Company Secret

World’s first smell sensing technology based on human olfaction

Comprehensive Digitalization Technology of All Flavor/Smell Notes Using Human Odorant Receptor-expressing Cell Array Sensor (hOR Sensor)

匂いを数値化する会社
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2020 11 30 (Non-NDA)

How do humans sense and distinguish smells?

How smells are perceived

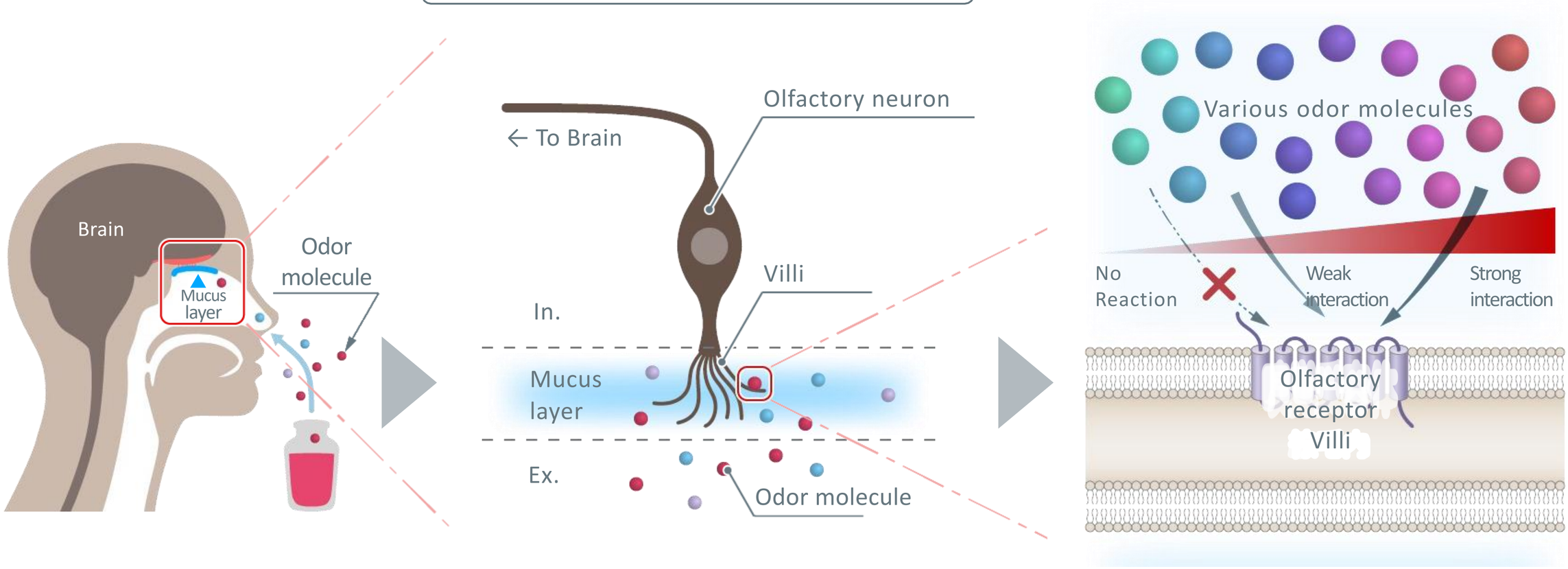
Odor molecules penetrate into the mucus layer of the olfactory epithelium at the back of the nostrils.

Olfactory neurons in the olfactory epithelium capture odor molecules with villi stretched across the mucus layer.

- Humans have about 400 different olfactory receptors.
- Each olfactory neuron has only one type of olfactory receptor.

Each olfactory receptor binds several types of odor molecules with different intensities.

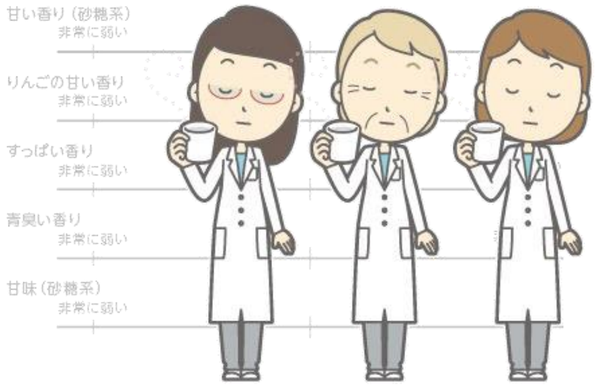
Interactions can be strong or weak (strength of association) and be long or short (length of time to react).



Difficulties in digitalizing the perception of smell

Pros and cons of conventional odor analysis technologies

【Sensory testing by smell】



Pros

- ○ Advanced judgment based on senses

Cons

- × Inability to communicate accurately and reliably
- × Difficult to train personnel due to high level of expertise
- × High cost
- × Low reproducibility
- × Difficult to mechanize

Implemented in food production, brewing, cosmetics and fragrances manufacturing, etc.

【Chemical and physical gas sensors】

Pros

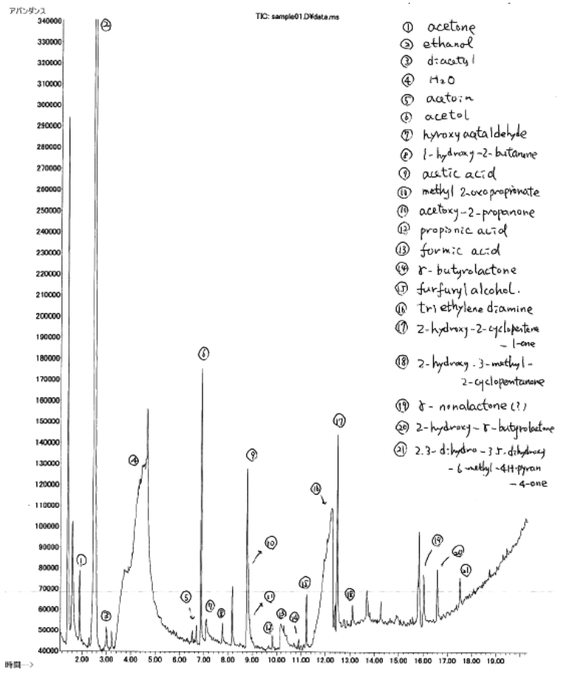
- ○ Easy to integrate devices
- ○ High stability
- ○ Low cost

Cons

- × Limited types of odor components
- × Need a sensor for each odor component

Gas detectors

【Gas chromatography】



Pros

- ○ Comprehensive detection of a large number of molecules at once

Cons

- × Detects unwanted molecules that have no smell

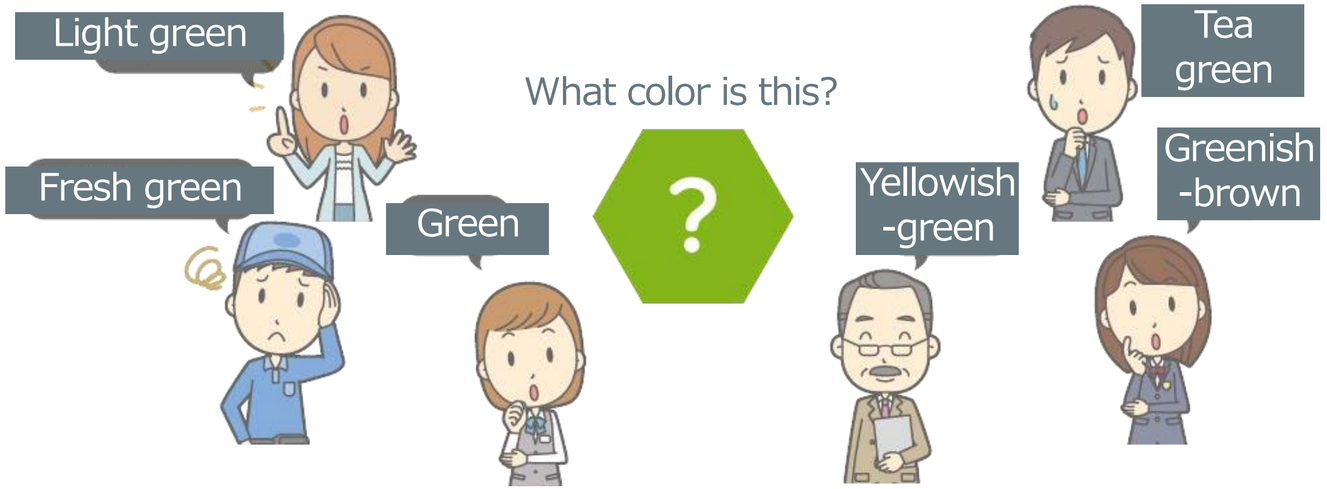
Analysis of components in gas

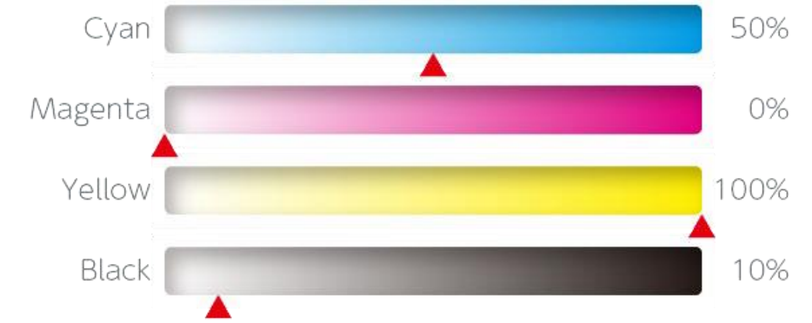
Difficulties in digitalizing the perception of smell

What is digitalization of senses ?

Digitalization of colors

Colors can be communicated by reconstructing standardized colors with numerical values.



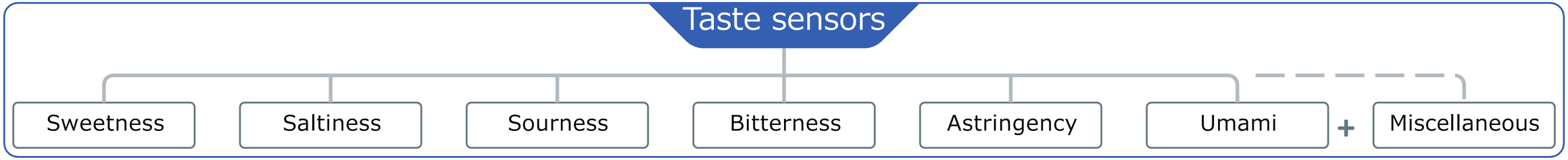


C: 50 / M: 0 / Y: 100 / K: 10

Quantification (digitalization)

Digitalization of taste

Taste can be communicated by seven different taste sensors.



Difficulties in digitalizing the perception of smell

Why was it impossible to digitalize the smell?

The human sense of smell is extremely complex

Unlike the case of taste, odor has no standard for calibration.
Only olfactory receptors can be used as a reference.

Human olfactory receptors (about 400) have a complex function.

- A single olfactory receptor responds to a number of odor molecules.
- The strength of the response has a strength (strength of the interaction).
- Perceive different smells as different over time.

“Pattern recognition” by a group of olfactory receptors

- About 400 olfactory receptors can distinguish tens of thousands of odors.

Sensory testing by smell

Chemical and physical gas sensors

Gas chromatography

Digitalization has so far been impossible with existing odor analysis techniques

New Odor Digitalizing Technology Invented by Komi-Hakko Corp.

Difficulties in digitalizing the perception of smell

The world's first!! Odor digitalization system by Komi-Hakko Corp. [International patent pending]

Human olfactory receptor-expressing cell array
(“artificial nose” comprehensively loaded with human olfactory receptors)

Measurement of changes in intracellular calcium concentration in response to receptors over time

- Quantify the way humans perceive smells.
- Measurement of changes in human olfactory receptors over time allows us to measure even the lingering effects of odors.
- All human olfactory receptors of about 400 subtypes can be measured at once under the same conditions.

Digitalizing smells allows for objective and accurate communication that does not rely on the senses

Unlike sensory testing which relies on the sense of smell, and gas chromatography-mass spectrometry which detects components that are not detected by the sense of smell,

Digitalizing odors perceived by humans will strongly contribute to the establishment of various new business in a wide range of industries.

Explanation of our technology

Basic technology [Reproduction of the mechanism by which humans sense

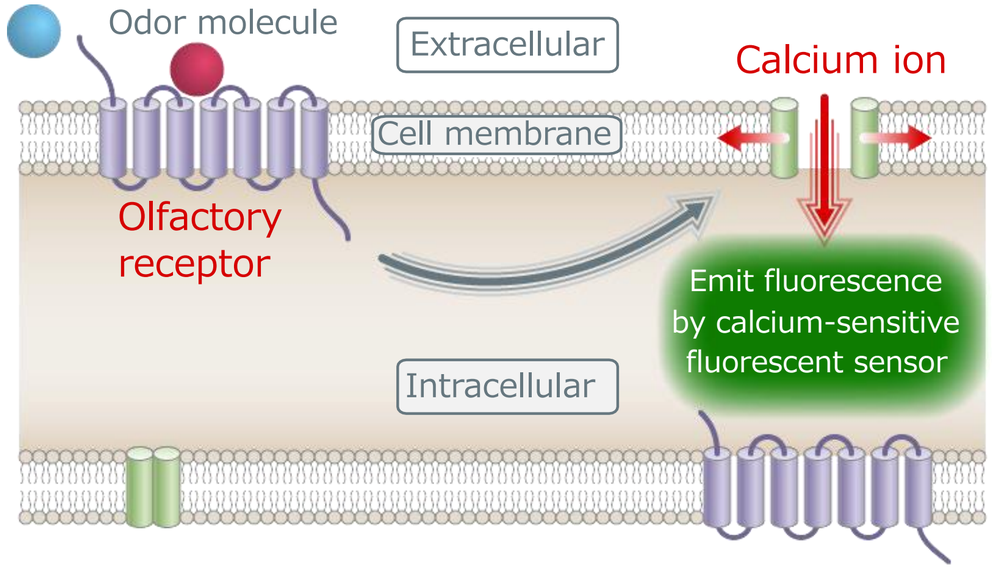
Two most important technologies (International patent pending)

We are the sole applicant for these patents, and no other party is involved.

Detection of intracellular influx of calcium ions in response to odor molecules

Odor molecule ⇒ Olfactory receptor ⇒ Influx of calcium ion

▶ Visualization with calcium ion-sensitive fluorescent sensor

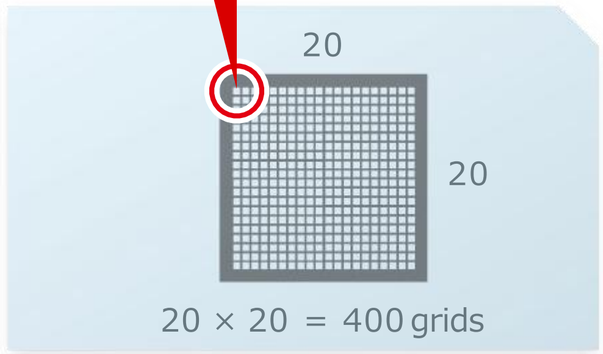


Human olfactory receptor-expressing cell array

"Artificial nose" comprehensively loaded with human olfactory receptors

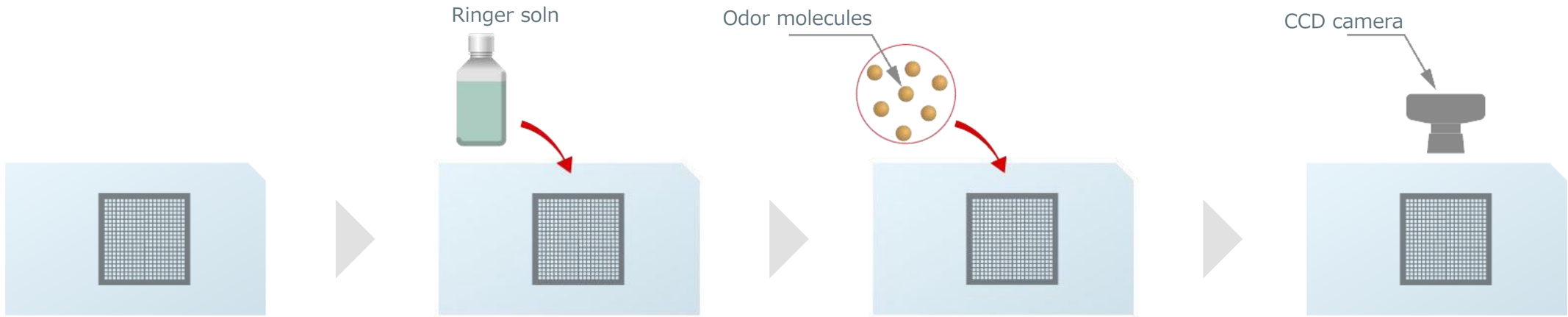
Using cells that fully mimic the human olfactory receptor system: Real-time odor analysis is possible.

Each human olfactory receptor-expressing cell was placed on each grid of the slide glass



Explanation of our technology

Flow chart of digitalization of human olfactory response using human olfactory receptor-expressing cell array



01
Human olfactory receptor-expressing cell array

Ringer soln

02
Immerse cell array in ringer soln

Odor molecules

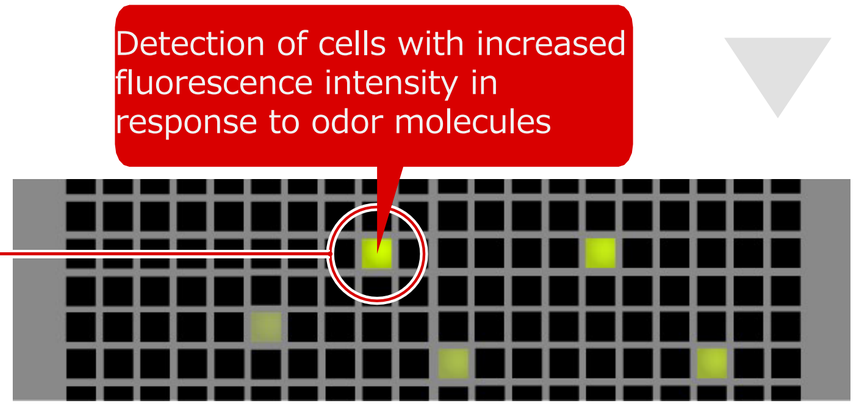
03
Contact with odor molecules

CCD camera

04
Camera records changes in fluorescence over time

Each human olfactory receptor-expressing cell was placed on each grid of the slide glass

Measurement of each cell in a grid of several hundred cells, which increases the number of cells examined and improves the accuracy dramatically

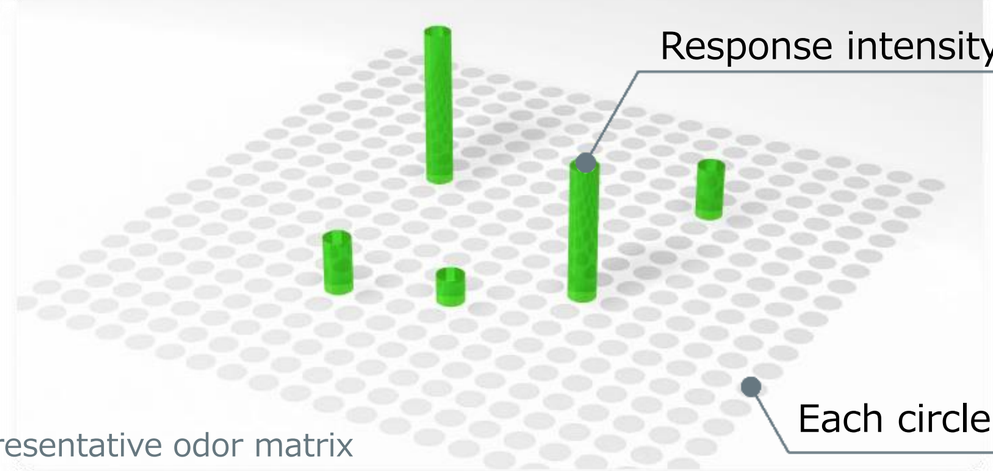


05
Only olfactory receptors that respond to odor molecules show an increase in fluorescence intensity according to the intensity of the response.

Explanation of our technology

How to express the digitalization of odor 【Odor Matrix】

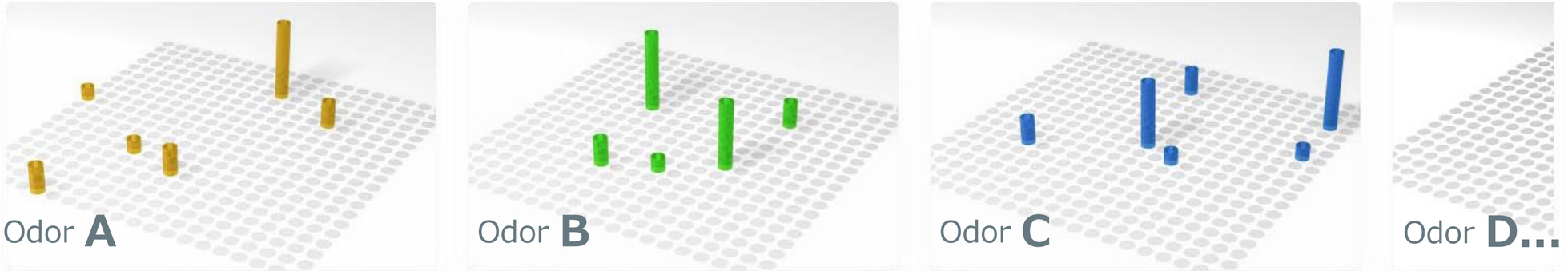
Visualization of the response of each olfactory receptor to odor by changes in fluorescence intensity



Representative odor matrix

The odor matrix represents human olfactory odor perception at a given moment, and changes over time can be represented by successive groups of odor matrices.

Different reactions to different odors (various odor matrices)



This odor matrix can be used to digitalizing all odors (both simple component and complex components)

Strengths of our technology compared to other technologies

Features of our method, the functions achieved firstly in the world

1) Measurement using human olfactory receptor-expressing cells

- Based on real human olfaction

2) Simultaneous and homogeneous measurement of all human olfactory receptors using its cell arrays

- Low inter-measurement variability

3) Realtime measurement

- Reduction in the measurement number compared to endpoint measurements

4) Single cell-based measurement

- Significant increase in the repeat number of measurements

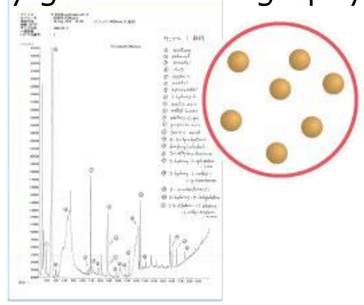
Strengths of our technology compared to other technologies

Technology to connect subjective data and objective data

Conventional technology

Objective data

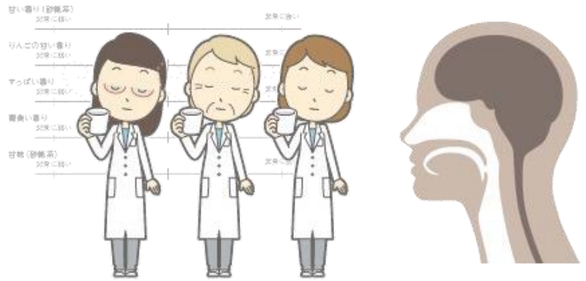
Composition of odorants by gas chromatography



Difficult to connect both data

Subjective data

Sensory testing by smell



Physiological effects

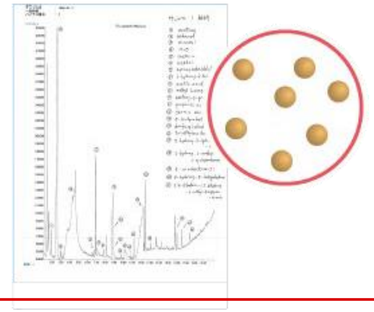
Relaxing effect
Sleep inducing effect
Appetite stimulating effect
Sedative effect
Concentration effect
etc.

Our technology

Easy to connect both data

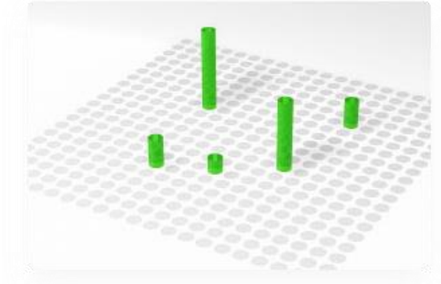
Objective data

Composition of odorants by gas chromatography



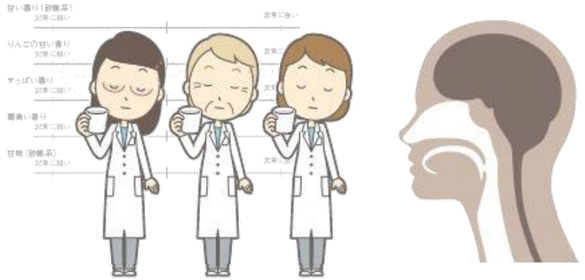
Odor matrix

Olfactory receptor rection



Subjective data

Sensory testing by smell



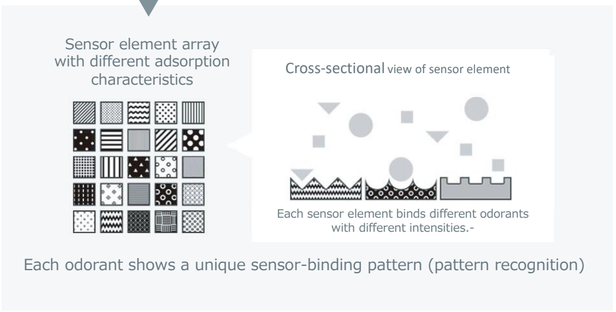
Physiological effects

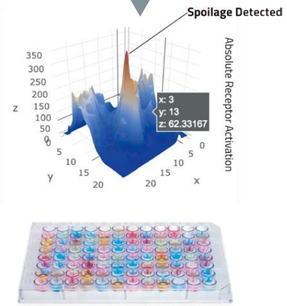
Relaxing effect
Sleep inducing effect
Appetite stimulating effect
Sedative effect
Concentration effect
etc.

Strengths of our technology compared to other technologies

Comparison with other companies' technologies

Origin and name of sensor	Shimadzu FF-2020	Aroma bit Aroma Coder-35Q	Duke University Luciferase assay	Aromyx EssenseChip	Our technology Olfactory receptor-expressing cell array
Detectable odorants	× 10 Metal sensors	△ 35 Polymer sensors	◎ 400 Human olfactory receptors	◎ 400 Human olfactory receptors	◎ 400 Human olfactory receptors
Consistency with temporal changes in sensory properties	×	×	× Human cells ・Endpoint measurement	× Yeast cells ・Endpoint measurement	◎ Mammalian cells (including human) ・Realtime measurement





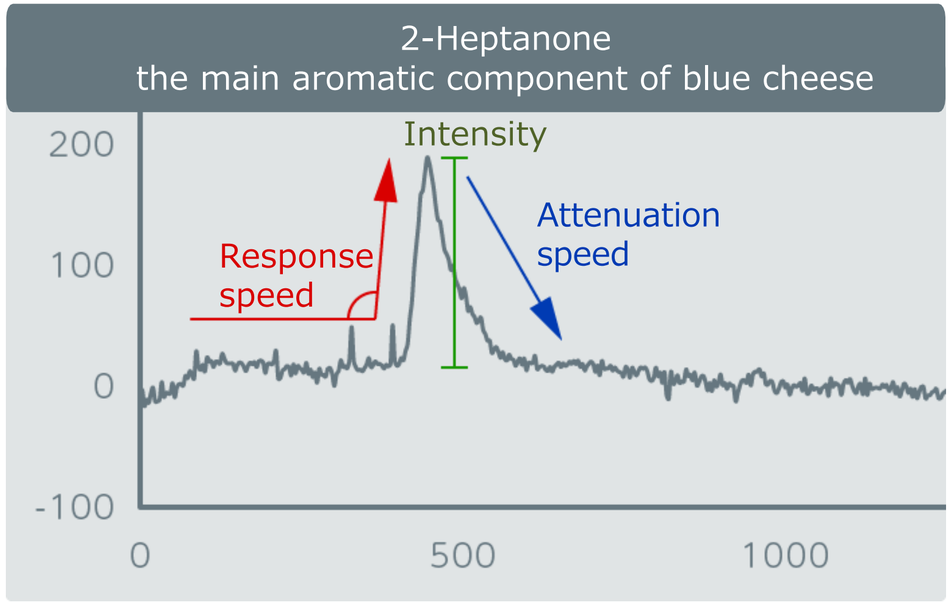
Only our technology can digitalize how human olfaction perceives odor over time in real time.

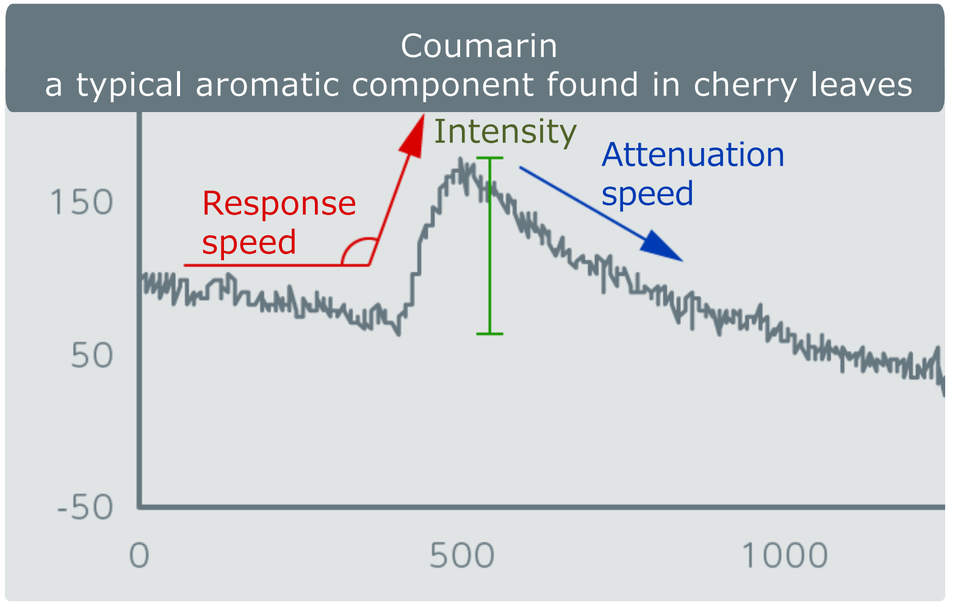
Strengths of our technology compared to other technologies

Why observation of changes over time is necessary for odor analysis

Even if one olfactory receptor shows similar response, different changes over time will result in different odor perceptions

・Both odorants elicit a response in the human olfactory receptor OR2W1, but the characteristics of the change over time are different.
・The receptor response over time (Realtime measurement) is the key to deciphering the mode of reception by the human olfactory system.





Odor molecule	Res. speed	Intensity	Attn. speed
2-Heptanone	+ +	+ +	+ + +
Coumarin	+	+	+

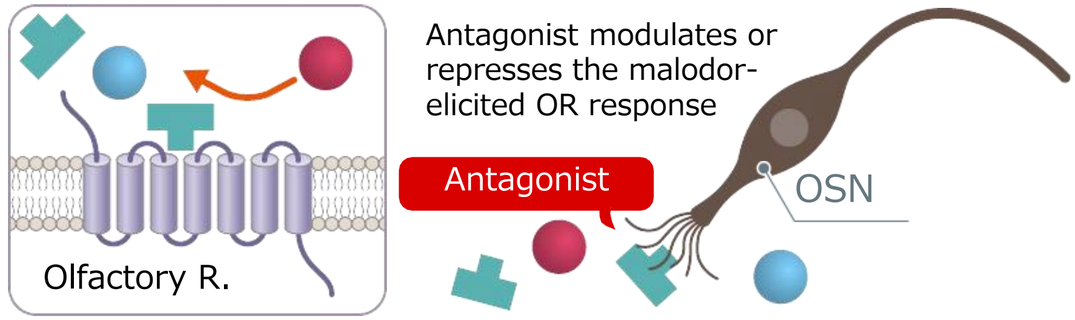
Current status of our business

Development of Novel Deodorants Targeting Malodor Responsive Olfactory Receptors

Development business of a completely new deodorant (antagonist deodorant)

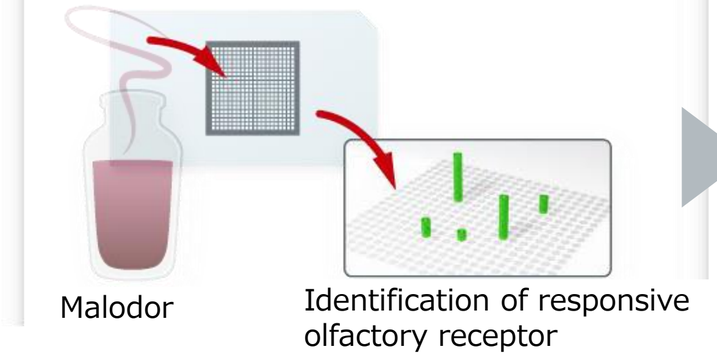
Recognition by binding of malodor molecules to receptors

Pre-emptively blocks the receptor site where malodor molecules bind

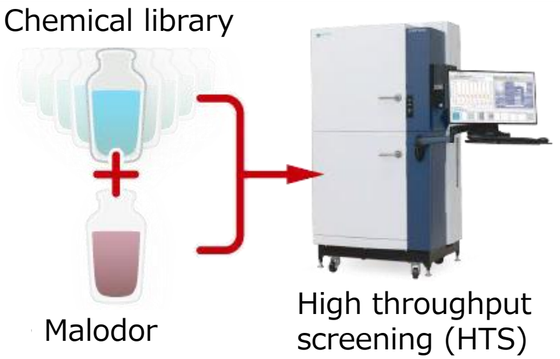


Development scheme for new deodorants

01. Search for Responsive Olfactory Receptors



02. Screening for molecules that block target receptors

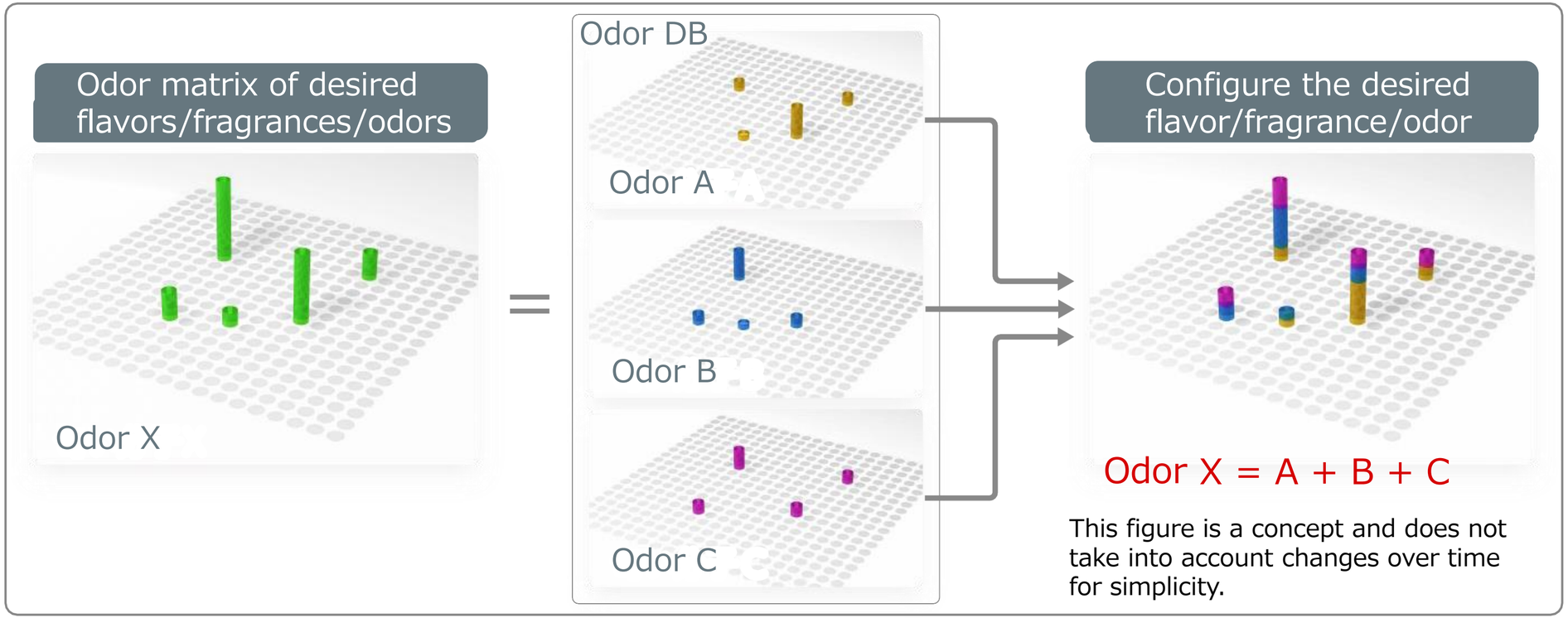


03. Commercialization of the ultimate deodorant

Reconstruction of flavors/fragrances/odors using odor molecule databases and AI

It is possible to build an odor database and configure the desired flavor/fragrance/odor

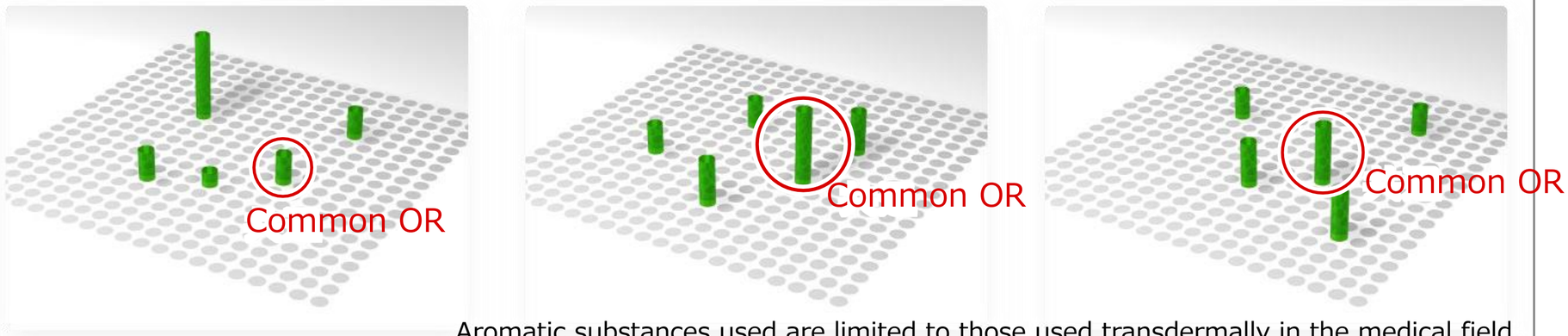
The desired flavors/fragrances/odors can be reconstructed by an AI program based on the respective odor matrix of each odor component (including changes over time).



Link between physiological effects and olfactory receptor's responses (odor matrix)

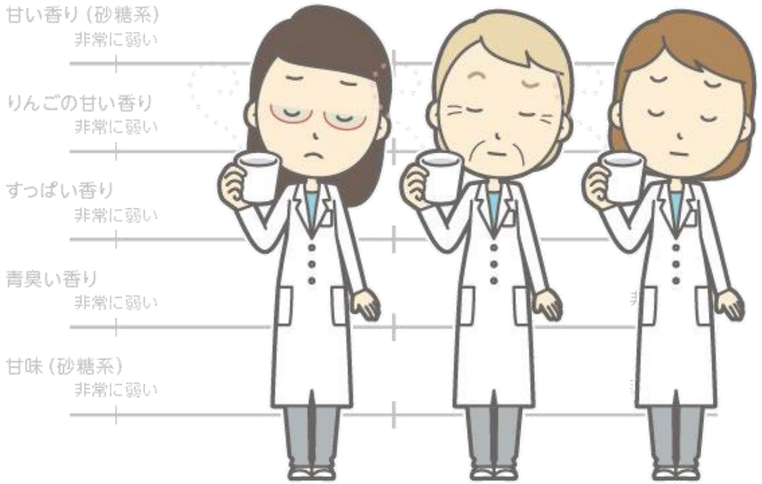
Olfactory receptor information-based medical aromatherapy

【Relaxing aroma substance A】 【Relaxing aroma substance B】 【Relaxing aroma substance C】



Aromatic substances used are limited to those used transdermally in the medical field.

AI



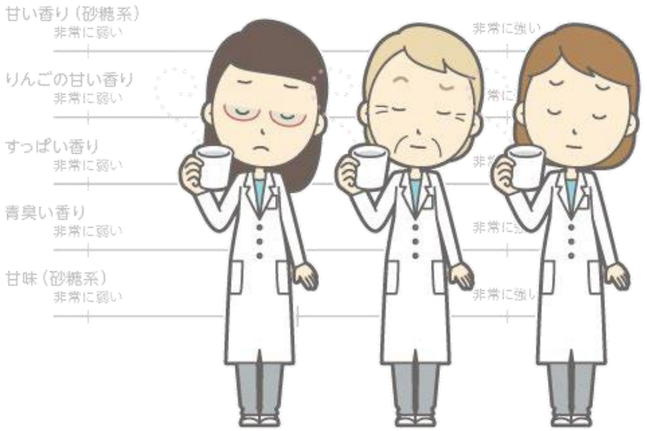
・Creating evidence-based relaxing aroma that works more efficiently
・Replacement of expensive natural materials with less expensive synthetic materials

This method will reveal the relationship between human olfactory receptor activation patterns and autonomic and emotional regulation, which will encourage the establishment of new businesses.

Application to quality control of products with fragrance

Quality control using an odor matrix

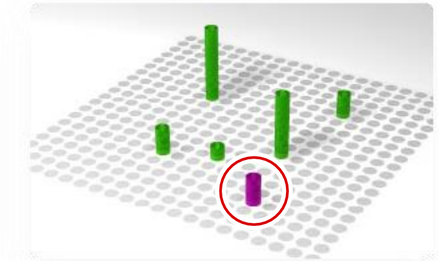
Sensory testing can lead to blurred data



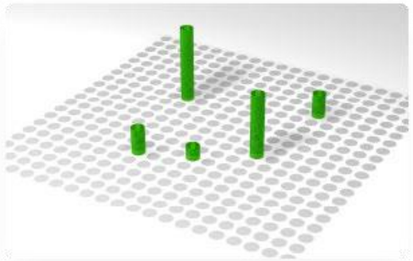
- Cannot make quantitative comparisons with normal/reference data
- Cannot compare with historical data accurately
- Affected by examiner's physical condition and age-related decline
- Inability to perform accurate handover due to personnel replacement

Can be compared with normal/reference data

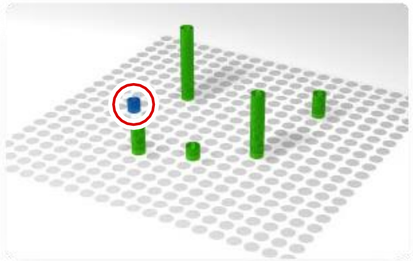
Check if the quality of the product is within the standard range



Failure
Unnecessary reaction

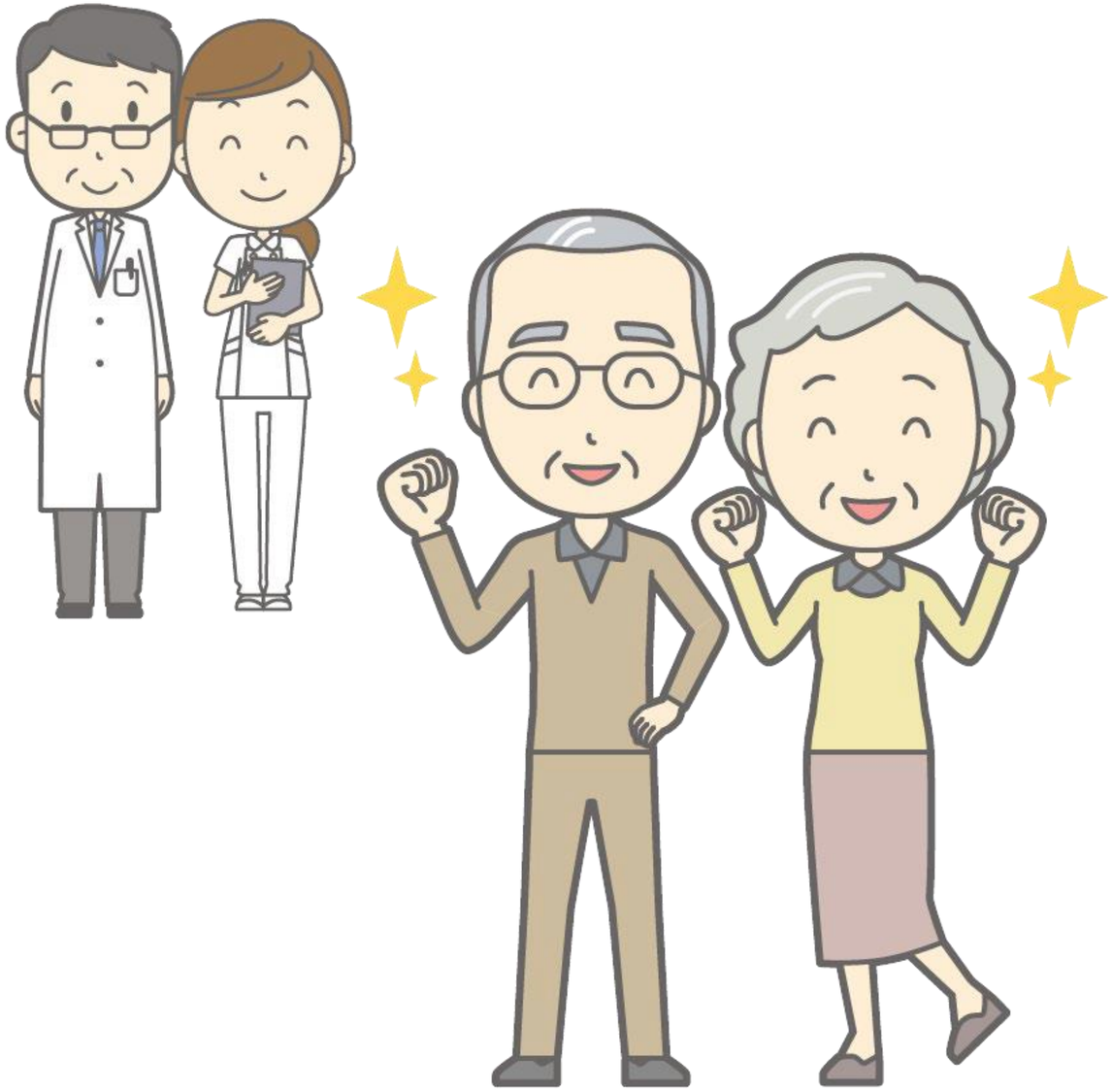


Pass
【within standards】



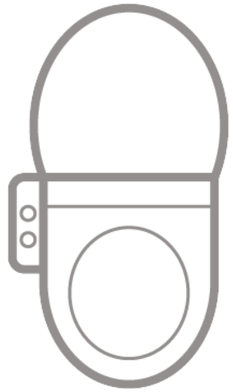
Failure
Insufficient reaction

Daily health check: Check diseases before onset by sick smells



It is known that in many diseases (especially cancer), patients emit a peculiar odor (sick smell). Cell array sensors are used to identify common odor components from feces, urine, sebum, and so on. By AI learning of cell array sensor responses and chemical sensor responses, chemical sensor for specific sick smell can be made for the home diagnostic devices.

Health Check Toilet



Health Check Toothbrush

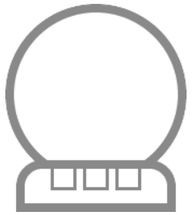
Dementia and Cancer Checker

Future development, business plan chart

Value addition to consumer electronics

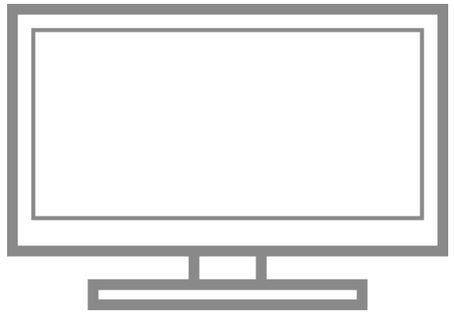
Aroma appliances and deodorizing appliances

Air conditioning to control emotions



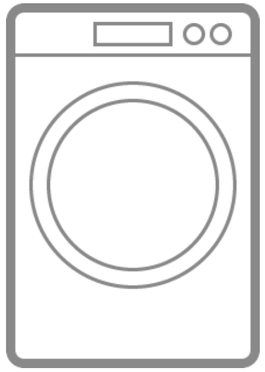
Aroma bed light to control sleeping and waking

Real-time incense dispensing display for AR & VR



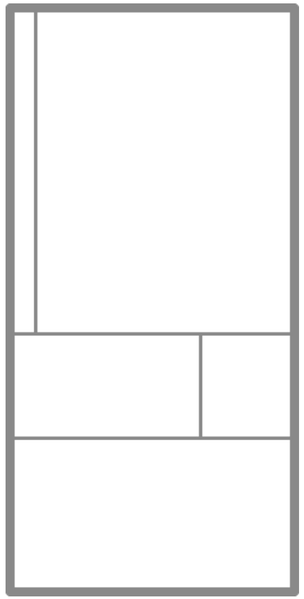
Odor projector

Home appliances with odor sensors (chemical)



Deodorizing washer and dryer

Cooker that tells you when it's time to eat

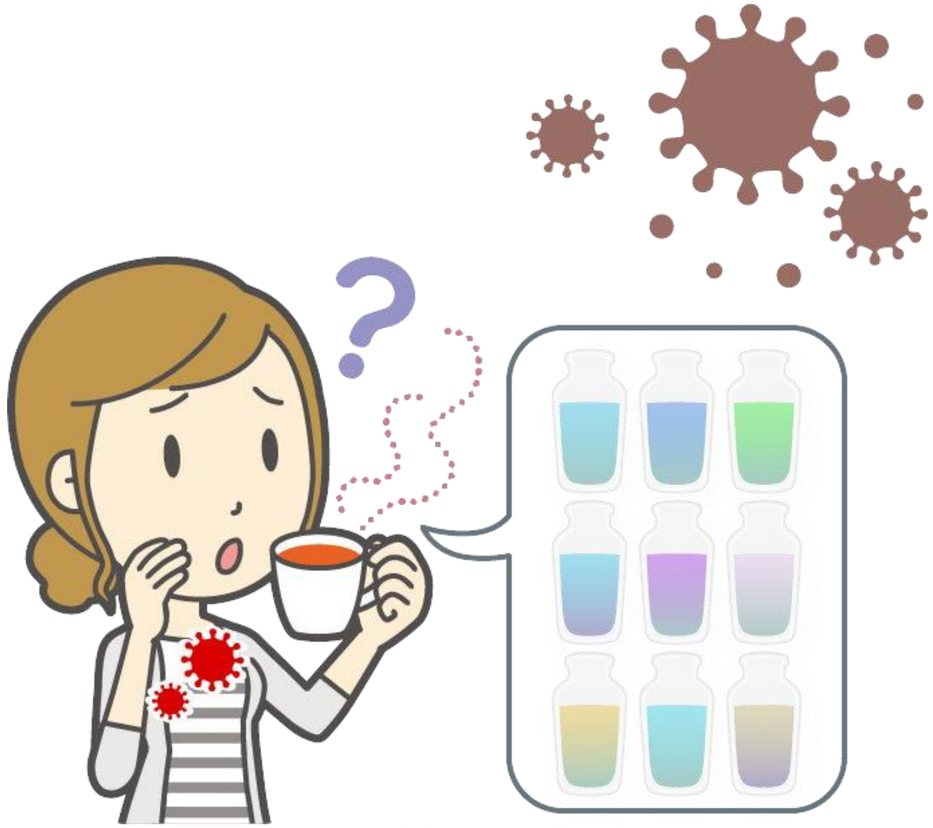


Refrigerator to find out when food is ready to eat or spoilage

Future development, business plan chart

Prevent new coronavirus pandemics and diseases transmission by mosquitoes, etc.

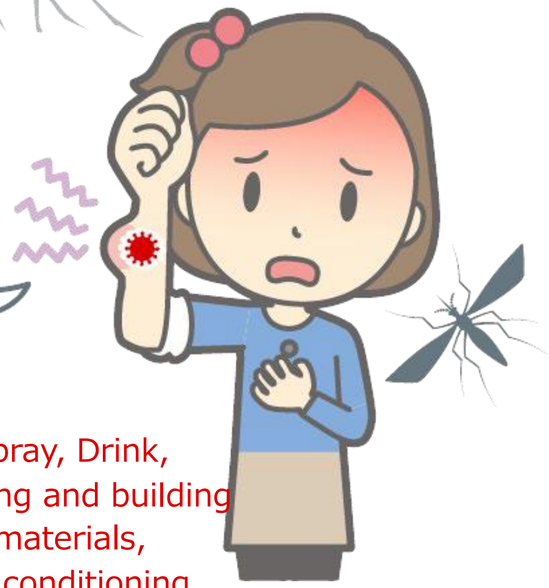
Protecting people from infectious diseases with our technologies such as ultra-early infection diagnosis kits based on human olfaction, and mosquito repellents



Diagnostic kit for super early infection of new corona viruses

Dengue Fever
Malaria
Chikungunya fever

Mosquito repellents

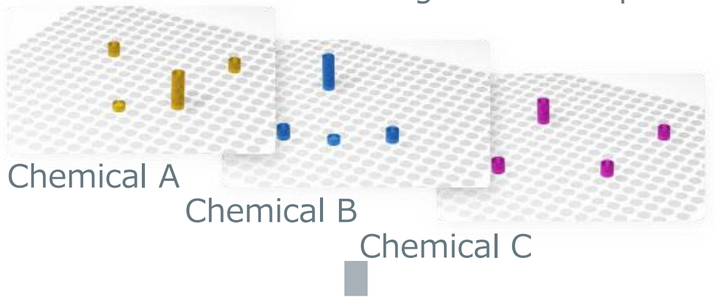


Spray, Drink,
Housing and building materials,
Air conditioning
(Public, commercial, household)

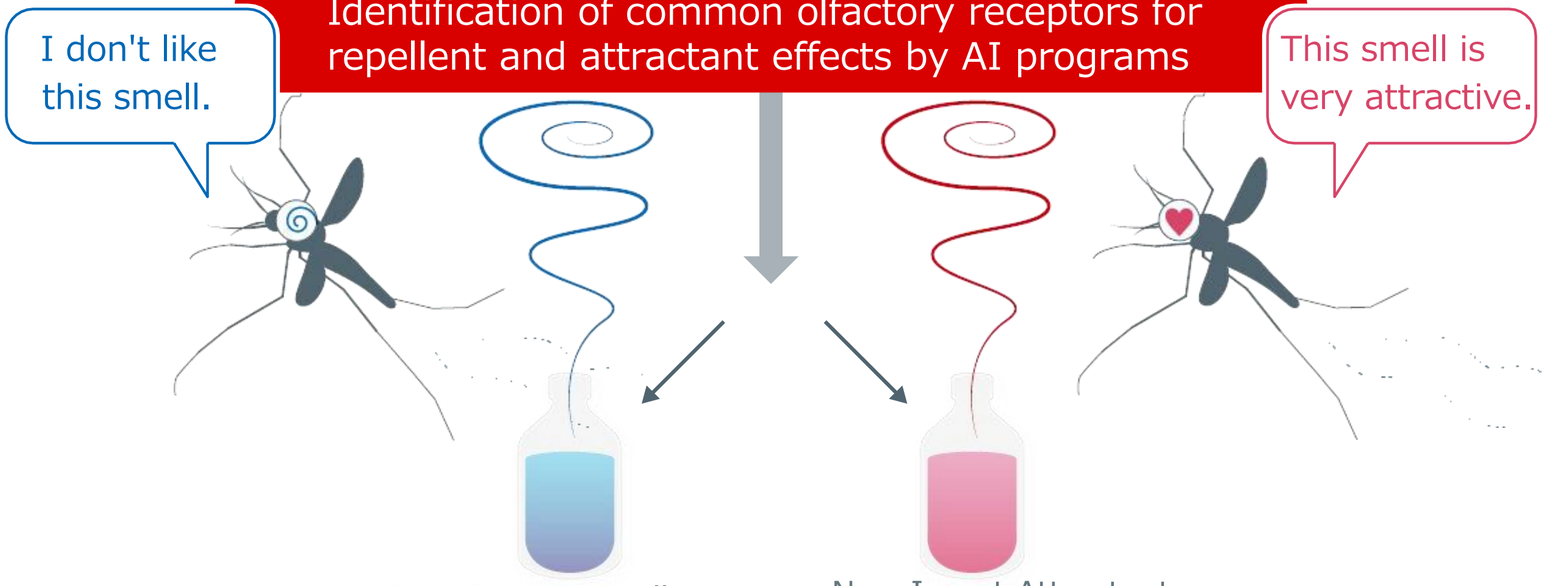
Development of insect repellents and attractants

Mosquito olfactory receptor-expressing cell array sensor: Search for effective insect repellents and attractants rooted in mosquito olfaction

Mosquito odor matrix database of existing and new repellents and attractants



Identification of common olfactory receptors for repellent and attractant effects by AI programs



New Insect Repellents Discovered by AI

New Insect Attractants Discovered by AI

In-house development: 8 pipelines

01. Malodor response receptor database

    Joint research and development with exclusive contractors: Identification of specific olfactory receptors of malodors (about 100 compounds), high throughput screening of modulator and deodorant, and commercialization

02. Flavor/fragrance response receptor database

    Identification of specific olfactory receptors of existing synthetic flavors/fragrances (about 8000 compounds), *de novo* design of new flavor/fragrance by AI programs

03. Mass production of olfactory receptor cell array sensor, development of its control software

04. Digital storage of odors of existing products for future patenting

05. Transform olfactory receptor-expressing cell array sensor to chemical sensor for integration into consumer electronics and handheld sensors

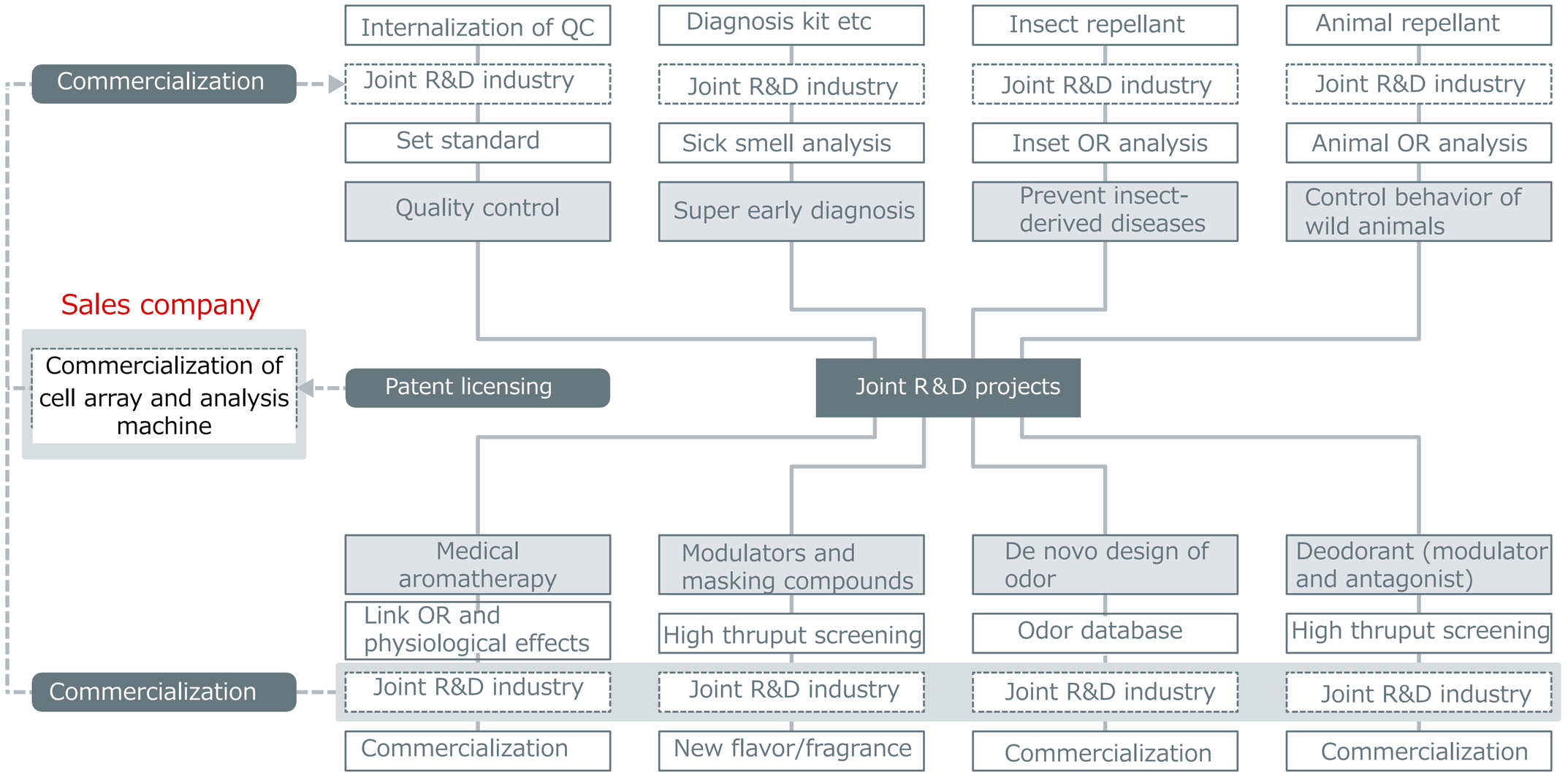
06. Development of agonists/antagonists/modulators that act on each of the approximately 400 human olfactory receptors for AR/VR display etc.

07. Establishment of an association for authorizing our sensor as domestic and international standard odor qualification method

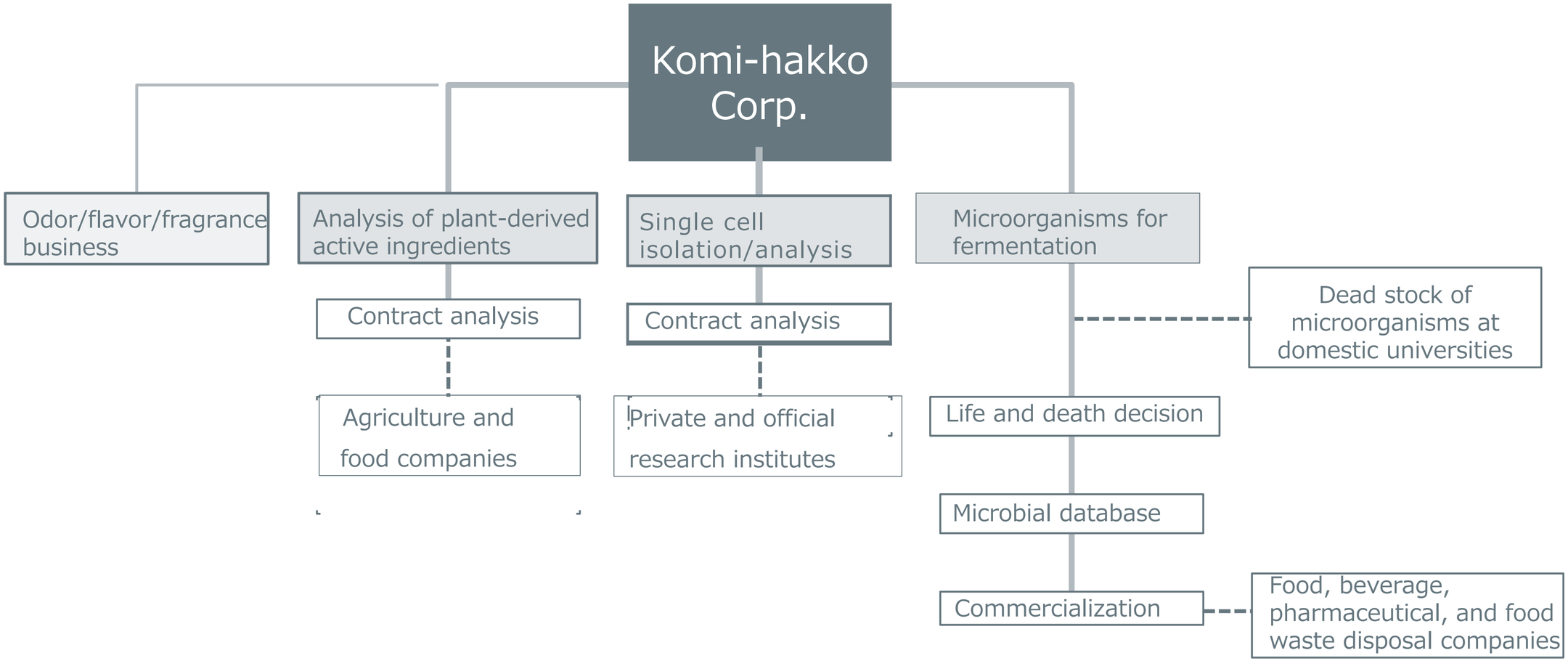
08. Patent licensing business

Future development, business plan chart

Launched 8 joint R&D projects

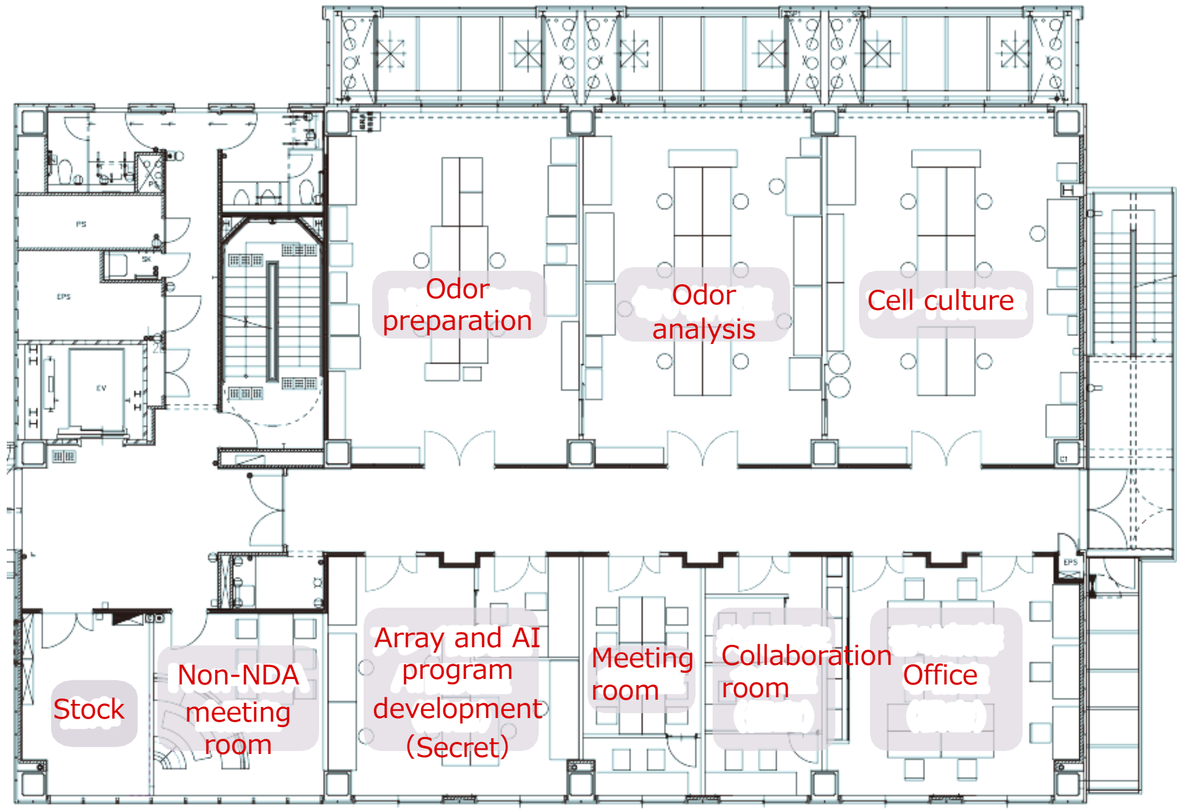


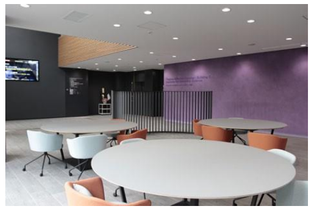
Our business other than smell-related business



Information on our R&D Center

R&D Center of Komi-hakko Corp. at Osaka university (Technoalliance C bldg)






R&D center (400 ㎡) can accept more than 10 researchers of joint research companies

R&D center: Techno-alliance building 3rd floor, Osaka university
2-8 Yamadaoka, Suita, Osaka Japan

Head office: TAT Edobori building 10th floor
1-24-12 Edobori, Nishi, Osaka, Osaka Japan