from-A Flavor-Receptor Ellipsoid Model for the Prediction of Flavor Sensory Thresholds

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Concept of Threshold Force

For many senses such as touch, hearing, and vision it is a pressure-like quality of the stimulus that is responsible for the sensation. Sound pressure of various intensities (orders of magnitude changes require a logarithmic scale defining the decibel) lead to the concept of threshold sound which can be frequency dependent. Touch requires a pressure that can best be sensed when the pressure is applied or removed. A constant pressure such as the pressure of the atmosphere, the pressure of clothes, or sitting on a chair become adapted to over a period of time and are only noticeable if the pressure condition is changed (getting out of the chair or removing the clothing). Even light can be considered a radiation pressure that stimulates and interacts with the visual system.

The pressure like quality of smell can certainly be related to the fact that gas vapors are responsible for the sensation and gas vapor has a pressure. However, air and water vapor are forever present in the nasal passage, and they appear to have a minimal odor. It is the presence of other flavor active materials in air and water vapor that are sensed as flavor and these flavors have their own vapor pressure. It is the presence of a new vapor that causes a variation in the pressure that affects the olfactory receptor by some mechanism.

The physical definition of pressure is a force per unit area. The changes in pressure then are related to changes in either the forces, the area or both. During breathing some changes in area of the nasal passage is possible which can change the internal pressure. The area of exposure of the receptor can also change. The force is changed by the presence of a new volatile material. This force can be thought of as a mechanical (translational and rotational) force of the molecules of the flavor in the vapor state, striking an area of the receptor. The transfer of these forces is a stimulus for the olfactory process.

If the concentration of the flavor is below threshold, then the force exerted on the receptor is below a threshold response. At the threshold concentration, the molecules in the vapor state exert a force, which is sufficient to cause a response of the olfactory receptor. This response then is converted to a nerve impulse that is interpreted as a presence of the given flavor compound (sensing the flavor is possible in the absence of other forces).

What is the nature of this mechanical force? From Newton's law this force is proportional to the product of a mass and acceleration

(1) $$\mathbf{F} = m*\mathbf{a}$$

where the bold letters indicate that these quantities are vectors. A vector property is a property that has both a magnitude and direction. The magnitude of a force may be constant, but the direction of the force can influence whether the force is effective. For example, the speed and direction of a tennis ball after a serve depends on the angle of the racquet to the ball, given the same amount of applied effort. Similarly, the force needed to stimulate the receptor site may not be available if the total translational and rotational energy of the molecule are not fully transferred to the site. For this reason, the force and acceleration terms are dependent on direction which implies that the threshold force for a receptor will depend on the directional quality of the accelerating molecules and their mass.

In general, the directional properties are the three independent directions in space required to define a point in space. It will later be shown that this also depends on the coordinate system used to define this space. For example, in cylindrical coordinates a radial vector and two angles define a point in space. The geometry of the model will influence the coordinate system used. As an initial geometry, the Cartesian x,y,z, coordinates of a molecule will be used. The components of force and acceleration are the values in the corresponding coordinate direction. The force will have components in the x,y,z direction given as F_x, F_y, F_z and the acceleration will be given as a_x,a_y,a_z. The magnitude of a vector is defined as the square root of the sum of the squares of the components.

(2) $$\text{magnitude of } \mathbf{a} = |a| = (a_x^2 + a_y^2 + a_z^2)^{1/2}$$

where the magnitude is a scalar (value is independent of direction).

A familiar example in physics of an acceleration vector is gravitation. The gravitational constant **g** for the earth slightly varies with longitude but is usually considered of a constant magnitude (9.80 meters/sec/sec). The direction of this force is always to the center of the earth (downward z direction) so the force or weight of objects is directed downward. The force of a human on the earth is $F_z = m*g_z$ where m is the mass of the human and F is in newtons or pounds force. (A 50 kilogram human weighs 50*9.8 newtons*1 lbf/4.4482 newtons = 110.2 lbf. (pounds) on earth but substantially more on Jupiter.)

This example shows that an acceleration constant can be defined for a given environment (Earth versus Jupiter). Similarly, an acceleration constant could be defined for the olfactory senses. If this value was constant, then the force exerted on a receptor would depend only on the mass (molecular weight or concentration) of the flavor. This model would be contrary to the experimental observation that threshold concentrations range 5 to 6 orders of magnitude for chemicals with molecular weights only ranging 2 fold. It could be argued that there are specific receptors that have sensitivities differing by 5-6 orders of magnitude. If such receptors were present, they would need a chemical specificity (docking model) in order to avoid their saturation at normal concentrations of most flavors. It would be difficult to relate a linear model such as Newton's law to these selective receptor thresholds. Although selective receptor thresholds may be present, their response mechanism based on force thresholds may be similar to all other olfactory receptors. In this case the setting of minimal force thresholds for each flavor would be required. A model could be found which predicts the value of receptor force thresholds. Since little is known about these receptors quantitative information would be difficult to obtain.

Since more is known about the flavor molecule than its receptor and receptor site it is more convenient to model threshold values around each flavor molecule. This model would assume that the force threshold values for most flavors is constant. The value of this constant force can vary for several reasons:

1. Adaptation to flavors may lower of increase the force threshold
2. Other flavors or taste molecules may alter the force threshold
3. Genetic variations may alter these thresholds and explain genetic insensitivity to some flavors and tastes.
4. Matrix effects may alter the force threshold.

In most cases experimental data would be required to determine the magnitude of changes to the force threshold. It would be assumed that these changes would be of a general nature and affect many flavors rather than be selective.

If the selectivity of the olfactory receptor to flavors is to be identified with the type of flavor as opposed to the type of receptor, then the acceleration constant is a property of the flavor only. Let g_f be the effective flavor dependent constant then,

(3) $$\mathbf{F}_t = m_t * \mathbf{g}_f$$

where m_t is the flavor threshold concentration in the liquid and F_t is a constant flavor force threshold. Note that both **F** and **g** are vector quantities that are important to this model. The value of $\mathbf{g}_f$ is *dependent only on the properties of the flavor molecule,* a statement that is also an important assumption of this model.

The linear model suggests that each flavor will have an associated $\mathbf{g}_f$ vector and that the interactions to a first approximation will obey linear vector properties. This means that if flavor A has vector $\mathbf{g}_{fA}$ and flavor B has vector $\mathbf{g}_{fB}$ then:

(4) $$\mathbf{F} = m_A * \mathbf{g}_{fA} + m_B * \mathbf{g}_{fB}$$

Presently there are many conclusions that can be made with this equation, but they may not agree with experimental observations. For example, both m_A and m_B can be below their threshold concentrations but the force **F** at or above the threshold force. Certainly, the additive flavor impact may be detected which is important to many fruit and vegetable extracts which contain many flavors below their threshold values, but which are important to the overall impact of the extract. Can there be a finite number of flavors in solution below threshold concentrations and their summation below the threshold force? If yes to this question, then the threshold force is proportional to flavor properties and not related to receptor properties. If one flavor is at threshold and another below, what is the nature of the combined flavor, A like, or A and B like?

Some of these questions will be examined as the model is developed and the vector properties are further explored. For example, from vector operations:

(5) $$\mathbf{g}_{fA} * \mathbf{g}_{fB} = g_{fAx} * g_{fBx} + g_{fAy} * g_{fBy} + g_{fAz} * g_{fBz}$$

with the summation given as the product of components of g in the x, y, z direction.

This vector property suggests that each flavor has a g vector composed of a magnitude given by equation (2) and a directional vector that establishes the magnitude at each component direction.

If the magnitude of the z component of the threshold force is constant, then the vector product of two flavors in the z direction gives a magnitude of the flavors:

(6) $$F_z = m_A * g_{fAz} + m_B * g_{fBz}$$

(7) $$m_C * g_{fCz} = m_A * g_{fAz} + m_B * g_{fBz}$$

If the magnitude of $g_{fCz} = g_{fAz} * g_{fBz}$ then dividing and solving for the threshold value of flavor C gives:

(8) $$m_C = m_A / g_{fBz} + m_B / g_{fAz}$$

The theory indicates that given the component g values and the concentration threshold values of some flavors, the threshold values of other components can be calculated directly. The application of this theory to the formulation of flavors would be valuable.