the tears in the dog
influences oxytocin in the humans.
I hope I'm getting this right.
No, I absolutely believe this.
I mean, from the time I brought Costello home at eight weeks old,
Costello is your dog.
He's my dog, unfortunately, passed away,
but having a long time.
Actually, the only time I can recall crying,
listen, I've certainly cried before,
many times in my life, many, many times.
The only time I ever recall crying to the point
where I wasn't sure that I could keep producing two years,
but somehow it is when I had to put him down, right?
Is this like, you know, and if I talk about too long now,
I'll start crying to the, you know,
it's one of those things.
I think it's a healthy emotional state.
But I recall when he was a puppy,
thinking this oxytocin thing must be real
because I can recall being in faculty meetings,
which, you know, fairly stated are not always that interesting,
but they could be pretty interesting.
And someone presenting data in my mind thinking,
I hope Costello is okay.
What's he doing down in my office?
This is when he was very little.
And also not needing to eat,
not being able to focus on anything else,
except my attachment to him
for about the first two or three weeks that I had him.
Then it was easy.
Then I could focus off on other things.
And I think that dogs, perhaps through oxytocin,
hijack the circuitry that's intended for childbirth.
I really do.
Otherwise, why would people be so ridiculously attached
to their dogs?
I mean, hence all the posts of everyone thinks their dog
is the cutest dog,

the same way everyone thinks their children
are the cutest children.
You know, Costello, by the way,
was a very handsome bulldog.
So again, to put another nail in that story
of tears are uniquely human.
So they're not dogs shed emotional tears.
And so that group really didn't like this.
And they went ahead and tried to replicate.
And to your listeners,
I'm showing double quotations on the replicate,
only the behavioral part,
the ratings of arousal in women of women
and fail to replicate that.
I see.
Now, this was just sharing on how science works
and it doesn't work in my notion in this case.
So at the time, after they got this accepted
in some journal, not a field journal,
in the journal of memory of something,
they contacted me for a response.
And I wrote to the authors and I said,
look, you know, this is very odd to me.
Why don't you come?
You know, why don't we replicate this again together
and see if it doesn't work?
If it doesn't work,
I'll publish it with you that it doesn't work, but you know.
And so I said, why don't you send over a graduate student
or the lead author and we'll do it here
and we'll show them how it's done
because they did it very wrongly in the paper.
And so they replied that, no, they don't have money
to send over a graduate student to do it.
So I replied saying, okay, I'll fund the graduate student
coming over and I'll fund the entire study
and their stay and so on and so forth
and let's do this together.
And they replied, no, they're not willing to do that,
which I don't think is the way things should work.
And they published this sort of failed behavioral effect
in that paper.
So I'm just sharing this, you know, that it's not only,

there was that successful replication
with the effect on testosterone,
but there was supposedly the failed replication
on the effect in behavior.
And then I published a rebuttal on that,
which I don't know if I should have done, but I did.
Well, I think it's interesting.
I mean, I think provided studies are done correctly,
I mean, the positive result almost always trumps
the negative result.
And yet I think replication is key.
The problem, as you pointed out,
is that replication is rarely pure replication
of the exact study.
Yeah, this one is not even remotely,
but I published the detail.
So actually they hid something in their data
that did partially work.
So I asked for their data and I reanalyzed it
and that's what I published in the rebuttal.
But you know, this is just sharing on how science works.
I took advice, so it's not that I'm friends with him,
but at that time I was communicating a bit
because we were on some board with Daniel Kahneman,
who's Nobel Laureate.
He's fast and slow.
And so I asked him, how should I deal with this?
Give me some advice here.
I was really, it was emotionally not fun
to be in that position.
And he said, never publish a rebuttal, don't do anything.
I was, how can I?
I have to do something.
Because once you do that,
then people don't go into the details.
They won't read the details of your rebuttal.
They'll be like, well, there's a group that says this
and there's a group that says that.
So it's unclear.
Well, I mean, I appreciate that you're bringing it up today
and I do appreciate that you published the rebuttal
and that you offered in a very magnanimous way
to do a collaboration.

That's what he then said.
So Kahneman's advice after that was that, well,
if you insist, then just publish, write a response
that you offered them to come do it together.
They refused and there's nothing you can do about that.
It's a lot like fight sports, right?
People talk a lot of trash.
Although in science, you know, I will say this,
you know, as long as we're on the sociology of science,
science is very different than podcasting or social media
or other fields because in science,
people generally are very kind to your face
and then you get it in the neck on grant reviews
or anonymous reviews.
I was on a grants review panel this morning.
I'm a nice reviewer, meaning I judge things objectively,
but I try to always think from the perspective
of the graduate student or author of the proposal.
Listen, I think that science is a game of people
who most of them are seeking facts.
However, the ego is strongly woven into it
like anything else.
So I think it was very magnanimous of you
to offer the collaboration.
So I'm gonna tell this lab whose name I can't pronounce.
Please accept the collaboration.
Then we can invite everyone on here for a round table.
I appreciate that you shared that story
and I know a number of other people will
for a number of reasons.
I have a couple of more questions and I realize,
and thank you by the way for your willingness and stamina
because it is probably 1 a.m. Israel time now
and you just arrived, but you're doing terrifically well.
So if you'll indulge us just a touch further,
there are two topics that I wanna touch on.
If you wanna cover these in shorter thrift,
that's fine, although don't feel any obligation to.
The first one is, I think most people are familiar
with the scent of food or foods as a signal
of the nutrient contents of those foods.
An orange that smells great
or the smell of something baking,

it suggests something about the contents
and quality of that food.
After all, you and I both separately lived
in the same apartment in Berkeley above the cheeseboard,
which the smell of cheese wafting up through the cheeseboard
is something I will never forget and the breads.
Never forget it.
Amazing bread.
I mean, I don't know if you've conveyed that clearly enough
to listeners or watchers.
No, the probability.
We really just discovered that we lived in the same,
we never met, I mean, a fit like this before.
Yep.
And we lived in the same apartment.
Exactly.
Are we click friends?
I had it in a lingering way, I guess.
Absolutely.
Through the floorboards, it had a great floor in that place.
It had a great wooden floor.
It was an amazing place.
I lived there with my girlfriend for a year and a half
and then it was an amazing place.
We won't give it out at the address
out of respect for the people that live there now.
But do check out the cheeseboard if you ever in Berkeley.
Their hours are weird, so you have to look online,
but it's a unique place with great bread and cheese
and some good flavors of pizza.
In any case, I'm wondering whether or not smell
can signal things about the nutrient contents of foods
in a way that's divorced from the smell
that we are perceiving.
So for instance, I could imagine,
based on what you've told us about smell today,
that, you know, I don't know,
I smell a piece of meat cooking
and it smells great to me.
And I think of it as, oh, that's so savory
and my mouth is watering and I love the smell of this.
And I'm thinking, okay, this is protein and fat
and I love the taste of steak and a little bit of char,

but that nature has co-opted that to ensure,
or I should say, increase the likelihood
that I will ingest some other thing that's in steak
for that has no odor,
but whose nutrient content is very important to me.
For instance, amino acids, right?
I mean, amino acids are essential to life.
And yet we don't go around sniffing for amino acids,
we go around sniffing for savouriness, umami type tastes
and things of that sort.
So I could imagine a million different examples of this.
In the same way, I could imagine that the scent
of somebody that we fall in love with
or become romantically attached to
or sexually attracted to
is signaling all sorts of things about,
sure, the potential for offspring
of a particular immune status.
That's a long-term game,
but also something about pleasure and safety
of a potential interaction.
So what I'm asking here is about
that whether or not there are subconscious signals
that the olfactory system has learned to seek,
but learned to seek through more overt signals,
sort of the tip of the iceberg for them and on.
So, you know, I don't have a good answer for you,
although I think it's a really good question
or a good idea, in fact.
So whether there's, you know,
older cues on nutrient value is a really good idea.
Moreover, it's probably good to the extent
that somebody probably did it and I should know and don't.
We haven't done anything on that line.
So I don't know.
I don't know if the nutrient value of food
is systematically encoded in odor.
If that's not been done,
and I will check after our meeting today,
then it should be.
That's a really good idea.
I mean, one of the reasons I asked this is because,
you know, the obesity crisis in the U.S. is a huge issue

and elsewhere and highly processed foods,
you know, have a lot of things that are problematic,
but one of the things that they don't have often
is a direct relationship between the scent,
the taste and the nutrient content.
And I don't mean macronutrient sugar fat,
excuse me, carbohydrates, fats and proteins,
but the vitamins and micronutrients,
things that support the microbiome,
whereas foods that are not highly processed,
for instance, meat or a piece of fruit,
contain many micronutrients
that are vital to aspects of our biology,
but we don't go around sniffing for probiotics.
I'll tell you one sort of factoid
that may support your hypothesis here.
And that is that there appears to be potential
olfactory perceptual similarity in metabolic products.
So something that's metabolized from something else
has perceptual similarity across those two things.
So metabolic cascades play into the coding
of olfactory space, and that is consistent
with the direction you're implying.
But again, I don't know of a direct test
of nutritional value in the smell.
And again, the fact that I don't know
doesn't mean, of course, that it doesn't exist.
And in this case, I would suspect that it should exist
in scientific press, and if not there,
then with the companies that have vested interest in this,
which are many.
I can briefly share, just please.
An amusing anecdote to share with you
is that we've received two independent
companies who have turned to our lab recently
asking for help to bring odor to engineered meat.
That's a growing thing.
And all these meats that are not off.
Yeah, to bring it up, this audience is going to be
very polarized along the lines of engineered meat.
You're not promoting.
Oh, no, no, no, no, I'm agnostic.
But we've had two companies turn to us and say,

look, we have this great product,
but it just doesn't smell like meat.
So help us make it smell like meat.
Interesting.
The reason it's so polarizing is that anything
related to nutrition on social media
is a total barbed wire topic.
We've had experts on nutrition come on here.
We'll have more, but don't worry.
You're safe.
No, don't worry.
No one is not, and is not promoting.
He hasn't even said whether or not
he's going to help them out.
No, we're not actually.
No, no, because yeah, it just never, it didn't happen.
Yeah.
No, the whether or not those engineered meats
are yum, yuck, or meh is a personal issue
to people in terms of taste.
Whether or not they are better for neutral or worse for you
and the planet than given the ingredients
that are required, that's a whole world we'll avoid now.
I won't, but you know, I'll take the opportunity
to highlight something related maybe
because on what we were saying on the scale,
you know, there's this, you know,
I'll take the opportunity to dispel another misconception
about olfaction, right?
There's this common notion that our sense of smell
is incredibly subjective, right?
And that what you might like in the smell,
I will not like in the smell and that we all have our own,
you know, totally subjective world of olfaction.
I think I know the study you're gonna tell me.
There are many.
The cross-cultural similarity.
There are many, that is utterly untrue.
Many, not only from my lab, there are many from many labs.
Please clarify for those that don't follow this literature.
So yeah, so humans are incredibly similar to one another
in their olfactory perception.
And this is in contrast to what most people think.

So why is there this misconception?
The misconception is there are two reasons.
First of all, or for several reasons,
but two are stand out.
First of all, we're attracted by outliers
because, you know, I'll tell somebody look, you know,
for example, olfactory pleasantness
is highly correlated amongst humans.
And let's first put this in numbers.
You'll take a bunch of humans and a bunch of odorants
and have them write pleasantness.
The correlation across the humans will be about 0.8.
That's incredibly high, incredibly high.
What do you think is pleasant, I think is pleasant.
Yeah, yeah.
Now, why is that go against what culturally people think
for two reasons?
First of all, we're attracted or biased by outliers,
but that's particularly that shows, in fact,
the result, what do I mean?
So you'll tell somebody, look,
people are very similar in their pleasantness estimates.
And the cell, you know, that can't be, I love cilantro.
And you know, my girlfriend hates the smell of cilantro,
right, or, and there are a few classic examples,
they're guava, right, you know,
is another polarizing odor.
So there are a few polarizing odors, right?
And that's true, right?
So that's true that, you know, half of the population
loves the smell of cilantro and half hates it,
half loves guava, half hates it.
That's true.
Microwave popcorn.
However, I assure you that, you know,
you can come to our lab,
we have about a thousand odorants in our lab, okay?
We won't smell the thousand, right?
But I assure you, you know, take a hundred odorants,
okay, from our mixtures and labs, right?
And we'll smell them, right?
And out of the hundred odors,
90 will totally agree on, right?

And including, I mean, you know,
nobody will say they like the smell of feces
or fecal smells, and everybody will say
they like the smell of rose and flowery smells.
There will be rare, rare exceptions.
And the correlation is about 0.8 across individuals.
So on 90 of a hundred will usually be in high agreement,
then five odorants will be in sort of intermediate agreement.
And yes, there'll be the five odorants
that we're in total disagreement on.
But I ask you, you know, if we agree on 95
and disagree on five, are we the same or are we different?
We're the same, they're just outliers to this rule.
And so one reason is this issue of outliers
attract how we think about things,
but no, we're actually much more similar than what we think.
And the second thing that drives this cultural effect
is our poor application of language to affection, right?
So in other sensory systems, we grow up with,
we develop with anchors, right?
So since you're a little kid, you know,
your mother shows you a cow and says,
what does a cow do moo, right?
And we all know moo moo.
And what color is this?
It's, well, this is kind of an odd black,
but it's black, right?
Or what color is that?
It's red, right?
So you have these anchors, but as you all know,
you know, the red that I'm seeing
is not necessarily the red that you're seeing,
we just both know to call that red.
And since you say red and I say red,
I think why we're seeing the same thing,
but no, we're not seeing the same thing, right?
And in odor, we don't have those anchors, right?
We don't, from childhood, you know,
our mom doesn't tell us, so what's this smell
and what's that smell, right?
And so we don't have these language anchors
that make us think that we're perceiving the same thing.
Now, how can you quantify that?

The most important term in measuring sensory systems
is similarity, right?
That's the measure, right?
So what can you do?
Let's say we take 10 odorants
and I have you rate all the pairwise similarities, right?
So you end up with 45 numbers, right?
So, you know, how similar is one to two,
one to three, one to four, and then two,
and all the possible pairwise similarities,
let's say you rate similarity from one,
which is totally dissimilar to 100,
exactly the same, right?
So now I have a similarity matrix
that describes Andrew's perception of smell, right?
I have, you know, based on these 10 odorants that I selected.
Now I can run my similarity matrix,
and then I can see if the similarity matrix
are correlated, right?
And then we've gotten rid of the issue of names and odors,
right?
It doesn't matter if I'll call this lemon and this orange,
and you call this sweet potato and this marshmallow, right?
It doesn't matter.
If I think that these two are highly similar
and you agree, and I think that these two
are very different and you agree, right?
We perceive the world in the same way.
If our similarity matrices are aligned, right?
And what's nice about that is that then you can do that
for vision, audition, and all faction in a common group.
And you can see where we're more alike each other or not.
And we've done that for color vision,
all faction, and tonal audition, okay?
And we are most dissimilar in color vision, okay?
In color vision, the variance is about 100%.
Amazing.
That's quite different.
Yeah, and there's tons of literature on this,
tons of it, tons of it, right?
And in all faction and audition, they're about the same.
So we're not different, we're very similar.
We're just very poor at appreciating this.

And mind you, not that there's not variability,
there is variability.
And of course the system is malleable,
as all sensory systems are,
so you can learn to like an odor,
and that will change you and learn to dislike an odor, right?
But just the way you can learn to like a sound
or dislike a sound.
So this doesn't take away from the hardwired link
of a structure to its perception
that they're malleable.
And we're not very variable, we're actually kind of similar.
That's a perfect segue to the question I have next,
which is if in general people perceive certain odors similarly,
you could imagine that odors could be manufactured,
co-opted, et cetera,
in order to elicit richer sensory experiences
and drive choice making.
That's obvious at the level of the smell of a hotdog stand
or freshly baked bread, et cetera.
But what I'm talking about here,
and I'd like to ask you about is doing this at scale
and scientists, geeks like to say in silico,
through computers.
So for a long time now, there's been this idea
that there will soon be Google smell,
not to call out Google is the only search engine,
but duck, duck, go, smell.
For those of you that don't want to hear smell.
Chat GPT.
Chat GPT, and on and on.
In other words, vision, visual information
is sent through computer interfaces
as is auditory information.
Not so much haptic somatosensory,
although it can, our lab uses VR.
It can be done, but it hasn't really taken hold.
However, smell being such a rich source of behavioral
and hormonal and other sorts of deep, deep information
that can drive people into yum, yuck, or meh
type decision making, seems like an amazing candidate.
So what is your experience with generating smells
in silico in computers?

And here folks, if for those of you
that aren't catching on to this,
and I don't expect that everyone would,
because what we're really alluding to here
is the idea that you'll look at,
you'll put into a search engine blueberry pancakes recipe,
and that not only will you get photos
of those blueberry pancakes and a recipe,
but you will get the hopefully validated odor
of those pancakes and that recipe coming at you
in real time through the computer.
So I'll start off answering from the name
you threw out there, Google.
So about, probably about five years ago,
Google had an April Fool's spoof.
All right, and they put out this video of Google smell,
okay, and it had all these classic sales images
of holding up your phone to a rose,
and it generating rose, and all these things, right?
So Google is now trying to do that.
And they just published,
I mean, I know they've been trying to do it for a while.
They visited our lab, but they just sort of went public
with this that really just like about a month ago
or something, that they have this offshoot startup.
I think it's called Osmo or something like that
that started off with a ridiculous sum of money
for a startup, like, yeah, I don't know, tons of money.
There's a lot of money in that world.
Yeah, in Google, yeah, to digitize smell.
And there are other companies
that are trying to do this as well.
And we've been talking now for quite a while
about our lab's chemo signaling work,
but actually half of our lab is devoted to this question
of ultimately digitizing smell.
And so this is a very, very active field of research.
And I'll say one thing that dovetails
with what you were talking about before,
in many ways, COVID is going to be one of the best things
that ever happened to all faction research,
because suddenly all the world is, are all the world.
Lots of people are very cognizant

of the importance of smell.
And the smell is like way up there
in people's awareness because of COVID.
And this is driving a renaissance of all faction research
and awareness to all faction is something
that's worth paying attention to.
And our lab has been involved in this way
in this effort for a long time
where the initial part of this effort
is in fact to develop a set of rules
that link odor structure to odor perception.
That is, the going saying was that until recently,
at least there was no scientist or a perfumer
for that matter who could look at the structure
of a novel molecular mixture
and predict for you how it will smell
or a smell something
and tell you what a molecular structure could or should be.
So in contrast, let's say to trivial like color vision,
let's say, so if you know what the wavelength of the light is,
you more or less know what perceived color is gonna be.
Of course, there are exceptions to that
and all sorts of issues,
but as a rule you would know,
or the other way around,
you can generate a wavelength
and you would know what color light
it's going to be perceived.
So that's an example of where the rules linking structure
in this case measured by wavelength
and perception in this case experienced as color.
The rules are well-known.
In all factions, we didn't have that until recently,
but over the past few years, a bunch of labs
have really pushed this forward.
There's a bunch of work out of Leslie Voshall's lab
at Rockefeller and Andreas Keller working with Leslie,
who've done a lot of work on this front.
Also worked from Joel Mainland's lab at Monell
and Fair Discovery Joel was a graduate student in our lab.
And recently in our lab we've had,
and I hope this doesn't come across as overly arrogant,
but we've had a sort of mini breakthrough on this front.

To call something a mini breakthrough as far from arrogant.
And this is a paper led by Arm Ravia
from our lab and Kobe Snitz also a major contributor there,
a paper published in Nature about a year and a half ago
in the height of a COVID pandemic.
So nobody really, I won't say nobody,
but it wasn't noticed in the way otherwise would have been.
It was published in Nature really on like a week
where the whole world was like going berserk over COVID.
And in this paper, we develop an algorithmic framework
where we can predict the perceptual similarity
of any two molecular mixtures with very, very high accuracy.
So if you give me two molecular mixtures,
I can predict how similar you will smell them to be, okay?
Now, not only could we predict that, but we could design it
so we can generate mixtures with known similarities.
And the result was highlighted
and you'll appreciate this coming from vision
is that using our algorithmic solution,
we generated olfactory metamers.
So we measured mixtures completely non-overlapping
in their molecular structure,
but they smell exactly the same, okay?
Now, if you would come to a classic perfumer
or most classic perfumers and tell them
that you can generate two mixtures
with zero molecules in common,
but smell exactly the same, they would tell you no.
And yet we did and anybody can recreate them.
This is simple actually.
And in the paper we do a few things,
like we generate a metamare for Chanel number five.
So you don't like perfume, so this one,
but we take, so we generate a Chanel number five
with no component from Chanel number five in it, okay?
And we actually have a publicly available website.
I'll give it to you for your links.
If you want that anybody can do this,
we built an engine that you can generate these metamers.
Now, once we did that,
in a way we've generated the infrastructure
for digitizing smell,
because again, what our algorithm predicts,

our framework predicts is similarity,
but in a way that's enough for you.
Why is that enough?
We have a map of 4,000 molecules.
For each one we know there are perceived smell.
Now you can make up any mixture you want for me.
I can project it into that map
and measure its pairwise distance
from all the points in the map.
If it falls on lemon,
then what you generated smells like lemon.
And if it falls on tomato,
then what you generated smells like tomato.
So we now solve that problem.
We can predict the odor of any molecular mixture.
We can say how it's going to smell.
What we can do is then find a set of components,
which we call odor primaries,
that can be used to mix any odor that you can perceive.
And that's what we're working on now.
And about a month ago,
so this is in collaboration with a lab
of Jonathan Williams and Max Planck in Munich.
Jonathan Williams is an atmospheric chemist,
but he's really good at using GCMS,
these tools that measure molecules.
So Jonathan Williams measured odorants in Germany,
transmitted the information to us over IP.
We fed that into our algorithmic framework
and recreated it from a device that mixes primaries.
And we tried to do four different odorants
in our proof of concept test.
One of them was rose and we failed at recreating rose.
We in fact recreated something that had a precip,
but most people perceived it as bubble gum.
The second one we tried to do was anise
and we failed at recreating anise.
And most people said it was cherry,
which is not very far, but it failed.
The third was gasoline.
And we were slightly but significantly better than chance
at recreating gasoline.
And the fourth was violets

and 15 of 16 people said violets.
So the first odor ever transmitted over IP is violets
and we did that last month.
Of course, this is not anything near a practical solution.
The device that Jonathan was using to measure
is a $1.5 million device bigger than this table.
That's right, I remember when VCRs
half the audience won't even know what that is.
VCRs were like this big, so we're all good.
I'm all good with the prediction
that things will come down in size and cost.
Yeah, I was just saying,
don't hold your breath for this to be on your table tomorrow.
And again, even, all we have in hand
is this very initial proof of concept.
You know, it's not even yet close to being a paper
we are submitting because there's still lots of work to be done.
But we're on the path.
We're on the path and, you know, Google will probably beat us to it.
They got a lot.
No, you seem pretty dogged in there.
Yeah, but they have so much more resources
that at this stage and they've already published
two papers from that effort that are good.
Yeah, you know, they definitely have a lot of dollars and a lot of people,
a lot of good neuroscience and other biology, engineering,
graduate students and postdocs go there.
But but the real question is, are they getting the best people?
Because as you and I both know in science, the oftentimes it's small groups
of the very best and most creative people that can out run and out gun large groups.
And here I don't have anything against Google.
Yeah, I know.
I use it all the time.
I'm not a betting man, but I would put my my money on Google on this race.
But I'll give I'll try and give them a run for their money.
There you go.
That was since I mostly just want to see the problem solved
regardless of who gets there first.
What I'll say is you better get going, Google, because no one was being
he's humble and he's dogged.
So better better get cracking there.
We just cost the weekends of and broke up the relationships of a bunch of scientists.
I remember when I was a graduate student at Berkeley, I remember hearing

there was a guy in in our common friend Irving Zooker's lab that worked
a hundred hours a week.
So I was like, oh, I'll work 102 hours a week, which was not a good choice.
In any case, it's it's it's abundantly clear that you're making progress here.
And I and I go to some of the earlier discussions we had.
And I think we're not just talking about transferring recipes and smells of food.
Gasoline from the people watching the the F1 race or something.
But I'm thinking dating apps.
I'm thinking you nowadays, everyone knows that when you travel and you want
to see your family, your grandkids or kids, you better to get on FaceTime
and see them resume than to just hear their voice.
We're all talking about being able to smell them.
I'll tell you more than that.
I'll tell you more than that.
I mean, we're talking now of trying to achieve the olfactory equivalent
of circa 1956, black and white TV, OK, basically, right?
I mean, you know, I'm not dreaming, let's say, of being able to transmit
to you the difference between a Cabernet or a Merlot, right?
But if I can generate something that's vaguely wine, that will be
an amazing success from my perspective, right?
But jump ahead in your imagination to to 4K order transmission.
Then medical diagnostics is what you want to be talking about.
Because in this is this is over extension.
But you can almost say that every disease will have an odor.
I mean, every disease is a specific metabolic process.
Metabolic process have metabolites, metabolites have a smell.
All faction, once it's digitized and and high resolution, which again,
in our hands, it's not going to be.
I mean, we're talking, you know, in my retirement, maybe I'll read
about this one day if I'll still have vision.
I mean, this is not close.
But when when all faction digitization is brought to the equivalent
of 4K vision and audition that you have now, then it will be in medical diagnosis.
You'll have excuse me for the the imagery, but you will have an electronic
nose in your bathroom, each one of us will have in the toilet.
And it will be doing diagnostics all the time.
And and that's that's where it's going to go.
But again, not anywhere in the very close future.
Well, it's it's certainly an exciting proposition.
And I'm delighted that you and other groups who are so strong are working on it.
I have really am.
No, my I want to say thank you for your time today.
First of all, this was a tremendously interesting conversation.

And we touched on so many things.
Hormone smells the architecture of the olfactory system.
I know that people listening to this are realizing, but I'm going to say it anyway.
What an incredible gift you've given us.
And as a as a expert in this field, giving us this tour of the work
that you and others who you credit so generously have done to elucidate
this incredible system that we call olfaction and chemo sensation.
Also, just for the incredibly pioneering work that you've done, you know, I.
I don't have many heroes in science.
I have heroes outside of science and a few in science.
But I'm going to I'm going to purposely embarrass myself a little bit by saying
that from the time I was at Berkeley and I then and saw that experiment being done
of people foraging falling scent trails.
And then when I was until I was a junior professor, I used that in my teaching slides
in a class that I taught that was sort of the early origins of this podcast in many way.
And over and over again, when your laboratory publishes papers,
I find like this is super interesting, super cool.
And I find myself telling everybody about it.
And that's really what I do for for a living is I learn and then I blab about it to to the world.
So thank you so much for the work that you've done and the spirit that you bring to it.
Whatever drives that spirit as the great late Ben Barris used to say,
keep going because we are all benefiting tremendously.
And and I also just want to say that, you know, for people listening to this,
that the spirit of science is one of, as you mentioned, there's complex politics
and all these things, but it's absolutely clear that you delight in the work you do.
And so I delight in it.
I'm grateful for it.
I'm grateful for your time today.
And so on behalf of me and the many, many people listening to this,
I just want to extend a huge debt of gratitude.
Thank you so much.
Oh, so I'm I'm I'm blushing.
I don't know if this doesn't come across on the on the radio podcast,
but thank you so much for very warm words.
I mean, you know, we, as you know, when you work in your lab,
you don't there's these moments where you suddenly discover that somebody
is like cares a bit about it.
And those are always very rewarding moments
because usually you function without that.
I mean, I guess that's one of the things you need to be a scientist
is to have the, you know, the drive to work without that
because it comes only rarely.
There's immense gratitude and appreciation for you and what you do from me.

And now I know from a large segment of the world as well.
So my only request is that you come back
and tell us about the next results sometime not too long now.
Yeah. Well, I'm going to catch you live now,
although you have the power to edit this, I guess that's not fair.
But first, you come visit us in Israel and tell us both about the science
and the public science work you're doing, and then I'll come again.
A good bargain. And again, I accept. Delighted.
Thank you so much.
Yeah, pleasure.
Thank you for joining me for today's discussion
about olfaction and chemo sensation with Dr. Noam Sobel.
If you'd like to learn more about the work in the Sobel laboratory
or read some of the papers described during today's episode,
as well as learn about the current and future projects in the Sobel laboratory,
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Once again, I'd like to thank you for joining me for today's discussion
about olfaction and chemo sensation with Dr. Noam Sobel.
And last but certainly not least, thank you for your interest in science.