Electronic Tongues–A Review

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***Abstract*— Sensing technologies for objective evaluation such as the discrimination and quantification of tastes have been developed since around 1990, before the discovery of taste receptors. Electronic tongues aim to discriminate and analyze foods and beverages and are well known as sensing technologies that greatly contribute to quality management. A taste sensor, i.e., an electronic tongue with global selectivity, is developed to realize a sensor that responds to taste chemical substances and can be used to quantify the type of taste focusing on the fact that humans discriminate the taste of foods and beverages on the tongue with the five basic tastes. In this paper, we focus on the taste sensor and describe its sensing principle, its difference from general electronic tongues that do not aim to quantify tastes, examples of its use, and the recent trend of research of electronic tongues.**

***Index Terms*— Electronic tongue, taste sensor, global selectivity, lipid/polymer membrane.**

I. Introduction

THE SENSE of tastes consists of five basic tastes, i.e., sourness, saltiness, umami, bitterness, and sweetness. When tasting a food or beverage, humans perceive each type of taste on sensory organs called taste buds on the tongue. Taste buds are composed of approximately 50-100 cells. Research on the mechanism behind the reception of taste substances [1], [2] has a short history; Taste-2 receptors (T2Rs), bitterness receptors present in taste cells, were discovered in 2000 [3]–[5] followed by the discovery of sweetness receptors (T1R2+T1R3) [6] and umami receptors (T1R1+T1R3) [7]. Each taste receptor receives multiple chemical substances constituting a single taste. Namely, taste receptors exhibit semi-selectivity rather than rigid and high selectivity. High selectivity means one-to-one correspondence to a particular chemical substance. Although the mechanisms behind the reception of sourness and saltiness have not yet been completely clarified, poly-cystic kidney disease 2-like 1 protein (PKD2L) [8], [9] and epithelial sodium channel (ENaC) [10] have been identified as the candidate receptors, respectively. Taste information perceived by taste buds is transmitted to taste nerves as a result of the release of neurotransmitters and finally reaches the gustatory area in the brain as a central tissue. It has been clarified that sweetness, umami, and bitterness receptors are expressed at not only the taste buds in the tongue but also digestive organs, kidneys, and even the brain [11], and the clarification of their physiological significance is expected in the future.

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While the above-mentioned research on the molecular and cellular biology of taste reception has been carried out, sensing technologies for objective evaluation such as the discrimination and quantification of tastes have been developed since around 1990, prior to the discovery of taste receptors. As a background for this, sensory tests, in which experienced evaluators called sensory panelists actually taste samples to evaluate them, are the main method of evaluating taste in the food industry; however, they have some problems such as low objectivity and reproducibility as well as the great stress imposed on the panelists. To resolve this problem, a sensing technology for objectively discriminating and quantifying the taste of foods, called the electronic tongue, has been developed. This was named after the similarity to the taste sense of humans. Although the concept of chemical sensors is generally to detect a target chemical substance specifically at a high sensitivity, the taste receptors of humans do not necessarily recognize individual chemical substances. As mentioned above, each of the receptors for the five basic tastes simultaneously receives multiple chemical substances, showing a semi-selective property. Therefore, it is practically impossible to measure the taste of foods containing several hundreds of types of taste substance by chemical analysis methods, such as liquid and gas chromatography, although they can be used to measure the concentration of chemical substances. Moreover, there are interactions between different tastes and between taste substances. For example, the bitterness of coffee is suppressed by adding sugar and a synergetic effect for umami can be obtained by mixing glutamine acid, an amino acid, and nucleotide-derived inosinic acid.

Toko *et al.* applied for a patent of their taste sensor in 1989 and developed a taste sensor equipped with multichannel electrodes using a lipid/polymer membrane for the transducer [12]. This taste sensor is considered to be an electronic tongue with global selectivity [13], [14]. Here, global selectivity is a term originally proposed by Toko *et al.* and is defined as the decomposition of the characteristics of a chemical substance into those of each type of taste and their quantification, rather than the discrimination of individual chemical substances, by mimicking the human tongue, on which the taste of foods is decomposed into each type of taste by each taste receptor [15]–[19]. The taste sensor is commercialized taste sensing systems SA 402B and TS-5000Z, which are the world's first commercialized electronic tongue system and are currently well known to be able to discriminate and quantify tastes [13], [14], [20]–[22]. Meanwhile, the electronic tongue proposed in 1995 is defined as a sensor used to analyze solutions using the arrays of nonspecific chemical sensors and pattern recognition [23]–[26].

A commercialized electronic tongue and taste sensor are the Astree II e-tongue Sensor (Alpha MOS, France) and the SA 402B and TS-5000Z taste sensing systems (Intelligent Sensor Technology Inc., Japan), respectively. The Astree II e-tongue Sensor is used to discriminate solution samples, whereas the both of SA 402B and TS-5000Z taste sensing systems are mainly used to quantify the intensity of each type of taste identified by the human tongue using a taste "scale" [27]–[29]. Currently, these sensing systems are used to evaluate the bitterness of pharmaceuticals as well as for the quality control of foods and beverages.

Thus far, many review papers on electronic tongues have been published [14]–[23], [25], [26], [29]. In this paper, we focus on the taste sensor, i.e., an electronic tongue with global selectivity, and describe its sensing principle, difference from general electronic tongues that do not aim to quantify tastes, examples of its use, and the recent trend of its research.

II. Electronic Tongues

Electronic tongues aim to discriminate and analyze foods and beverages and are well known as sensing technologies that greatly contribute to quality management. Winquist and Lundström reported a voltammetric electronic tongue in 1997 [30] and then developed a hybrid electronic tongue by combining the technologies for measuring potentiometry, voltammetry, and conductivity [26], [31]–[33]. Six different types of metallic electrode were used for the measurement electrodes in voltammetric measurements to obtain different potential responses, and principal component analysis (PCA) was used to analyze the obtained data and discriminate foods [26], [34].

Legin and coworkers applied solid-state crystalline ion-selective electrodes based on chalcogenide glass to an electronic tongue [35], [36], and presented examples of applying their system to the analysis and quality management of foods and beverages such as wine [37]–[39] and mineral water by PCA and analysis using neural network techniques [23].

Aissy Inc., Japan, a venture from Keio University, provides accurate analysis using its original taste sensors and services useful for the development of new products and marketing in the food industry [40].

The features of electronic tongues based on sensor arrays are (1) low selectivity and high cross-selectivity instead of high selectivity and (2) a capability of statistically analyzing the outputs from multiple sensors. Sensing technologies based on these features, i.e., low selectivity, high cross-selectivity, and statistical analysis, have started to be studied in relation to electronic noses [41]–[48] and currently with electronic tongues, generating new measurement technologies.

III. Taste Sensor

The fundamental concepts of the taste sensor and electronic tongues are totally different except for the electrical detection of sample information [14]–[23], [29], [49]. Electronic tongues aim to discriminate and analyze foods and beverages using sensor arrays such as ion-selective electrodes with different specificity property and statistical analysis such as PCA and neural network techniques. On the other hand, the taste sensor using a lipid polymer membrane was developed to realize a sensor that responds to taste chemical substances and can be used to quantify the type of taste focusing on the fact that humans discriminate the taste of foods on the tongue on the basis of the five basic tastes. It is needless to say that samples can be discriminated if the five basic tastes can be discriminated and quantified. Sensors for astringency, which is perceived from a physical stimulus that affects foods, rather than taste substances [50], have also been developed. Fig. 1 shows the commercially available TS-5000Z taste sensing system. This system has the following four concepts: (1) The taste sensing system must respond consistently to the same taste like the human tongue (global selectivity). (2) The taste sensor threshold must be the same as the human taste threshold. (3) There must be a clearly defined unit of information from the taste sensing system. (4) The taste sensing system must detect interactions between taste substances.

Fig. 1. TS-5000Z taste sensing system (Intelligent Sensor Technology, Inc.).

A lipid/polymer membrane comprising a lipid, polyvinyl chloride, and a plasticizer is used for the stage of receiving taste substances, the key technology of the taste sensor. The thickness of the membrane is about 200 μm, and the membrane can be used about 3,000 times. The development of taste sensor with the lipid/polymer membrane was started before the mechanism behind the reception of tastes by humans was elucidated. Initially, researchers attempted to realize the reception of taste substances by mimicking biological cell membranes composed of lipids [12], [17].

The taste sensor has sensor electrodes (working electrodes) to which a lipid/polymer membrane is attached and a reference electrode, and measures changes in the membrane potential generated when these electrodes are immersed in a sample solution. The measurement procedure is as follows (Fig. 2). First, the membrane potential for a reference solution (30 mM KCl, 0.3 mM tartaric acid), V_r, is measured. Next, the membrane potential for a sample solution, V_s, is measured. The difference between V_s and V_r, i.e., $V_s - V_r$, is used as a relative value. Then, the membrane potential for the reference solution is measured again (V_r'). The difference between V_r' and V_r, i.e., $V_r' - V_r$, is defined

TABLE I
CHEMICAL COMPONENTS OF TASTE SENSORS

Taste sensor	Lipid	Plasticizer
Saltiness	Tetradodecylammonium bromide *n*-Tetradecyl alcohol	Dioctyl phenylphosphonate
Sourness	Phosphoric acid di(2-ethylhexyl) ester, Oleic acid, Trioctylmethylammonium chloride	Dioctyl phenylphosphonate
Umami	Phosphoric acid di(2-ethylhexyl) ester, Trioctylmethylammonium chloride	Dioctyl phenylphosphonate
Acidic bitterness	Phosphoric acid di-*n*-decyl ester	Bis(1-butylpentyl) adipate Tributyl *O*-acetylcitrate
Basic bitterness	Tetradodecylammonium bromide	Dioctyl phenylphosphonate
Astringency	Tetradodecylammonium bromide	2-Nitrophenyl octyl ether
Sweetness	Tetradodecylammonium bromide Trimeritic acid	Dioctyl phenylphosphonate

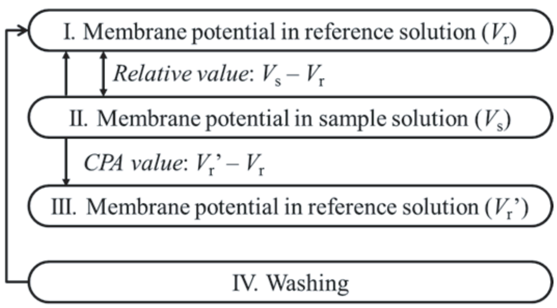

Fig. 2. Measurement procedure of taste sensing.

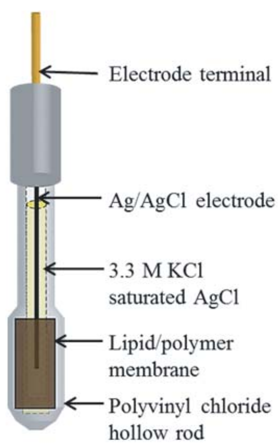

Fig. 3. Sensor electrode.

as the change in membrane potential caused by adsorption (CPA). Finally, the membrane is rinsed with a sensor rinsing solution (30 vol% EtOH, 100 mM HCl or 30 vol% EtOH, 10 mM KOH and 100 mM KCl). Here, the lipid/polymer membranes of sensor electrodes to measure bitterness and astringency also respond to taste substances other than bitter and astringent substances, respectively, shown as relative value (V_s–V_r). On the other hand, CPA value (V_r'–V_r) of these membranes can selectively respond to bitter and astringent substances, respectively, because bitter or astringent substances are adsorbed onto the lipid/polymer membrane of the sensor electrodes. [29].

IV. PRINCIPLE OF TASTE SENSOR

The commercialized taste sensor, i.e., the taste sensing system (Fig. 1) consists of a working electrode with a lipid/polymer membrane used to receive taste substances, a handle, and a data processing unit. In the electrode structure, a Ag/AgCl electrode, inner solution (3.3 M KCl saturated AgCl) is contained in a polyvinyl chloride hollow rod with a lipid/polymer membrane attached (Fig. 3). The potential of the lipid/polymer membrane changes upon electrostatic interaction with taste substances and their physicochemical adsorption [15]–[17], [19], [29]. Table 1 shows lipids and plasticizers used in the taste sensor.

The composition of the membrane is designed considering the charges on the membrane surface and hydrophobicity on the basis of physicochemical properties of substances with each basic taste; for example, an electrical potential change for bitterness is induced when bitter substances are adsorbed onto the membrane owing to the electrostatic and hydrophobic interactions of their charges with the membrane, and a potential change for sourness is induced when protons bind to the membrane [29], [51]. A bitterness sensor, i.e., sensor electrode to measure bitterness, has a membrane with a lower content of charged lipids to increase hydrophobicity. In contrast, a saltiness sensor, i.e., sensor electrode to measure saltiness, has a membrane with a higher content of charged lipids to increase hydrophilicity and easily induce the electrostatic interaction with ions. In addition, the content of lipids is selected from the optimal range and an appropriate plasticizer is adopted so that marked changes in the membrane potential can be obtained by adding a small amount of taste substances. Fig. 4 shows schematics of the membranes in saltiness and bitterness sensors used for the evaluation of foods. NaCl and iso-α acid, which is well known as the bitterness component of beer, are shown as examples of salty and bitter substances, respectively. A larger amount of lipids is included in for the saltiness sensor (Fig. 4(a)) than the bitterness sensor (Fig. 4(b)). Here, iso-α acid is present in the lipid/polymer membrane, which will be explained with the results of measuring the amount of adsorbed taste substance.

The electrode with a lipid/polymer membrane immersed into a sample solution containing taste substances can be used

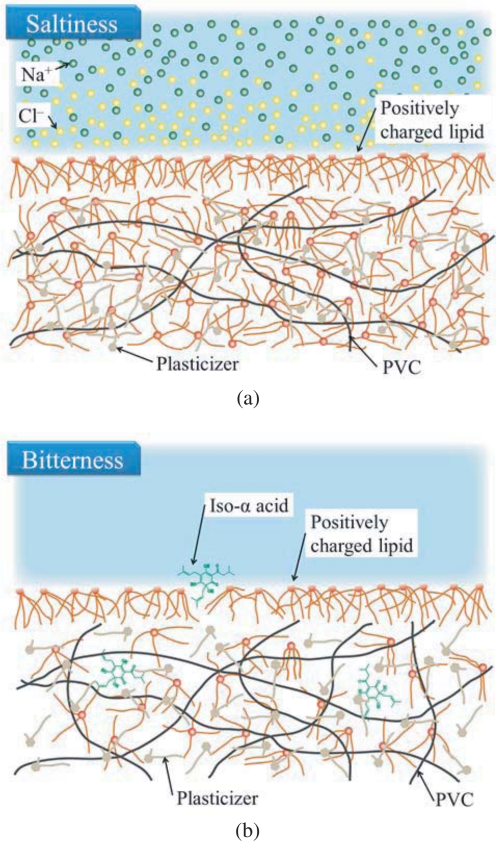

Fig. 4. (a) Schematic illustration of lipid/polymer membranes for salty substances and (b) acidic bitter substances.

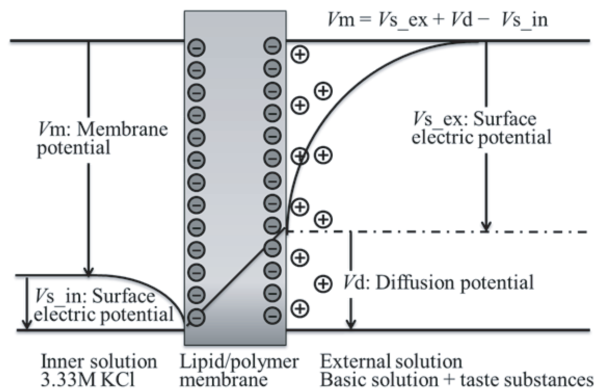

Fig. 5. Membrane electric potential in a negatively charged membrane.

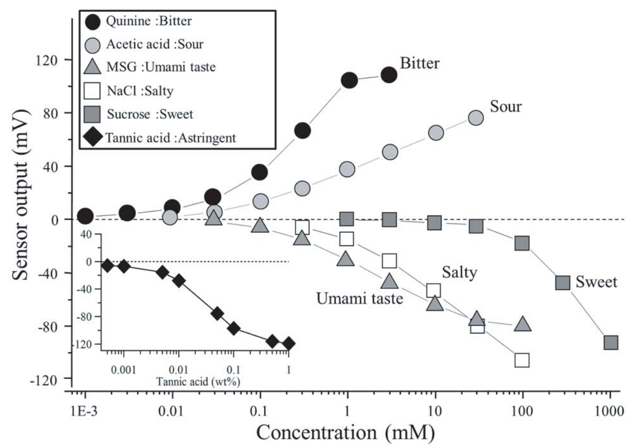

Fig. 6. Concentration dependence of six types of electrode on the five basic tastes and the astringent taste. MSG is the abbreviation of monosodium glutamate.

to determine the intensity of the taste by detecting changes in the potential of the lipid/polymer membrane and by evaluating the difference between the membrane potential of the sample solution and that of the reference solution. Fig. 5 shows the response mechanism of a negatively charged membrane. When the concentrations of the inner and outer solutions across the membrane are different, the membrane potential is the difference between the potential of the inner solution and that of the outer solution. The membrane potential comprises a surface potential generated at the interface between the membrane surface and the solution and a diffusion potential in the membrane. Regarding the surface potential, a diffuse electrical double layer is formed in the solution layer near the membrane surface. When the lipid/polymer membrane comes into contact with an electrolyte solution, it is charged as a result of the ionization of dissociative groups of the lipid in the membrane surface and the adsorption of ions. For negatively charged lipid/polymer membranes, cations are attracted to the vicinity of the membrane surface owing to the electrostatic interaction, whereas anions move away from the membrane surface. Thus, a diffuse electrical double layer is formed by the negative charges and cations on the membrane surface. The diffusion potential in the membrane is a potential difference caused by the difference between the mobility of cations and that of anions in the membrane.

V. Application of the Taste Sensor

A. Measurement of Basic Tastes

Similar to the above-mentioned electronic tongues, the initial taste sensor discriminated and quantified tastes by statistically analyzing the PCA values and other parameters using the responses from multiple sensor electrodes with a lipid/polymer membrane [12], [15]–[17]. However, researchers succeeded in expressing the intensity of each type of taste directly from the response of the electrodes by improving the selectivity and sensitivity of the sensor electrodes with respect to each taste, i.e., realizing a global selectivity. Specifically, when the change in the membrane potential of a sample solution (even unknown) is smaller than that of the reference solution, the intensity of the taste is low. In contrast, the larger the change, the higher the intensity of the taste. Fig. 6 shows responses of sensor electrodes used in the commercially available taste sensing system. The threshold for tastes identified by humans is low for signals of toxic and rotten substances, i.e., bitterness and sourness (increasing in this order), and is highest for sweet substances, the energy source for humans. Following these biological properties, the threshold and sensitivity of each sensor electrode are adjusted in the taste sensing system. Unlike electronic tongues, the taste

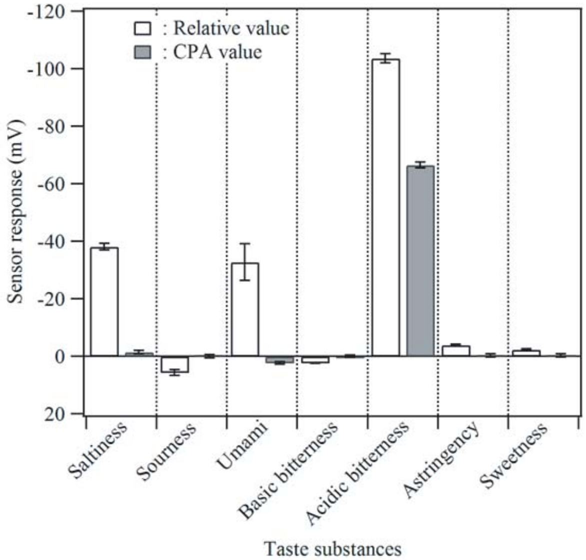

Fig. 7. Relative values and CPA values of the acidic bitterness sensor response to each taste substance ($n = 5$): saltiness; 300 mM KCl, 0.3 mM tartaric acid, sourness; 30 mM KCl, 3mM tartaric acid, umami; 10 mM MSG, basic bitterness; 0.1 mM quinine-HCl, acidic bitterness; 0.01 vol% iso-α acid, astringency; 0.05 wt% tannic acid, sweetness; 1 M sucrose. Umami, basic bitterness, acidic bitterness, astringency and sweetness samples include 30 mM KCl and 0.3 mM tartaric acid.

sensor can convert the measured values into sensory values by simple linear regression or multiple regression analysis using two sensor outputs without using any complicated statistical methods such as pattern recognition, and can provide a taste scale [29].

B. Global Selectivity

Fig. 7 shows the relative and CPA values obtained from an acidic bitterness sensor, i.e., sensor electrode for acidic bitterness (Table 1) for samples with basic tastes. The relative value for the acidic bitter substance is –100 mV, whereas those for the salty and umami substances are approximately –40 mV. In contrast, the CPA value is –67 mV for the acidic bitter substance but is nearly zero for other taste substances. Namely, the CPA value of the acidic bitterness sensor is highly selective to acidic bitter substances. Fig. 8 shows the measurement results obtained from a basic bitterness sensor, i.e., sensor electrode for basic bitterness. Four bitter substances and other taste substances [29] were tested. From the CPA values, the basic bitterness sensor responds to all bitter substances but does not respond to other taste substances. These results support the fact that the basic bitterness sensor has global selectivity. In addition, the CPA value highly correlates with the results of sensory evaluation, as shown in Fig. 8. As mentioned above, the basic bitterness sensor conforms to the concept of the taste sensing system described in Section 3.

C. Application to Foods and Beverages

As electronic tongues are used in the quality control of foods and beverages, the taste sensing system has been similarly applied to not only quality control but also services for

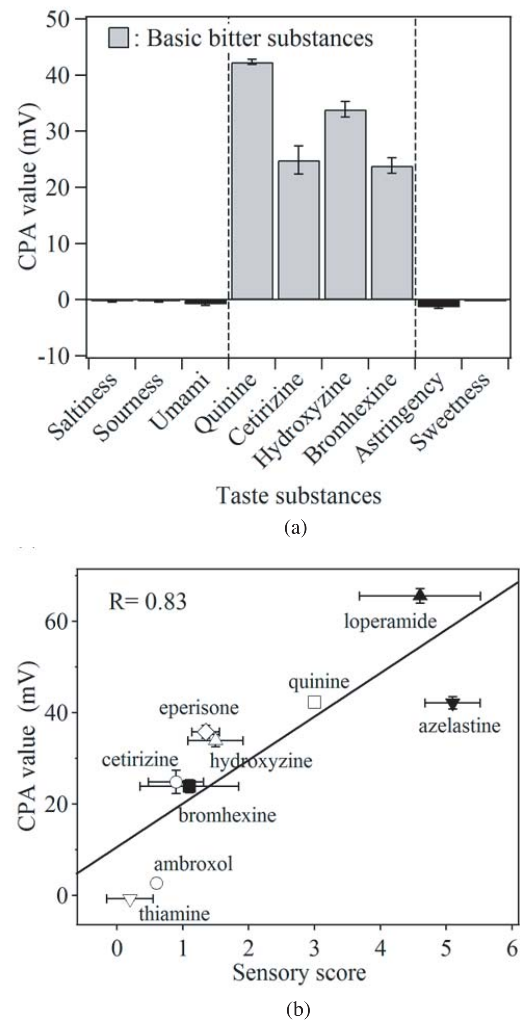

Fig. 8. Sensor performances of the basic bitterness sensor [29]. (a) CPA values of response to six taste substances. (b) Relationship between results of CPA values of the basic bitter substances and human sensory score. The bitter substance materials: 0.1 mM of hydrochloride salts. Data are expressed as mean $\pm$ SD ($n = 4$). All samples include 30 mM KCl and 0.3 mM tartaric acid as a supporting electrolyte.

consumers and marketing in the food industry. Moreover, methods of determining the expiration date of foods using the taste sensing system have been developed [29]. In practice, the tastes of various foods and beverages, including black tea [52], green tea [53], milk [54], Prosciutto ham [29], rice [55], pork [56], table salt [57], and ginseng [58], have been quantified using the taste sensing system. Fig. 9 shows a taste map where the intensities of taste for beer in various countries are mapped. In the map, the ordinate represents the bitterness intensity and the abscissa represents the sourness intensity, providing the visualized information of taste as well as the discrimination of products.

The taste sensing system has also been examined for use in the selection of feed appropriate for the growth of local chickens with the aim of reducing the breeding cost [59]. The feed in the reference shows greater responses to umami and koku than other types of feed. Here, koku is also called kokumi in academic fields and is generally known as rich taste, thick taste, or good body. Kokumi, or koku, substances

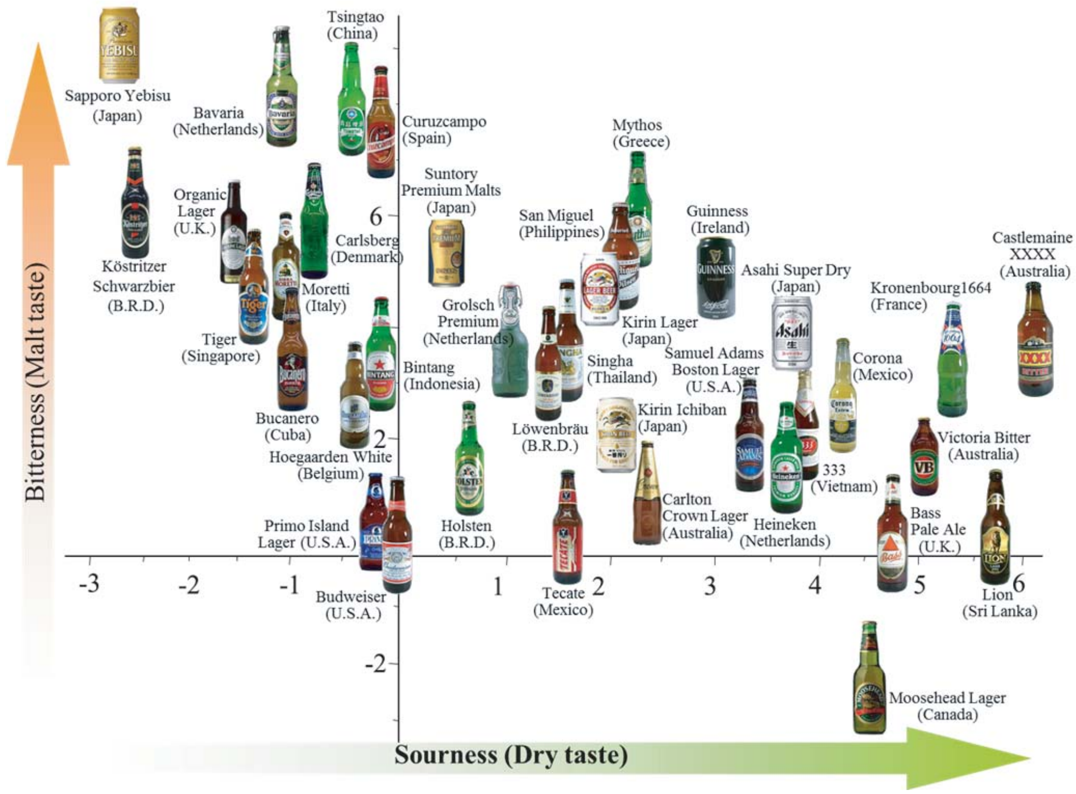

Fig. 9. Taste map of beer.

were discovered by Ueda *et al*. [60] and its receptor has also been discovered recently [61]. Koku substances add thickness, mouthfulness, and continuity to the taste of foods. A typical koku substance is glutathione (γ-L-glutamyl-L-cysteinylglycine). The taste sensing system can be used to quantify koku by measuring the CPA value for umami. In actuality, the effect of kokumi flavor in noodle soup base has been demonstrated and quantified using the taste sensing system [29], [62].

The above applications of the taste sensing system can be used to provide taste information (type and intensity of taste) to consumers and as a marketing tool in the food industry as well as to compare own products with others and determine consumers' preference. In other words, the taste sensing system can be used not only for quality management based on the discrimination and analysis of foods, which is the aim of electronic tongues, but also to add taste information to products as an added value. It is a device that can indicate consumers' preference of foods.

Moreover, arbitrary tastes can easily be created by utilizing the database obtained from measurements using the taste sensing system. On the basis of this concept, coffee provided by Japan Airlines is designed using the taste sensing system. Manually making coffee with a desired taste will be a time-consuming trial-and-error task. The taste sensing system enables us to accurately create a desired taste in a short period of time.

The taste sensing system can be used to detect the interaction between taste substances, as described in Section 5.6 in detail. It is known that cooking oil generally makes the taste of foods milder. The changes in taste when cooking oil was added to solutions with various tastes such as sourness, bitterness, and astringency were measured [29], [62]. The results revealed that the responses to bitterness and astringency markedly decreased. In contrast, the responses to other tastes including umami and saltiness remained unchanged. These results indicate that cooking oil suppresses bitterness and astringency, which are relatively stimulating and sustained, to make the taste of foods milder.

D. Sweetness Sensor

The development of sweetness sensor, i.e., sensor electrode for sweetness was behind that of other taste sensor electrode. This is mainly because sweet substances are nonelectrolytes, i.e., substances without charges, and the potential of lipid/polymer membranes is hardly changed by sweet substances. Although Brix meters may be used as an alternative method of measuring sweetness, they perform indirect measurements in which the refraction index of solutions is measured. Therefore, measurement results greatly depend on the composition of solutions, and it is difficult to accurately measure the intensity of sweetness. In actuality, general solutions with a high viscosity also show a high refraction index (i.e., they respond to Brix meters). Toyota *et al*. succeeded in detecting sweet substances, such as sucrose, glucose, fructose, and raffinose, by modifying lipid/polymer membranes using substances that electrostatically interact with sweet substances (sweet-responsive substances, SRSs) in advance. They found a clue to resolving the problem related to sweetness sensors, and their developed sweetness sensors have already been practically used [63], [64]. For realizing highly functional sweetness sensors, it is also an urgent task to develop methods of quantifying high-intensity sweeteners, such as aspartame, acesulfame-K, and saccharin, which are popularly used in sweet foods and beverages because of their low calorie content.

E. Measurement of Amino Acids

Amino acids are the basic building blocks of proteins essential to human lives and important components in foods. Some amino acids have two types of taste, for example, sweetness and bitterness. Methods of evaluating the taste of amino acids were examined [65]. The relative values were measured using taste sensor for L-alanine (L-Ala) as the sweet amino acid, L-tryptophan (L-Trp), L-leucine (L-Leu), and L-isoleucine (L-Ile) as the bitter amino acids, and L-methionine (L-Met) as the amino acid with a composite taste. The results were compared with those of sensory evaluation. The correlation coefficient between the relative value obtained from the sweetness sensor for L-Ala and the value obtained by the sensory evaluation was 0.97, and between the relative values obtained from the bitterness sensor for L-Trp, L-Leu, and L-Ile and the values obtained by the sensory evaluation was also 0.97, indicating that the intensity of taste of each amino acid can be measured using the taste sensors.

Moreover, the sensory evaluation revealed that 300 mM L-Met with a composite taste of bitterness and sweetness has bitterness corresponding to that of 30 mM L-Trp and sweetness corresponding to that of 300 mM L-Ala [65]. The estimated intensities of bitterness and sweetness obtained from the sensors for 300 mM L-Met corresponded to the bitterness of 10–30 mM L-Trp and the sweetness of 100–300 mM L-Ala, respectively. These results indicate that the estimated values obtained from the taste sensor and the results obtained by the sensory evaluation are in good agreement. Therefore, for L-Met with both sweetness and bitterness, i.e., amino acids with a composite taste, the intensities of coexisting tastes can be estimated using the bitterness and sweetness sensors. It is found that the taste sensor can be used to quantify the taste of amino acids.

F. Application to Pharmaceuticals

The bitterness of not only foods but also pharmaceuticals has been successfully quantified using taste sensor, which has now been practically used to evaluate the bitterness of pharmaceuticals [49], [66]–[71]. Most pharmaceuticals have strong bitterness, and enhancing the medication compliance by patients is an important task for pharmaceutical manufacturers. The taste of a sample prepared by mixing bitterness-masking materials used to suppress bitterness, i.e., sucrose, α-cyclodextrin, BMI-40 (Kao Corporation, Japan), with a bitter substance, in this case quinine chloride, was measured using taste sensor. The results highly correlated with the results obtained from sensory evaluation by sensory panelists, indicating the applicability of taste sensor to the detection of the effect on suppressing the bitterness of pharmaceuticals [29], [71]. Orally disintegrating tablets (ODTs) attracted much attention approximately 20 years after the start of their research and development and 10 years after commercialization. In particular, the use of ODTs has been rapidly promoted since 2000 and has been becoming the mainstream of oral medication. Harada *et al.* evaluated the bitterness of a carrageenan-containing propiverine hydrochloride ODT [66]. For ODTs containing pectin, agar, or λ-, ι-, or κ-carrageenan, the intensity of bitterness at the complete disintegration was measured using taste sensor and compared with the results of sensory evaluation by panelists, showing a strong correlation with a high correlation coefficient of $R = 0.907$. Moreover, propiverine hydrochloride eluted from these ODTs was sampled for different elution times and the intensity of bitterness was measured, demonstrating that the time dependence of the change in bitterness intensity can be evaluated using taste sensor.

A group led by Uekama and Arima reported the suppression of bitterness for various drugs using β-cyclodextrin [69]. Sawai Pharmaceutical Co., Ltd., a Japanese generic manufacturer, developed a generic drug with suppressed bitterness and was awarded the Generic Drug of the Year 2011 title by the Generic Drug Association, Japan. The development of a bitterness-free cetirizine hydrochloride ODT, for which the company won the award, was conventionally considered to be difficult because of the very strong bitterness and irritating taste of the raw materials. The strong bitterness of cetirizine hydrochloride was effectively suppressed using β-cyclodextrin to realize the above ODT. The outputs from taste sensor indicated that the irritating taste of cetirizine hydrochloride is attributable to sourness, and therefore, its sourness was suppressed using sodium citrate. These pretreatments enabled the development of the first-ever cetirizine hydrochloride ODT with sufficiently suppressed bitterness and irritating taste [70]. Considering the fact that medication is generally unpleasant and painful for healthy people, a stress imposed on panelists in sensory evaluation is very large and the taste sensor that enables objective evaluation can be used as a promising tool for developing pharmaceuticals. As above, the taste sensor is expected to be further applied to the pharmaceutical industry.

Woertz *et al.* compared the TS-5000Z taste sensing system with the Astree II e-tongue Sensor from the viewpoint of pharmaceutical formulation development. They described that the TS-5000Z provides more reliable (in vitro/in vivo correlation) and precise (reproducibility and repeatability) data than the Astree II e-tongue Sensor [27].

VI. Adsorption of Taste Substances

As mentioned above, the CPA value obtained using taste sensor reflects the change in the membrane potential caused by the adsorption of taste substances onto lipid/polymer membranes. The effect of weakly adsorptive substances such as salty and sour substances can be eliminated, showing a high selectivity to each taste. The amount of taste substances adsorbed onto the lipid/polymer membrane generally depends on the content of lipid in the membrane. The following experiment was carried out to confirm the relationship between the amount of taste substances adsorbed onto the lipid/polymer membrane and the CPA value.

A lipid/polymer membrane to be used for a bitterness sensor was formed on a petri dish, onto which 5 ml of 0.01 vol% iso-α acid solution was added dropwise and left to be immersed for 30 s. After that, 3 ml of the solution was taken from the petri dish to measure the absorbance of the solution. The concentration of iso-α acid remaining in the solution was calculated from the measured absorbance and a calibration curve obtained in advance. The difference between the concentration of the iso-α acid solution added dropwise and the calculated concentration was defined as the amount of adsorbed iso-α acid. This value was divided by the area of the petri dish to obtain the amount of iso-α acid adsorbed per square centimeter. A CPA is generated when a taste substance adsorbs onto the surface of a lipid/polymer membrane and the electrical charge density of the membrane surface changes. As the concentration of positively charged lipids increases, the surface charge density of the lipid/polymer membrane increases and the hydrophobicity of the membrane decreases. Iso-α acid is negatively charged in solution. When the surface charge density of the membrane increases, iso-α acid tends to be attracted to the membrane surface by electrostatic interaction, resulting in the increased amount of iso-α acid adsorbed onto the membrane surface. The increased surface charge density is a factor increasing the potential response. In contrast, the amount of iso-α acid adsorbed onto the membrane surface or into the membrane interior decreases when the hydrophobicity of the membrane decreases. The decreased hydrophobicity is a factor decreasing the potential response. These opposite factors indicate that a peak should exist in the lipid concentration dependence of the CPA value.

A measurement was carried out for membranes with lipid concentrations of 0.001–10 wt%. The amount of adsorbed iso-α acid increased with the lipid concentration to its maximum when the lipid concentration was 0.715 wt%, then decreased when the lipid concentration further increased, as expected. The maximum amount of adsorbed iso-α acid was approximately 1 μg/cm^2 (Fig. 10). The relationship between the amount of adsorbed iso-α acid and the CPA value was evaluated using a lipid/polymer membrane with a lipid concentration of 0.715 wt%. For an amount of adsorbed iso-α acid of 2 μg/cm^2 or more, the CPA value saturated, meaning that the taste substances were adsorbed onto the membrane surface or into the membrane interior, as illustrated in Fig. 4. This adsorption causes the suppression of dissociation and the screening effect by paired ions, resulting in the reduced change in the surface charge density of the membrane.

In a previous study, the amount of adsorbed quinine chloride was measured using a bitterness sensor and peaks were observed in the lipid concentration and the amount of adsorbed quinine chloride [72]. In addition, the CPA value saturated for an amount of adsorbed quinine chloride of 3 μg/cm^2 or more. Therefore, quinine chloride and iso-α acid show similar adsorption behaviors. This fundamental finding on the CPA

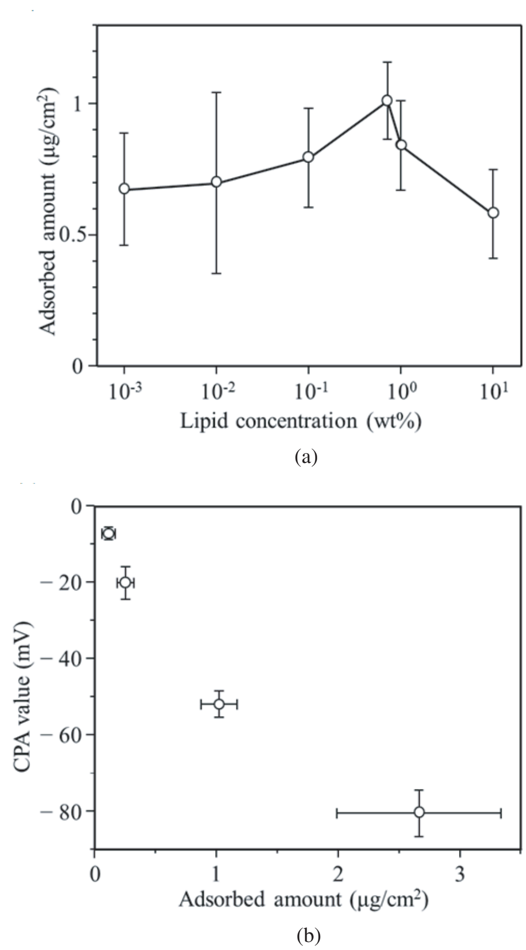

Fig. 10. (a) Amount of iso-α acid adsorbed on the acidic bitterness membrane. (b) Relationship between the CPA value and the amount of adsorbed iso-α acid.

value will contribute to the development of new lipid/polymer membranes and the further improvement of global selectivity.

VII. Portable Taste Sensor

The commercialized taste sensing system is large and can be used only by particular users at limited places. We are developing a portable sensor with the aim of downsizing the conventional taste sensing system [73], [74]. Measurement targets of taste sensor include foods and pharmaceuticals, which are compounds containing many chemical and biochemical substances. Therefore, working and reference electrodes must be rinsed with alcohol to ensure the reproducibility and stability of sensor outputs, requiring physical and chemical durabilities. The prototype portable taste sensor that we fabricated consists of a taste sensor chip and device and is as small as a USB memory for portability, forming a hand-held-type sensor. For practical application, the sensor chip has a structure that can contain a reference electrode and multiple working electrodes fabricated on a low-cost highly versatile polycarbonate substrate. The taste sensor chip is integrated in the taste sensor device, which can be held in a hand and is connected to a PC to process the measurement data.

The taste sensor chip consists of electrodes fabricated on polycarbonate substrates, polyimide double-faced tapes, and

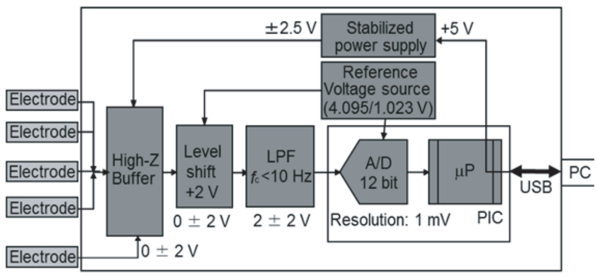

Fig. 11. Block diagram of portable taste sensor device [74].

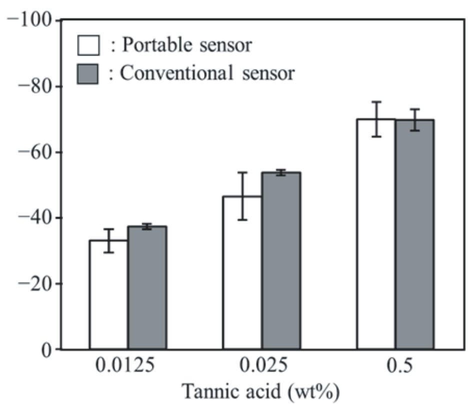

Fig. 12. CPA value of the portable taste sensor to tannic acid [74].

partitions (polycarbonate, 1.0 mm in thickness). To fabricate the electrodes on plastic substrates, polycarbonate substrates with a thickness of 1.0 mm were used and a Ti/Ag layer was formed on the substrates using a high-frequency sputtering device. The electrode pattern was formed by photolithography. For the sensing stage, a polyimide double-faced tape with a 3-mm-diameter pore was attached to the Ag/AgCl electrode obtained by coating a Ag layer with Ag/AgCl ink, and then a poly-hydroxyethyl methacrylate (pHEMA) mixed solution (60 wt% hydroxyethyl metacrylate, 38 wt% ethylene glycol, 1 wt% dimethoxy-2-phenylacethophenone, 1 wt% tetraethylene glycol dimethacrylate) was added onto the Ag/AgCl electrode to polymerize the polymer gel pHEMA by UV irradiation. Next, a partition with a 4.5-mm-diameter pore was bonded to the electrode, onto the pHEMA of which KCl solution was dropped as an electrolyte for overnight incubation.

The circuit of the taste sensor device consists of a high-input-impedance buffer amplifier, a level shift circuit, a low-pass filter (LPF), a peripheral interface controller (PIC) microcomputer, and a stabilized power supply unit. The PIC microcomputer has a 12-bit AD converter. The fabricated taste sensor device is connected via USB to perform data processing on the PC. In addition to this communication of signals with the PC, power is supplied to the device via USB (Fig. 11).

The performance of the fabricated portable taste sensor was compared with that of the TS-5000Z. The astringency sensor in this portable taste sensor showed a similar level of sensor output to that of the astringency sensor in the conventional taste sensing system (Fig. 12). As explained above, the TS-5000Z and SA 402B, commercially available taste sensing systems, show sensor outputs in good agreement with the results of sensory evaluation by panelists. Therefore, the practicality of the portable taste sensor that is highly compatible with conventional taste sensing systems has been demonstrated.

VIII. Discussion and Conclusion

In this paper, we have reviewed the concept of the taste sensor, i.e., an electronic tongue with global selectivity, and its applications to foods, beverages, and pharmaceuticals. The taste sensor enabled the quantification of the five basic tastes and astringency identified by the human tongue, and successfully provided the sensor outputs in good agreement with the results of sensory evaluation by panelists. For pungency, a type of taste in a broad sense, the development of a surface plasmon resonance (SPR) immunosensor that can detect capsaicin, a typical pungent substance, at ultrahigh sensitivity is under way. In the future, it will become possible to quantify the intensities of all types of taste of foods, including the five basic tastes, astringency, and pungency. Recently, researchers have also been attempting to develop biosensors using biological tissues such as taste cells and receptors by genetic engineering technologies [75]–[77]. A group led by Suslick has analyzed liquids such as beer and soft drinks using colorimetric sensor arrays that comprise multiple chemically responsive dyes [78]–[80].

Technologies for detecting pesticide residues to ensure the security and safety of foods have also been developed by applying the taste sensor [81]. Pesticides are composed of 1) active ingredients (AIs), 2) inert ingredients added to support the AIs and facilitate the formulation, and 3) surfactants; the latter two are called pesticide adjuvants. The taste sensor detects the changes in the electrical potential of lipid/polymer membranes caused by the physicochemical interaction between the membranes and chemical substances. By applying this principle, we develop a technology that can detect pesticide residues that exceed the acceptable level and aim to realize portable pesticide sensors.

Recently, the spread of the Internet has enabled consumers to easily search for information and products that meet their requirements. In accordance with this, their requirement and expectation for tastes will increase in the future. Humans perceive tastes by the tongue and also systematically sense tastes on the basis of odor, texture, visual appearance, and factors based on cultural background such as taste preference, experience, and memories. In the future, sensing technologies that can be used to quantify comprehensive tastes, or palatability, are expected to be realized by advancing comprehensive research on various fields, such as brain science, genetic engineering, psychology, and physics.

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