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(54) Title: APPARATUS AND METHOD FOR DRY EYE FORECAST AND TREATMENT RECOMMENDATION

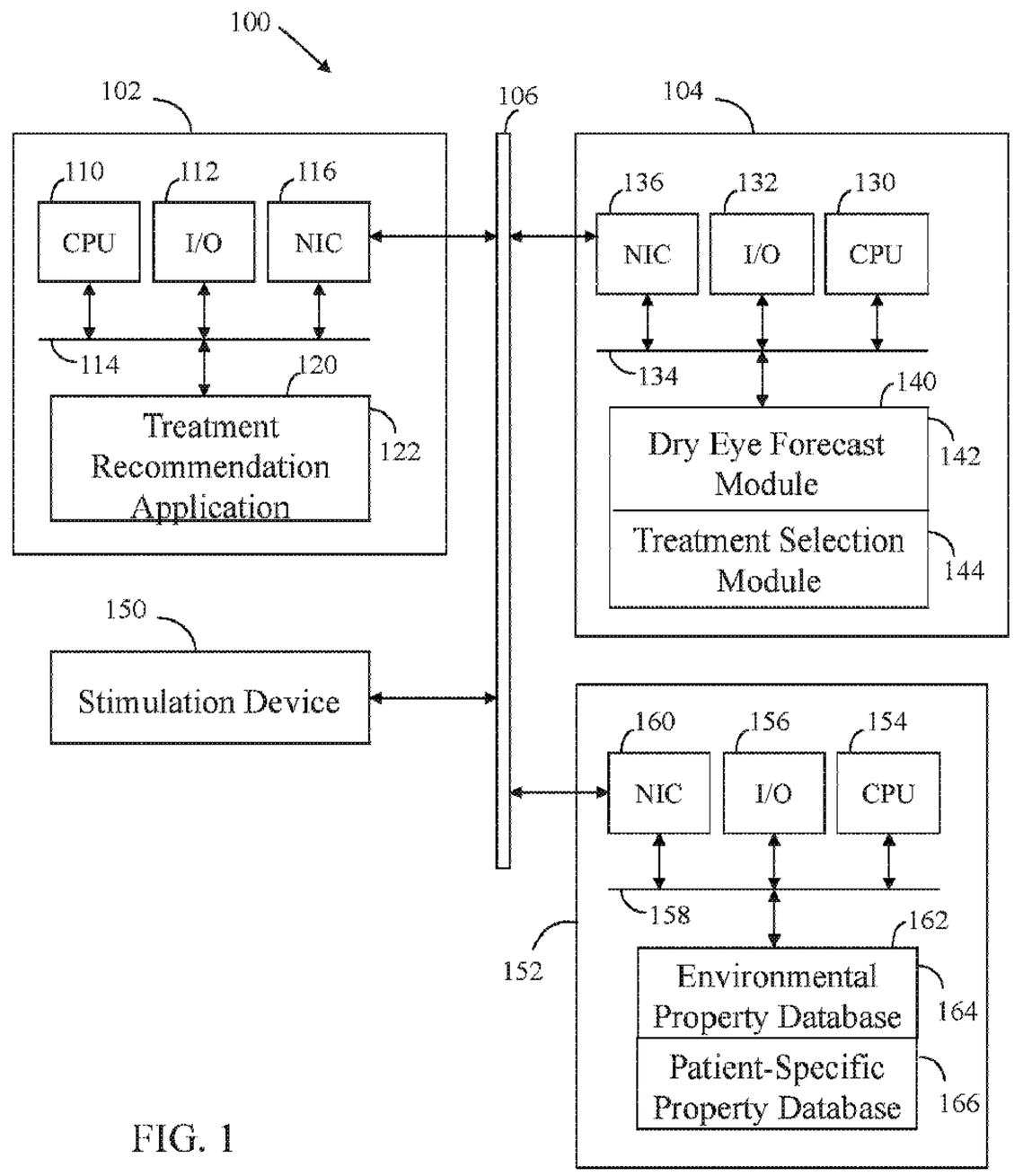

FIG. 1

(57) Abrégé/Abstract:
Generally, a machine may include a processor and a memory connected to the processor, where the memory stores instructions executed by the processor to determine first and second properties related to dry eye symptoms of a patient. The properties may

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be used to form a dry eye forecast. A treatment recommendation may be selected based at least in part upon the dry eye forecast. The treatment recommendation may be supplied to a device.

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(54) Title: APPARATUS AND METHOD FOR DRY EYE FORECAST AND TREATMENT RECOMMENDATION

(57) Abstract: Generally, a machine may include a processor and a memory connected to the processor, where the memory stores instructions executed by the processor to determine first and second properties related to dry eye symptoms of a patient. The properties may be used to form a dry eye forecast. A treatment recommendation may be selected based at least in part upon the dry eye forecast. The treatment recommendation may be supplied to a device.

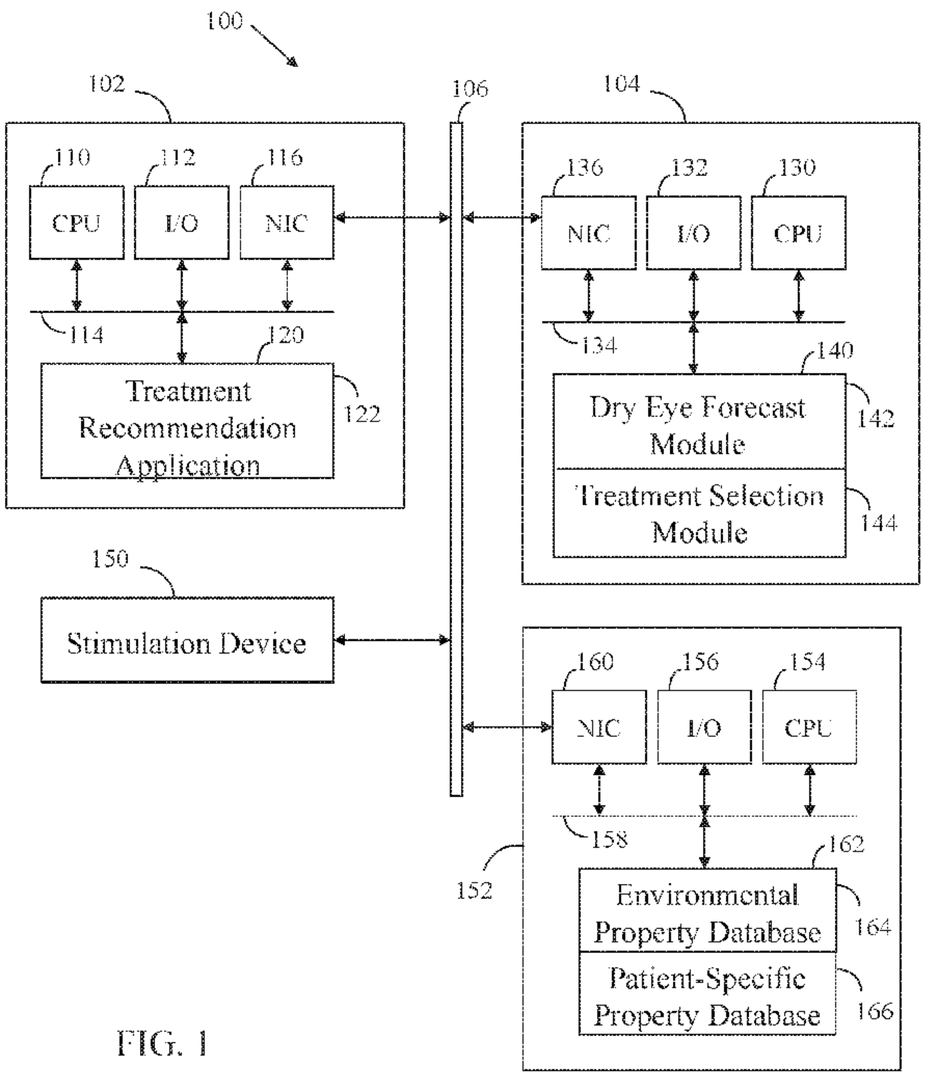

FIG. 1

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APPARATUS AND METHOD FOR DRY EYE FORECAST AND TREATMENT RECOMMENDATION

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority to U.S. Provisional Patent Application No. 62/429,694 filed December 02, 2016, and U.S. Provisional Patent Application No. 62/469,440 filed March 09, 2017. Each of these applications is hereby incorporated in its entirety by this reference.

FIELD

[0002] This invention relates generally to treatment of dry eye. More particularly, this invention relates to forming a dry eye forecast. The dry eye forecast may be based on properties related to dry eye symptoms. A treatment recommendation may be selected based on the dry eye forecast. Treatment may be applied according to the treatment recommendation.

BACKGROUND

[0003] Dry Eye Disease ("DED") is a condition that affects millions of people worldwide. More than 40 million people in North America have some form of dry eye, and many millions more suffer worldwide. DED results from the disruption of the natural tear film on the surface of the eye, and can result in ocular discomfort, visual disturbance, and a reduction in vision-related quality of life. Activities of daily living such as driving, computer use, housework, and reading have also been shown to be negatively impacted by DED. Patients with severe cases of DED are at risk for serious ocular health deficiencies such as corneal ulceration, and can experience a quality of life deficiency comparable to that of moderate-severe angina.

[0004] DED is progressive in nature, and fundamentally results from insufficient tear coverage on the surface of the eye. This poor tear coverage prevents healthy gas exchange and nutrient transport for the ocular surface, promotes cellular desiccation and creates a poor refractive surface for vision. Poor tear coverage typically results from: 1) insufficient aqueous tear production from the lacrimal glands (e.g. secondary to post-menopausal hormonal deficiency, auto-immune disease, LASIK surgery, etc.), and/or 2) excessive evaporation of aqueous tear resulting from dysfunction of the meibomian glands. Low tear volume causes a hyperosmolar environment that induces an inflamed state of the ocular surface. This inflammatory response

induces apoptosis of the surface cells which in turn prevents proper distribution of the tear film on the ocular surface so that any given tear volume is rendered less effective. This initiates a vicious cycle where more inflammation can ensue causing more surface cell damage, etc. Additionally, the neural control loop, which controls reflex tear activation, is disrupted because the sensory neurons in the surface of the eye are damaged. As a result, fewer tears are secreted and a second vicious cycle develops that results in further progression of the disease (fewer tears cause nerve cell loss, which results in fewer tears, etc.).

[0005] Commonly assigned U.S. Patent Application No. 14/256,915, filed April 18, 2014, and titled "NASAL STIMULATION DEVICES AND METHODS," U.S. Patent Application No. 14/630,471, filed February 24, 2015, and titled "POLYMER FORMULATIONS FOR NASOLACRIMAL STIMULATION," U.S. Patent Application No. 14/809,109, filed July 24, 2015, and titled "STIMULATION PATTERNS FOR TREATING DRY EYE," and U.S. Patent Application No. 14/920,860, filed October 22, 2015, and titled "STIMULATION DEVICES AND METHODS FOR TREATING DRY EYE," each of which is hereby incorporated by reference in its entirety, describe devices and methods for application of electrical stimulation to sensory neurons in the nasal cavity to activate the nasolacrimal reflex and thereby increase tear production. However, it would be desirable to additionally supply a patient with a treatment recommendation for stimulus delivery.

SUMMARY

[0006] Generally, a machine may include a processor and a memory connected to the processor, where the memory stores instructions executed by the processor to determine first and second properties related to dry eye symptoms of a patient. The properties may be used to form a dry eye forecast. A treatment recommendation may be selected based at least in part upon the dry eye forecast. The treatment recommendation may be supplied to a device. In some variations, the machine may further include instructions executed by the processor to determine a third property related to dry eye symptoms of the patient, wherein the instructions to form the dry eye forecast utilize the first, second, and third properties. In some variations, the machine may include instructions executed by the processor to supply the treatment recommendation to the device implemented as a computer device. In some variations, the machine may include instructions executed by the processor to supply the treatment recommendation to the device implemented as a stimulation device.

[0007] The properties related to dry eye symptoms may include one or more of an environmental property proximate to the patient or a patient-specific property. For example, a property may be a humidity, a relative humidity, an ambient temperature, a wind speed, a pollution level, a pollen count, condensation data, an air pressure, a vapor pressure, a UV index, a wind chill, a schedule of a patient, or a medical condition of a patient. In one non-limiting example, a first property is a relative humidity (*RH*) proximate to the patient, a second property is an ambient temperature (*T*) proximate to the patient, and the dry eye forecast is a value equal to

$$\begin{cases} 0, & RH * P(T) > 6.28 \\ 100 * [6.28 - RH * P(T)]/6.28, & RH * P(T) \leq 6.28 \end{cases}$$

where *P(T)* is the saturated water vapor pressure at temperature *T*. In another non-limiting example, the first property is a relative humidity (*RH*) proximate to the patient, the second property is an ambient temperature (*T*) proximate to the patient, and the dry eye forecast is a value equal to

$$\begin{cases} 0, & RH * P(T) < 3.768 \\ \dfrac{(100 * [6.28 - RH * P(T)]/6.28) - 40}{60} * 100, & RH * P(T) \geq 3.768 \end{cases}$$

where *P(T)* is the saturated water vapor pressure at temperature *T*.

[0008] The treatment recommendation may include stimulus delivery to a patient. The stimulus delivery may be an electrical stimulus delivery. The stimulus delivery may include delivery to a nasal mucosa of the patient. The treatment recommendation may specify characteristics of the stimulus delivery, such as a duration of stimulus delivery, a time of stimulus delivery, or a number of periods of stimulus delivery.

BRIEF DESCRIPTION OF THE FIGURES

[0009] FIG. 1 illustrates a system configured in accordance with an embodiment of the invention.

[0010] FIG. 2 illustrates a method performed in accordance with an embodiment of the invention.

[0011] FIG. 3 illustrates a stimulation device utilized in accordance with an embodiment of the invention.

[0012] FIGS. 4A-4D are scatterplots of evaporation rate versus relative humidity (FIGS. 4A and 4C) and versus temperature (FIGS. 4B and 4D) for first (FIGS. 4A-4B) and second (FIGS. 4C-4D) geographic locations.

[0013] FIGS. 5A-5B show exemplary displays utilized in accordance with an embodiment of the invention.

DETAILED DESCRIPTION

[0014] Described herein are systems and methods for selecting and supplying a treatment recommendation for dry eye. The treatment recommendation may be based on a dry eye forecast representing past, present, or future expected severity of dry eye symptoms of a patient. The dry eye forecast may be based on, for example, environmental properties proximate to a patient or patient-specific properties, such as a patient's schedule or medical history. The treatment recommendation may be selected to reduce current dry eye symptoms and/or prevent future dry eye symptoms. As such, supplying such a treatment recommendation may allow for reduction in symptoms using a minimum amount of treatment, may allow treatment to be tailored for a particular patient and/or environment, and/or may allow a patient to avoid or reduce future symptoms by administering prophylactic treatment. The recommended treatment may include stimulus delivery (e.g., electrical stimulus delivery) to the patient (e.g., to nasal mucosa of the patient). The treatment recommendation may specify characteristics of the stimulus delivery, such as the timing for stimulus delivery, duration of stimulus delivery, and/or parameters of stimulus delivery (e.g., waveform of an electrical stimulus).

Systems

[0015] In general, the systems described herein may comprise a stimulation device and a patient device comprising a treatment recommendation application. The systems may further comprise a server, which may comprise a dry eye forecast module and a treatment selection module, and a database server, which may comprise an environmental property database and a patient-specific property database. Some or all of the stimulation device, patient device, server, and database server may communicate via a network.

[0016] As one example, FIG. 1 illustrates a system 100 configured in accordance with an embodiment of the invention. The system 100 includes a stimulation device 150 and a patient device 102 that communicates with a server 104 via a network 106, which may be any combination of wired and/or wireless networks. The system 100 also includes a database server 152 that communicates with the server 104 via the network 106.

Patient Device

[0017] In an exemplary variation, the patient device 102 includes a central processing unit 110 linked to input/output devices 112 via a bus 114. The input/output devices 112 may include a keyboard, mouse, touch display, and the like. A network interface circuit 116 may also be connected to the bus 114. The network interface circuit 116 may provide connectivity to network 106. A memory 120 may also be connected to the bus 114. The memory 120 may store a treatment recommendation application 122 with instructions executed by the central processing unit 110 to implement operations disclosed herein. In some variations, the memory 120 may also store patient-specific properties related to dry eye symptoms, such as a schedule of a patient or a medical condition of a patient. The patient device 102 may be a computer, tablet, smart phone, and the like.

[0018] In some variations, the patient device 102 may comprise one or more sensors for determining a property, such as an environmental property proximate to the sensor. For example, the patient device 102 may comprise a temperature sensor, humidity sensor, wind sensor, and/or air pressure sensor. In some variations, a sensor (e.g., temperature sensor, humidity sensor, wind sensor, air pressure sensor) may be located in a separate device (i.e., separate from the patient device), such as but not limited to a keychain dongle, belt clip, or other wearable device, that is connected to the network 106. In some variations, a sensor may be located in a stimulation device such as the stimulation device 300 described with respect to FIG. 3. In some variations, the sensor may be located in a base unit configured for charging and/or sending/retrieving data from a stimulation device, where the base unit is connected to the network 106.

Server

[0019] Server 104 may also include components including a central processing unit 130, input/output devices 132, a bus 134, and a network interface circuit 136. A memory 140 may be

connected to the bus 134. The memory 140 may store instructions executed by the central processing unit 130 to implement operations disclosed herein. In one embodiment, the memory stores a dry eye forecast module 142. The dry eye forecast module determines properties related to dry eye symptoms of a patient and uses them to form a dry eye forecast for the patient. The memory 140 also may also store a treatment selection module 144. The treatment selection module 144 selects a treatment recommendation based upon the dry eye forecast. It should be appreciated that modules 142 and 144 may be incorporated into the treatment recommendation application 122. In such a variation, all processing may be performed by the patient device 102 without communicating with server 104.

Database Server

[0020] The database server 152 may also include components including a central processing unit 154, input/output devices 156, a bus 158, and a network interface circuit 160. A memory 162 may store an environmental property database 164 and a patient-specific property database 166.

[0021] The environmental property database 164 may contain one or more environmental properties related to dry eye symptoms. For example, the property may be a humidity or relative humidity, an ambient temperature, a wind speed, a pollution level, a pollen count, condensation data, an air pressure, a vapor pressure, a UV index, and/or a wind chill. When the property is an environmental property, the environmental property may be associated with a location proximate to the patient. The environmental property may also be associated with a time. For example, the environmental property may be associated with a current time, a past time, or a future time.

[0022] The patient-specific property database 166 may contain one or more patient-specific properties related to dry eye symptoms. For example, the property may be a schedule of a patient, a medical condition of a patient, a treatment history of a patient, or a reported symptom severity of a patient. It should be appreciated that in other variations, patient-specific properties may additionally or alternatively be stored by the memory 120 of patient device 102. It should also be appreciated that in these or other variations, the environmental property database and patient-specific property database may be on different database servers, each containing a central processing unit, input/output devices, a bus, a network interface circuit, and a memory.

Methods

[0023] The methods described herein may comprise forming a dry eye forecast from one or more properties related to dry eye symptoms of a patient, and using the dry eye forecast to select a treatment recommendation. The treatment recommendation may be supplied and used to provide treatment (e.g., stimulus delivery) to a patient.

Determine First Property

[0024] FIG. 2 illustrates operations associated with an embodiment of the invention. Initially, a first property is determined 200. The first property may be any of the properties described herein, such as an environmental property or a patient-specific property. The dry eye forecast module 142 may be used to implement this operation. For example, the dry eye forecast module 142 may retrieve one or more properties from the database server 152.

[0025] In variations in which the property is an environmental property, the environmental property may be associated with a location proximate to the patient. Accordingly, in some variations the dry eye forecast module 142 may provide a location interface to the patient device 102. The location interface may be displayed by an output device (e.g., a display) 112 associated with the patient device 102. The patient may use the location interface to input a location (e.g., a zip code, a city and state, a point on a displayed map, etc.). In other variations, a location of a patient may be determined using a location application stored by the memory 120 of the patient device 102, such as a global positioning system application. The first property may be retrieved from the environmental property database based on the location. In other variations, the first property may be retrieved from a sensor (e.g., a temperature sensor, humidity sensor, wind sensor, air pressure sensor, etc.) proximate to the patient. For example, the first property may be retrieved from a sensor on the patient device 102, on a separate wearable device, on a stimulation device, or on a base unit for a stimulation device. As one non-limiting example, the environmental property may be a humidity or a relative humidity proximate to the patient.

[0026] It should be appreciated that in other variations in which the property is an environmental property, the environmental property may be associated with a location not proximate to the patient at the time of determining the first property. For example, the location may be a location proximate to the patient at a future time, such as, for example, if the patient

intends to travel in the future. In some of these variations, the dry eye forecast module 142 may provide a location interface to the patient device 102. The location interface may be displayed by an output device (e.g., a display) 112 associated with the patient device 102. The patient may use the location interface to input a location (e.g., a zip code, a city and state, a point on a displayed map, etc.). The inputted location may, for example, correspond to an intended location of the patient at a future time. In other variations, the location of a patient may be determined using an application stored by the memory 120 of the patient device 102, such as a location stored for a future date in a calendar application.

[0027] In variations in which the property is a patient-specific property and a patient-specific property database 166 contains one or more patient-specific properties related to dry eye symptoms, the patient-specific property may be determined from the patient-specific property database 166. In variations in which the property is a patient-specific property and is stored by the memory 120 of the patient device 102, the patient-specific property may be retrieved from the patient device 102. In some variations the dry eye forecast module 142 may provide a patient-specific property interface to the patient device 102. The interface may be displayed by an output device (e.g., a display) 112 associated with the patient device 102. The patient may use the interface to input a patient-specific property. As non-limiting examples, for instance, the patient may use the interface to input a daily schedule or information about current dry eye symptom severity.

Determine Second Property

[0028] A second property may be determined 202. The second property may be any of the properties described herein, such as an environmental property or a patient-specific property. The dry eye forecast module 142 may be used to implement this operation. For example, the dry eye forecast module 142 may retrieve one or more properties from the database server 152.

[0029] In variations in which the property is an environmental property, the environmental property may be associated with a location proximate to the patient. Accordingly, in some variations the dry eye forecast module 142 may provide to the patient device 102 a location interface. The location interface may be displayed by an output device (e.g., a display) 112 associated with the patient device 102. The patient may use the location interface to input a location (e.g., a zip code, a city and state, a point on a displayed map, etc.). In other variations, a

location of a patient may be determined using a location application stored by the memory 120 of the patient device 102, such as a global positioning system application. The second property may be retrieved from the environmental property database based on the location. In yet other variations, the second property may be retrieved from the environmental property database using the location provided with respect to step 200 in which a first property was determined. In other variations, the second property may be retrieved from a sensor (e.g., a temperature sensor, humidity sensor, wind sensor, air pressure sensor, etc.) proximate to the patient. For example, the second property may be retrieved from a sensor on the patient device 102, on a separate wearable device, on a stimulation device, or on a base unit for a stimulation device. As one non-limiting example, the environmental property may be an ambient temperature proximate to the patient.

[0030] It should be appreciated that in other variations in which the property is an environmental property, the environmental property may be associated with a location not proximate to the patient at the time of determining the second property. For example, the location may be a location proximate to the patient at a future time, such as, for example, if the patient intends to travel in the future. In some of these variations, the dry eye forecast module 142 may provide a location interface to the patient device 102. The location interface may be displayed by an output device (e.g., a display) 112 associated with the patient device 102. The patient may use the location interface to input a location (e.g., a zip code, a city and state, a point on a displayed map, etc.). The inputted location may, for example, correspond to an intended location of the patient at a future time. In other variations, the location of a patient may be determined using an application stored by the memory 120 of the patient device 102, such as a location stored for a future date in a calendar application.

[0031] In variations in which the property is a patient-specific property and a patient-specific property database 166 contains one or more patient-specific properties related to dry eye symptoms, the patient-specific property may be determined from the patient-specific property database 166. In variations in which the property is a patient-specific property and is stored by the memory 120 of the patient device 102, the patient-specific property may be retrieved from the patient device 102. In some variations the dry eye forecast module 142 may provide a patient-specific property interface to the patient device 102. The interface may be displayed by an output device (e.g., a display) 112 associated with the patient device 102. The patient may use

the interface to input a patient-specific property. As a non-limiting example, for instance, the patient-specific property may be a medical condition of the patient.

Determine Third Property

[0032] A third property may be determined 204. The third property may be any of the properties described herein, such as an environmental property or a patient-specific property. The dry eye forecast module 142 may be used to implement this operation. For example, the dry eye forecast module 142 may retrieve one or more properties from the database server 152.

[0033] In variations in which the property is an environmental property, the environmental property may be associated with a location proximate to the patient. Accordingly, in some variations the dry eye forecast module 142 may provide to the patient device 102 a location interface. The location interface may be displayed by an output device (e.g., a display) 112 associated with the patient device 102. The patient may use the location interface to input a location (e.g., a zip code, a city and state, a point on a displayed map, etc.). In other variations, a location of a patient may be determined using a location application stored by the memory 120 of the patient device 102, such as a global positioning system application. The third property may be retrieved from the environmental property database using the location. In yet other variations, the third property may be retrieved from the environmental property database based on the location provided with respect to step 200 in which a first property was determined, or using the location provided with respect to step 202 in which a second property was determined. As non-limiting examples, the environmental property may be a wind speed, a pollution level, a pollen count, condensation data, an air pressure, a vapor pressure, a UV index, or a wind chill proximate to the patient. In other variations, the third property may be retrieved from a sensor (e.g., a temperature sensor, humidity sensor, wind sensor, air pressure sensor, etc.) proximate to the patient. For example, the third property may be retrieved from a sensor on the patient device 102, on a separate wearable device, on a stimulation device, or on a base unit for a stimulation device.

[0034] It should be appreciated that in other variations in which the property is an environmental property, the environmental property may be associated with a location not proximate to the patient at the time of determining the third property. For example, the location may be a location proximate to the patient at a future time, such as, for example, if the patient

intends to travel in the future. In some of these variations, the dry eye forecast module 142 may provide a location interface to the patient device 102. The location interface may be displayed by an output device (e.g., a display) 112 associated with the patient device 102. The patient may use the location interface to input a location (e.g., a zip code, a city and state, a point on a displayed map, etc.). The inputted location may, for example, correspond to an intended location of the patient at a future time. In other variations, the location of a patient may be determined using an application stored by the memory 120 of the patient device 102, such as a location stored for a future date in a calendar application.

[0035] In variations in which the property is a patient-specific property and a patient-specific property database 166 contains one or more patient-specific properties related to dry eye symptoms, the patient-specific property may be determined from the patient-specific property database 166. In variations in which the property is a patient-specific property and is stored by the memory 120 of the patient device 102, the patient-specific property may be retrieved from the patient device 102. In some variations the dry eye forecast module 142 may provide a patient-specific property interface to the patient device 102. The interface may be displayed by an output device (e.g., a display) 112 associated with the patient device 102. The patient may use the interface to input a patient-specific property.

[0036] It should be appreciated that any suitable number of properties may be determined as part of the methods described herein. For example, in some variations of the method, a single property may be determined and used to form a dry eye forecast. In other variations, two properties may be determined and used to form a dry eye forecast, or three properties may be determined and used to form a dry eye forecast. In yet other variations, more than three properties may be determined and used to form a dry eye forecast, such as but not limited to four, five, six, or more properties. Each property may be determined in a similar way as described herein with respect to the first, second, and third properties.

Form Dry Eye Forecast

[0037] The determined properties may be used to form a dry eye forecast 206. The dry eye forecast module 142 may implement operation 206. The dry eye forecast may be a representation of the expected severity of dry eye symptoms in a patient. In some variations, the dry eye forecast may represent the expected severity of dry eye symptoms at a single time point,

i.e., a past, current, or present time. In other variations, the dry eye forecast may represent the expected severity of dry eye symptoms over a period of time, e.g., over a period of hours or days.

[0038] The dry eye forecast may be formed based on the determined properties using a suitable operation. For example, in variations in which a determined property is a humidity or relative humidity level, the dry eye forecast may reflect an increased severity of dry eye symptoms associated with a low humidity or relative humidity level. In variations in which a determined property is an irritant level, such as a pollution level or a pollen count, the dry eye forecast may reflect an increased severity of dry eye symptoms associated with a high irritant level. In variations in which a determined property is a wind speed, the dry eye forecast may reflect an increased severity of dry eye symptoms associated with a high wind speed. In variations in which a determined property is a UV index, the dry eye forecast may reflect an increased severity of dry eye symptoms associated with a high UV index. In variations in which a determined property is a schedule of a patient, the dry eye forecast may reflect an increased severity of dry eye symptoms associated with certain activities, such as but not limited to airplane travel, nighttime driving, and computer use. In variations in which a determined property is a medical condition of a patient, the dry eye forecast may reflect an increased severity of dry eye symptoms associated with certain medical conditions, such as but not limited to Sjögren's syndrome. In variations in which a determined property is a treatment history of a patient, the dry eye forecast may reflect an increased severity of dry eye symptoms associated with a history of more extensive treatment for dry eye disease, such as but not limited to more frequent use of intranasal stimulation, longer duration of intranasal stimulation, and use of other therapies for dry eye (e.g., artificial tears, cyclosporine, etc.).

[0039] As one example, the dry eye forecast may be based at least partially on the amount of expected tear evaporation. Expected tear evaporation may be calculated using the properties described herein, such as environmental and patient-specific properties, as well as estimates of the surface area of tear in contact with air, and tear temperature. Any suitable method for estimating expected tear evaporation from the determined properties may be used in forming a dry eye forecast. For example, when E is the evaporation rate (Kg/min), P is water's vapor pressure at ambient temperature (kPa), V is the velocity of air above the water surface (m/s), A is the surface area of water (m^2), T_a is the ambient temperature (K), M is the molecular weight of

water (18.02 g/mol or dimensionless), R is the universal gas constant (8314.5 Pa·m³/(kmol·K)), $\emptyset$ is the evaporation coefficient (Kg/m²*h), Xs is the humidity ratio in saturated air (Kg Water /Kg of moist air), and X is the humidity ratio in air (Kg Water /Kg of dry air), the evaporation rate may be estimated according to one of the following equations

$$evaporation\ rate = \left[\frac{0.106PAM^{2/3}V^{0.78}}{RT_a}\right] \text{ or}$$

$$evaporation\ rate = \left[\frac{0.002VPAM}{RT_a}\right] \text{ or}$$

$$evaporation\ rate = \frac{\emptyset A(X_s - X)}{60}, \text{ where}$$

$$X_s = 0.622 * \frac{p_{ws}}{p_a - p_{ws}} \text{ and } p_{ws} = \frac{e^{(77.35+0.0057T-7235/T)}}{T^{8.2}}, \text{ and}$$

$$X = 0.622 * \frac{p_w}{p_a - p_w}$$

where p_w is the partial vapor pressure of water vapor in moist air (Pa) (relative humidity * p_{ws}), p_a is the atmospheric pressure of moist air (Pa), p_{ws} is the saturation pressure of water vapor, and T is the temperature (Kelvin). Because p_w is small relative to p_a, the relationship between X and Xs is almost linear.

[0040] For example, FIGS. 4A-4D show examples of expected tear evaporation when a first property is temperature, a second property is relative humidity, a third property is pressure, and a fourth property is wind speed. These figures show scatterplots of calculated average evaporation rates based on the environmental properties proximate to a patient of temperature, relative humidity, pressure, and wind speed, using the third formula above $\left(evaporation\ rate = \frac{\emptyset A(X_s - X)}{60}\right)$. FIGS. 4A-4B are scatterplots of evaporation rate (g/s) versus mean relative humidity (%) (FIG. 4A) and versus mean temperature (Celsius) (FIG. 4B) for a first geographic location. FIGS. 4C-4D are scatterplots of evaporation rate (g/s) versus mean relative humidity (%) (FIG. 4C) and versus mean temperature (Celsius) (FIG. 4D) for a second geographic location. Each data point is for a particular day. The surface area of the tear was assumed to be 2 cm², and the determined environmental properties (temperature, relative humidity, pressure, and wind

speed) were average values for each day. The range of average evaporation rates (g/s) at each location are shown in Table 1 below.

Location	Min	Max	Median	25%	75%
First Location	6.02e-9	3.43e-7	8.06e-8	4.85e-8	1.25e-7
Second Location	3.27e-8	8.43e-7	2.00e-7	1.07e-7	2.90e-7

Table 1. Range of average evaporation rates (g/s) at two locations.

[0041] The dry eye forecast for each day in each location may be based on the calculated evaporation rate. For example, in some variations the dry eye forecast may be a value equal to or positively correlated with the evaporation rate, with higher values corresponding to more severe dry eye symptoms, and lower values corresponding to less severe dry eye symptoms.

[0042] In other variations, expected tear evaporation may be at least partially based on other models using the relationship between water vapor pressure of air proximate to a patient and water vapor pressure of the tear film. For instance, the patient and tear film may be assumed to be a heat sink held at body temperature, which is 37°C (310.15 Kelvin). The patient's local environment may be assumed to be an independent heat sink, with temperature T and relative humidity RH. Air mixing may be assumed to be instantaneous and complete, so that no layer of warm air is formed above the eye. Based on these assumptions, the water vapor pressure of air (pressure exerted by water molecules arriving at a surface) is equal to

$$air\ water\ vapor\ pressure = RH * P(T)$$

where $P(T)$ is the saturated water vapor pressure at temperature T. Also based on these assumption, the water vapor pressure of a tear (pressure exerted by water molecules exiting the liquid phase and entering the gaseous phase) is equal to

$$tear\ water\ vapor\ pressure = P(37°\text{C}) = 6.28\ \text{kPa}.$$

[0043] The difference between the water vapor pressures, δ, of these two heat sinks is thus equal to

$$\delta = 6.28 - RH * P(T) \quad (\text{in kPa}).$$

[0044] This differential represents the underlying physical quantity that drives evaporation under these assumptions, and has a maximum of 6.28 kPa (when $RH = 0\%$).

[0045] Thus, when a first property is a relative humidity (RH) proximate to a patient and a second property is a temperature (T) proximate to the patient, this differential between the water vapor pressures may be used to form a dry eye forecast. For instance, in some variations the invention comprises a dry eye forecast that is a value between 0 (corresponding to the least severe dry eye symptoms) and 100 (corresponding to the most severe dry eye symptoms) derived from dry eye forecast formula (A) below:

$$dry\ eye\ forecast\ value =$$

$$\begin{cases} 0, & RH * P(T) > 6.28 \\ 100 * [6.28 - RH * P(T)]/6.28, & RH * P(T) \leq 6.28 \end{cases} \quad \text{(A)}$$

where $P(T)$ is the saturated water vapor pressure at temperature T, which may be calculated or looked up in a vapor pressure table. Exemplary dry eye forecast values for various relative humidities and temperatures are shown in Table 2 below.

Temperature (°F)	Humidity (%)	Dry Eye Forecast Value
109	19	74
107	10	87
106	21	74
104	19	78
103	25	72
93	62	49
92	59	53
92	62	51
89	70	49
89	74	46
78	66	66
69	54	79
68	54	80
67	47	83
66	46	84

Table 2. Example dry eye forecast values.

[0046] As another example, if a patient is traveling in an airplane, the relative humidity may be about 20% and the temperature may be about 20°C, resulting in a dry eye forecast value of 92. It should be appreciated that in other variations of the invention, tear evaporation may be modeled using other suitable methods, including methods not assuming perfect air mixing and thus modeling the transition layer. It should also be appreciated that in some variations of the invention, patient feedback regarding dry eye symptom intensity may be used to refine the formation of a dry eye forecast from determined properties. For example, a patient may indicate the severity of his or her dry eye symptoms on a user interface (e.g., on the patient device), where higher ratings of dry eye symptoms contribute to a higher dry eye forecast value (or adjusted dry eye forecast value, described below). In one exemplary variation, the patient may rate the severity of his or her dry eye symptoms on a numerical scale (e.g., 1 to 5, with 1 being not severe and 5 being extremely severe), and the rating may be correlated to a multiplier on the dry eye forecast value obtained via the dry eye forecast formula (A) above (or the adjusted dry eye forecast value formula described below).

[0047] In some variations of the invention in which the dry eye forecast is a value, the dry eye forecast may be based on a calculation designed such that the resulting values span a desired range. For example, the dry eye forecast formula (A) above may in theory mathematically result in values between 1 and 100, but real-world, global relative humidity and temperature values may in fact limit the range of resulting dry eye forecast values. In some variations of the invention, a formula for dry eye forecast values may be adjusted such that real-world, global relative humidity and temperature values result in a broader range of resulting dry eye forecast values. As one example, in some variations the invention comprises a dry eye forecast value calculated using the dry eye forecast formula (A) above that is adjusted as follows:

$$adjusted\ dry\ eye\ forecast\ value = \frac{value\ from\ dry\ eye\ forecast\ formula\ (A) - 40}{60} * 100$$

where negative adjusted dry eye forecast values are set to zero. That is, in these variations the invention comprises an adjusted dry eye forecast that is a value between 0 (corresponding to the least severe dry eye symptoms) and 100 (corresponding to the most severe dry eye symptoms) equal to

$$adjusted\ dry\ eye\ forecast\ value = \begin{cases} 0, & RH * P(T) < 3.768 \\ \frac{(100 * [6.28 - RH * P(T)]/6.28) - 40}{60} * 100, & RH * P(T) \geq 3.768 \end{cases}$$

where *P(T)* is the saturated water vapor pressure at temperature *T*, which may be calculated or looked up in a vapor pressure table. Example adjusted dry eye forecast values for various relative humidities and temperatures are shown in Table 3 below. As shown there, the values span a broader range (10 to 78) than the unadjusted values of Table 2 (46 to 87).

Temperature (°F)	Humidity (%)	Adjusted Dry Eye Forecast Value
109	19	57
107	10	78
106	21	57
104	19	63
103	25	53
93	62	15
92	59	22
92	62	18
89	70	15
89	74	10
78	66	43
69	54	65
68	54	67
67	47	72
66	46	73

Table 3. Example dry eye forecast values.

[0048] While the example above illustrates an adjustment that is implemented for all dry eye forecast values, in other variations of the invention, dry eye forecast values for one patient may be adjusted differently than dry eye forecast values for another patient. For instance, rather than adjusting all dry eye forecast values in the same way, regardless of a patient's location, dry eye forecast values may be adjusted instead at least partially based on a patient's location. Because certain geographic locations may have particular ranges of environmental properties (e.g., temperatures and humidities), dry eye forecast values based on environmental properties may result in a limited range of values. That is, the range of dry eye forecast values calculated using a universal formula (i.e., the same formula for all geographic locations) based on environmental properties may be limited to a particular range of values within the theoretical range of outputs of the universal formula, and that range may be different for different geographic locations. As another example, when a dry eye forecast is a value based on a patient-specific property such as, for example, a medical condition of the patient, dry eye forecast values for that patient may be limited to a particular range of values due to the medical condition. For example, when the dry

eye forecast is a value based on a medical condition of a patient, a patient having Sjögren's syndrome may have dry eye forecast values within a narrow range of severity.

[0049] When a patient's dry eye forecast values have variation only within a small range of values, the dry eye forecast values may be less useful for selecting treatment recommendations, and when provided to a patient, less meaningful for the patient. Thus, it may be desirable in some variations to use different formulas for dry eye forecast values (e.g., non-universal formulas) for different patients, such as different formulas for different locations, or different formulas for different medical conditions. In some variations, for example, the invention may comprise carrying out the same initial calculation regardless of location (e.g., using the dry eye forecast formula (A) above), and then applying a location-specific adjustment. In some variations of the invention, for example, such a location-specific adjustment may normalize the distribution of dry eye forecast values for a particular location (e.g., a zip code, a city, etc.) to a uniform distribution within a range (e.g., between 0 and 100). In other variations, for example, the invention may comprise carrying out the same initial calculation regardless of location (e.g., using the dry eye forecast formula (A) above), and then applying a patient-specific adjustment. In some variations of the invention, for example, such a patient-specific adjustment may normalize the distribution of dry eye forecast values for the particular patient to a uniform distribution within a range (e.g., between 0 and 100). The normalization of the distribution of dry eye forecast values may, for example, be based on all previous dry eye forecast values for the patient, or as another example, may be based on a subset of previous dry eye forecast values for the patient, such as but not limited to dry eye forecast values for the patient from the previous week, previous 2 weeks, previous month, previous 3 months, previous 6 months, previous year, or the like.

[0050] Once formed, the dry eye forecast may be provided to a patient. For example, the dry eye forecast may be provided to the patient device 102 and displayed by an output device (e.g., a display) 112 associated with the patient device 102. The dry eye forecast may have any suitable form. For example, the dry eye forecast may comprise a single value (e.g., representing the expected severity of dry eye symptoms at a single time point) or a plurality of values (e.g., representing the expected severity of dry eye symptoms over a period of time). When the dry eye forecast is a value or a plurality of values (e.g., between 0 and 100, with 100 representing the most severe symptoms; between 0 and 10, with 10 representing the most severe symptoms; etc.),

the value(s) may be displayed by an output device (e.g., a display) 112 as one or more numerals, a line graph, a bar chart, one or more colors, a combination of these forms, or the like.

[0051] For example, FIGS. 5A-5B show an exemplary display 500 that may be used to provide a dry eye forecast to a patient. In this example, the dry eye forecast is a value and is displayed via an indicator 502 that provides the value numerically, graphically, and/or with text indicating the severity of expected dry eye symptoms (here, "low"). The display 500 may also allow a patient to view properties related to dry eye symptoms, such as humidity, temperature, pollen count, pollution index, and wind, as shown in FIG. 5A. In some variations, the display 500 may present a plurality of dry eye forecasts to a patient, such as the dry eye forecast for a series of days or over a geographic region.

Select Treatment Recommendation

[0052] A treatment recommendation may be selected 208 based upon the dry eye forecast. The treatment selection module 144 may implement this operation.

[0053] The treatment recommendation may include stimulus delivery to the patient. The treatment recommendation may include various parameters of the stimulus delivery, such as but not limited to one or more of the duration of the stimulus delivery, the time of stimulus delivery, the number of periods of the stimulus delivery, and the form of stimulus delivery (e.g., stimulation waveform). Suitable treatment recommendations are described in commonly assigned U.S. Patent Application No. 14/256,915, filed April 18, 2014, U.S. Patent Application No. 14/809,109, filed July 24, 2015, and U.S. Patent Application No. 14/920,860, filed October 22, 2015, each of which was previously incorporated by reference in its entirety.

[0054] The treatment selection based on the dry eye forecast may be intended to achieve one or more goals. For example, in some variations, the treatment recommendation may be selected to prevent worsening of dry eye symptoms; based on the dry eye forecast, the treatment recommendation may include prophylactic stimulus delivery. Additionally or alternatively, the treatment recommendation may be selected to maximize symptom relief with a minimum amount of stimulus delivery, and/or may be selected to optimize the stimulation device battery life. In some variations, the treatment selection module 144 may utilize patient feedback regarding dry eye symptom intensity to refine the algorithm for treatment selection.

Supply Treatment Recommendation

[0055] The treatment recommendation may be supplied 210. In some variations, the treatment recommendation may include one or more of a stimulation intensity, stimulation duration, stimulation frequency, and stimulation amplitude. Additionally or alternatively, the treatment recommendation may include a recommendation for frequency of treatment sessions (e.g., every 30 minutes, every hour, etc.).

[0056] In the case of a server-based implementation, the treatment recommendation is supplied to the patient device 102 from the server 104 via network 106. In the case of a patient-side implementation, the treatment recommendation application 122 supplies the treatment recommendation to a display on the patient device. FIG. 5B shows the display 500 showing an icon 504 allowing a patient to view and/or supply a treatment recommendation. Also shown are icons 506, 508, 510, and 512, which may allow a patient to view other information, such as but not limited to instructions and support, historical dry eye forecasts, future dry eye forecasts (e.g., a 5-day outlook), data regarding past treatment sessions, and the like.

[0057] The treatment recommendation may also be supplied to a stimulation device 150 from either the patient device 102 or the server 104. In these variations, the treatment recommendation may be supplied to the stimulation device 150 either directly or via a base unit.

Use Treatment Recommendation to Apply Treatment

[0058] The final operation of FIG. 2 is to use the treatment recommendation to apply treatment 212. In one example, the treatment is electrical stimulation. Stimulation may be carried out manually in accordance with a displayed treatment recommendation. Alternately, stimulation may be automatically executed by the stimulation device 150. Commonly assigned U.S. Patent Application No. 14/256,915, filed April 18, 2014, U.S. Patent Application No. 14/630,471, filed February 24, 2015, U.S. Patent Application No. 14/809,109, filed July 24, 2015, and U.S. Patent Application No. 14/920,860, filed October 22, 2015, each of which was previously incorporated by reference in its entirety, disclose stimulation devices that may be used in accordance with embodiments of the invention.

[0059] FIG. 3 shows one variation of a stimulation device 300 that may be used in accordance with embodiments of the invention. Stimulation device 300 includes a stimulator probe 302

configured to deliver a stimulus to the patient and having a first nasal insertion prong 304 and a second nasal insertion prong 306, each of which has an electrode 308. The stimulation device 300 also includes a stimulator body 310 configured to generate the stimulus and having a housing 312 and a user interface 314 including indicator lights 320 and buttons 316 and 318. A patient may place the electrodes 308 in contact with nasal tissue (e.g., nasal mucosa adjacent the nasal septum) and deliver a stimulus in accordance with the treatment recommendation.

[0060] Additionally or alternatively, stimulation may be manually and/or automatically executed by other suitable stimulation devices. For example, electrical stimulation may be delivered by a microstimulator implant, such as those described in U.S. Patent Application No. 13/441,806, filed April 06, 2012 and titled "STIMULATION DEVICES AND METHODS", which is hereby incorporated in its entirety by this reference. Furthermore, other treatment may include ultrasound stimulation (e.g., via ultrasound transducers), chemical stimulation, or any suitable stimulation.

[0061] An embodiment of the present invention relates to a computer storage product with a non-transitory computer readable storage medium having computer code thereon for performing various computer-implemented operations. The media and computer code may be those specially designed and constructed for the purposes of the present invention, or they may be of the kind well known and available to those having skill in the computer software arts. Examples of computer-readable media include, but are not limited to: magnetic media, optical media, magneto-optical media and hardware devices that are specially configured to store and execute program code, such as application-specific integrated circuits ("ASICs"), programmable logic devices ("PLDs") and ROM and RAM devices. Examples of computer code include machine code, such as produced by a compiler, and files containing higher-level code that are executed by a computer using an interpreter. For example, an embodiment of the invention may be implemented using JAVA®, C++, JavaScript, or other object-oriented or functional programming languages and development tools. Another embodiment of the invention may be implemented in hardwired circuitry in place of, or in combination with, machine-executable software instructions.

[0062] The foregoing description, for purposes of explanation, used specific nomenclature to provide a thorough understanding of the invention. However, it will be apparent to one skilled in the art that specific details are not required in order to practice the invention. Thus, the foregoing

descriptions of specific embodiments of the invention are presented for purposes of illustration and description. They are not intended to be exhaustive or to limit the invention to the precise forms disclosed; obviously, many modifications and variations are possible in view of the above teachings. The embodiments were chosen and described in order to best explain the principles of the invention and its practical applications, they thereby enable others skilled in the art to best utilize the invention and various embodiments with various modifications as are suited to the particular use contemplated. It is intended that the following claims and their equivalents define the scope of the invention.

CLAIMS

1. A machine, comprising:

a processor; and

a memory connected to the processor, the memory storing instructions executed by the processor to:

determine a first property related to dry eye symptoms of a patient;

determine a second property related to dry eye symptoms of the patient;

form a dry eye forecast based upon the first property and the second property;

select a treatment recommendation based upon the dry eye forecast; and

supply the treatment recommendation to a device connected to the machine through a computer network.

2. The machine of claim 1, wherein the first property is a humidity or relative humidity proximate to the patient.

3. The machine of claim 1, wherein the second property is an ambient temperature proximate to the patient.

4. The machine of claim 1, further comprising instructions executed by the processor to determine a third property related to dry eye symptoms of the patient, wherein the instructions to form the dry eye forecast utilize the first property, the second property, and the third property.

5. The machine of claim 4, wherein the third property is an environmental property proximate to the patient.

6. The machine of claim 5, wherein the third property is a wind speed.

7. The machine of claim 5, wherein the third property is a pollution level.

8. The machine of claim 5, wherein the third property is a pollen count.

9. The machine of claim 5, wherein the third property is condensation data.

10. The machine of claim 5, wherein the third property is an air pressure.

11. The machine of claim 5, wherein the third property is a vapor pressure.

12. The machine of claim 5, wherein the third property is a UV index.

13. The machine of claim 5, wherein the third property is a wind chill.

14. The machine of claim 4, wherein the third property is a patient-specific property.

15. The machine of claim 14, wherein the third property is a schedule of the patient.

16. The machine of claim 14, wherein the third property is a medical condition of the patient.

17. The machine of claim 1, wherein the treatment recommendation includes stimulus delivery to the patient.

18. The machine of claim 17, wherein the treatment recommendation includes a duration of the stimulus delivery.

19. The machine of claim 17, wherein the treatment recommendation includes a time of the stimulus delivery.

20. The machine of claim 17, wherein the treatment recommendation includes a number of periods of the stimulus delivery.

21. The machine of claim 17, wherein the stimulus delivery is an electrical stimulus delivery.

22. The machine of claim 17, wherein the treatment recommendation includes stimulus delivery to a nasal mucosa of the patient.

23. The machine of claim 1, including instructions executed by the processor to supply the treatment recommendation to the device implemented as a computing device.

24. The machine of claim 1, including instructions executed by the processor to supply the treatment recommendation to the device implemented as a stimulation device.

25. The machine of claim 1, wherein the first property is a relative humidity (RH) proximate to the patient, the second property is an ambient temperature (T) proximate to the patient, and the dry eye forecast is a value equal to

$$\begin{cases} 0, & RH * P(T) > 6.28 \\ 100 * [6.28 - RH * P(T)]/6.28, & RH * P(T) \leq 6.28 \end{cases}$$

where $P(T)$ is the saturated water vapor pressure at temperature T.

26. The machine of claim 1, wherein the first property is a relative humidity (RH) proximate to the patient, the second property is an ambient temperature (T) proximate to the patient, and the dry eye forecast is a value equal to

$$\begin{cases} 0, & RH * P(T) < 3.768 \\ \dfrac{(100 * [6.28 - RH * P(T)]/6.28) - 40}{60} * 100, & RH * P(T) \geq 3.768 \end{cases}$$

where $P(T)$ is the saturated water vapor pressure at temperature T.

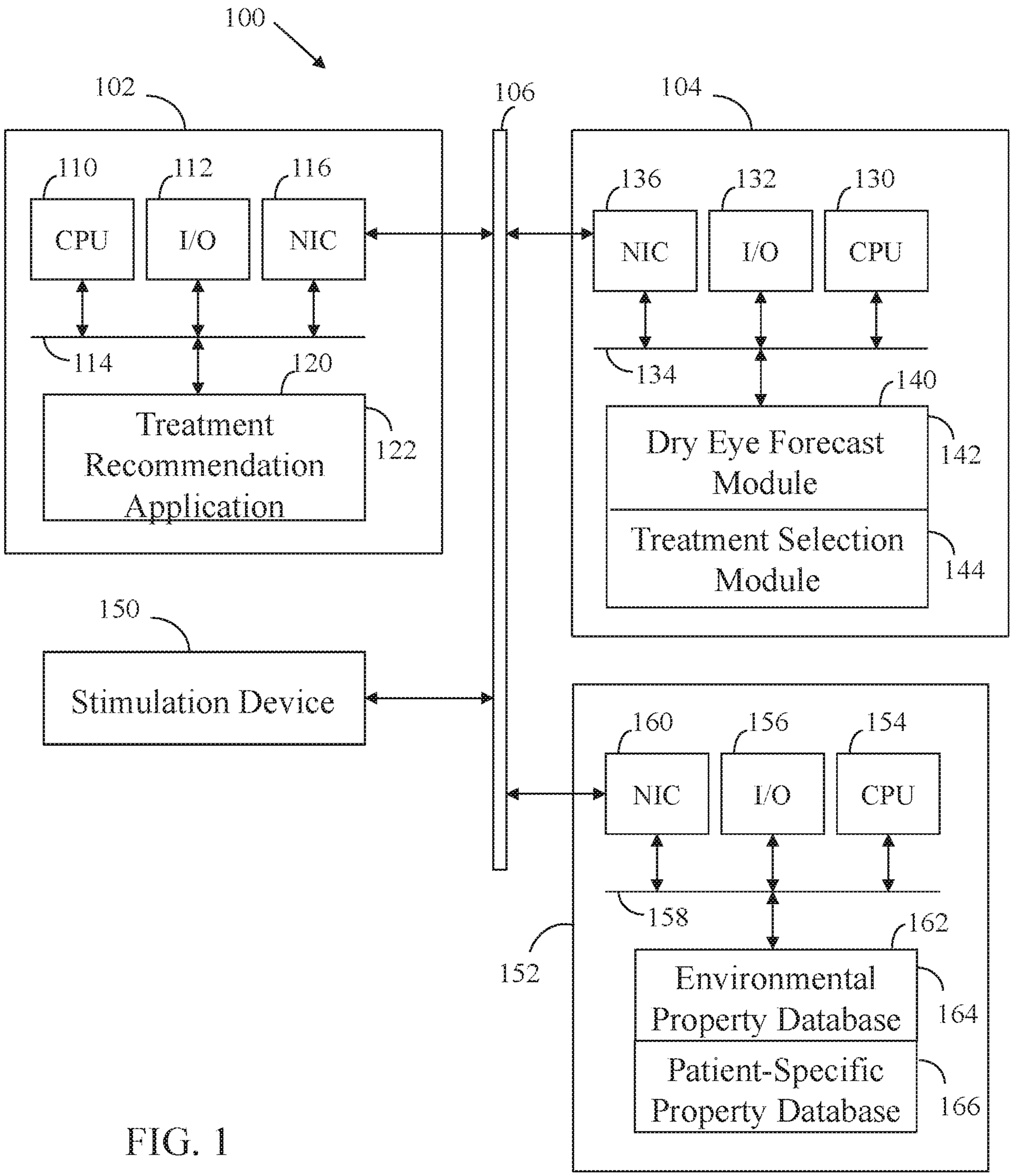
100
102
106
104
110
112
116
CPU
I/O
NIC
114
120
Treatment Recommendation Application
122
136
132
130
NIC
I/O
CPU
134
140
Dry Eye Forecast Module
142
Treatment Selection Module
144
150
Stimulation Device
160
156
154
NIC
I/O
CPU
158
162
152
Environmental Property Database
164
Patient-Specific Property Database
166

FIG. 1

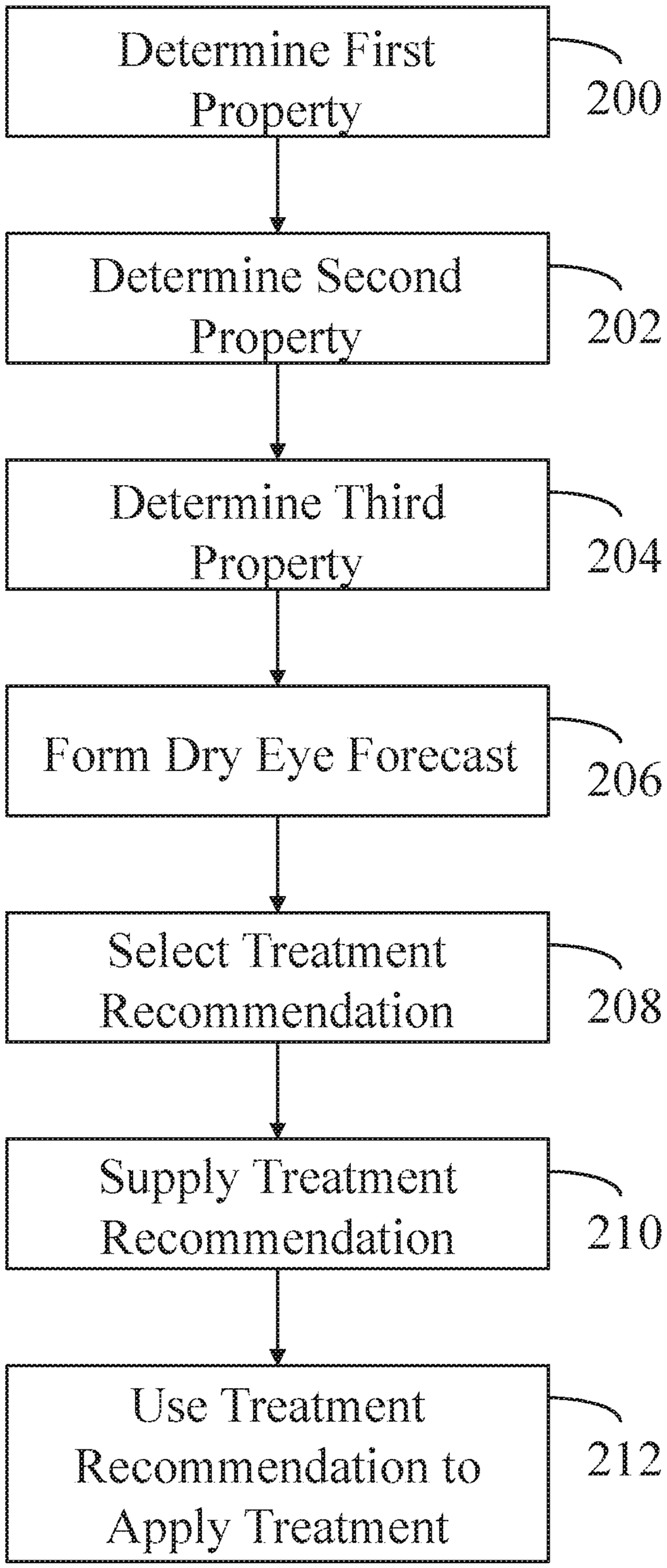
Determine First Property
200
Determine Second Property
202
Determine Third Property
204
Form Dry Eye Forecast
206
Select Treatment Recommendation
208
Supply Treatment Recommendation
210
Use Treatment Recommendation to Apply Treatment
212

FIG. 2

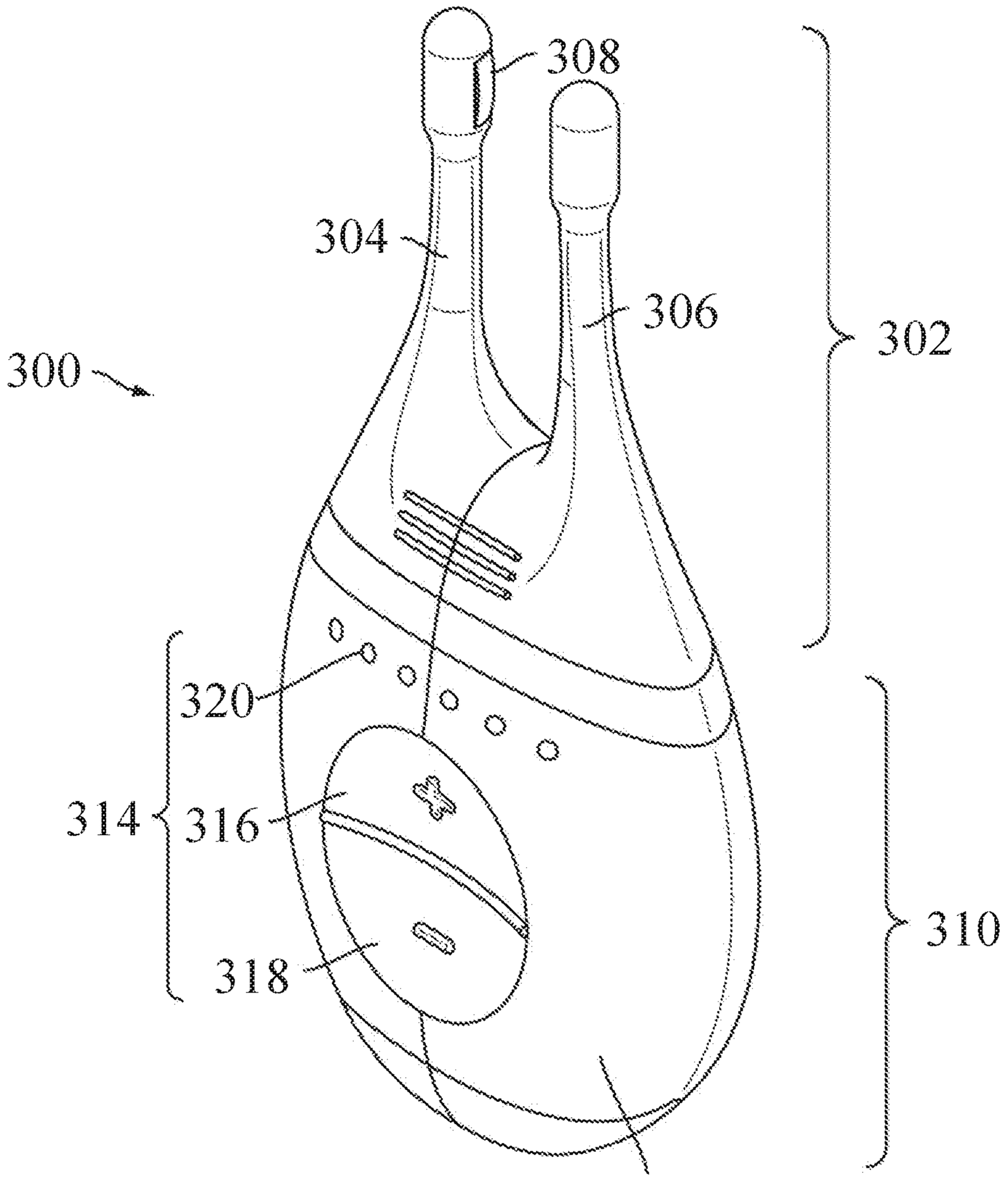

FIG. 3

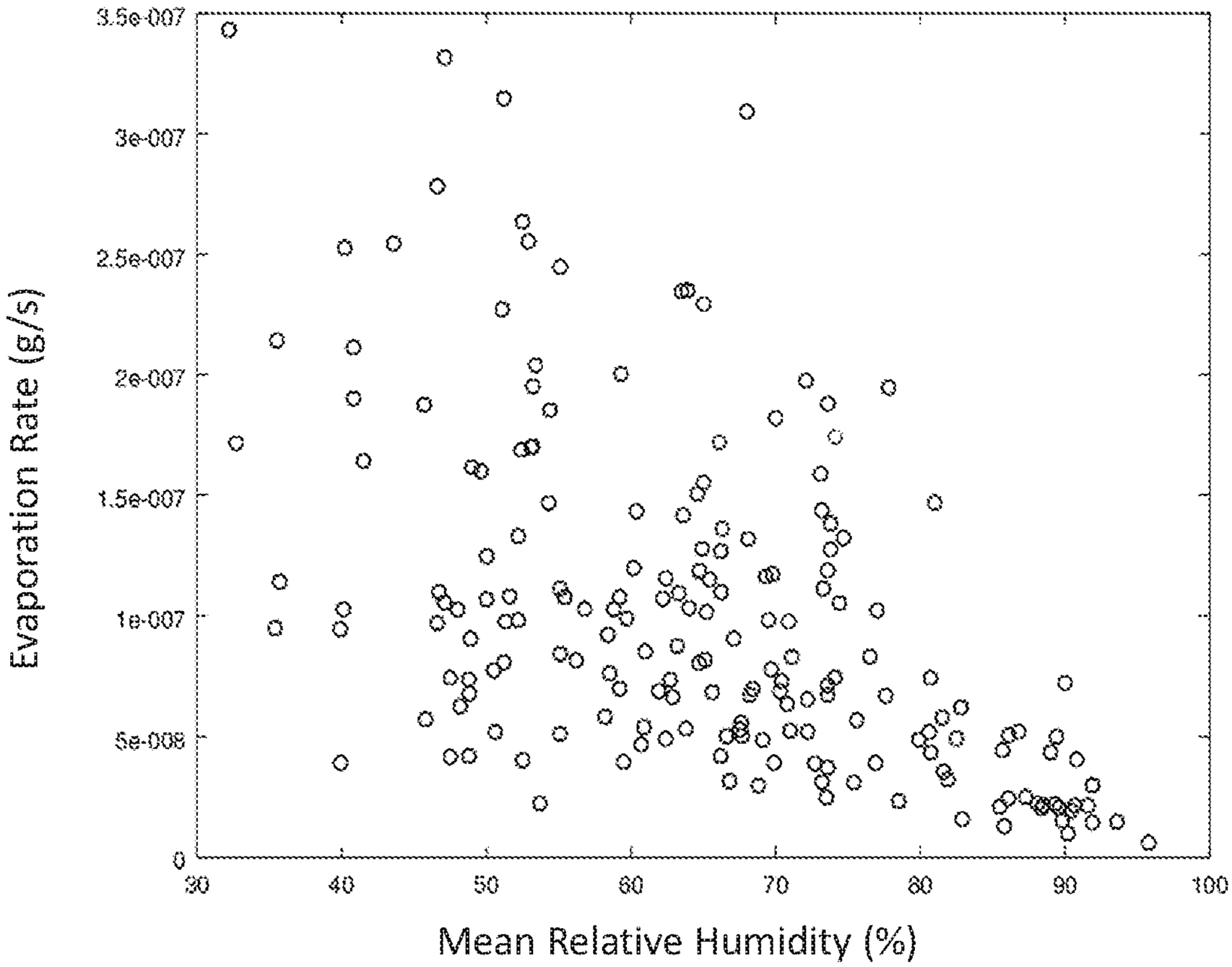
3.5e-007
3e-007
2.5e-007
2e-007
1.5e-007
1e-007
5e-008
0
Evaporation Rate (g/s)
30
40
50
60
70
80
90
100
Mean Relative Humidity (%)

FIG. 4A

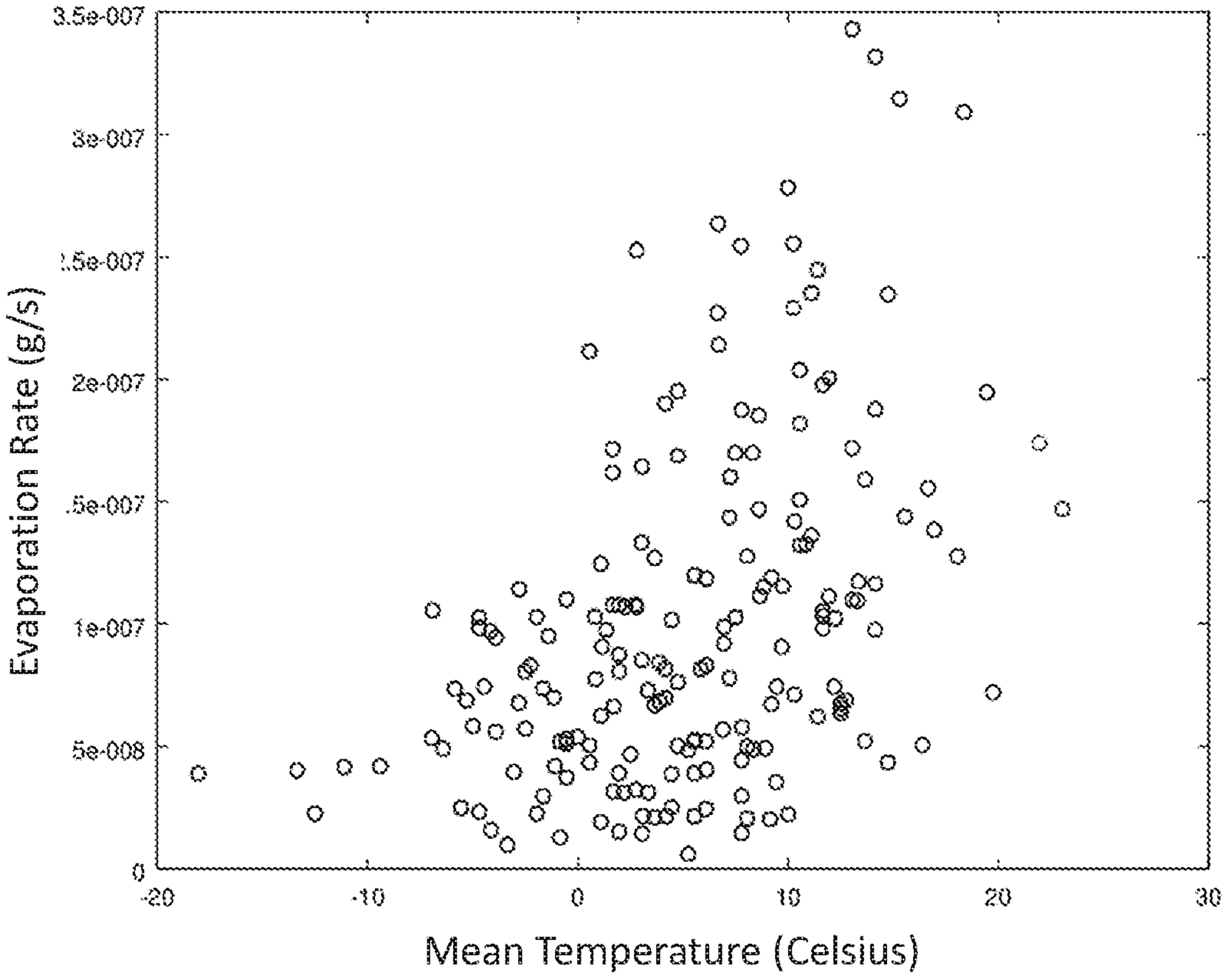
3.5e-007
3e-007
2e-007
1e-007
5e-008
0
Evaporation Rate (g/s)
-20
-10
0
10
20
30
Mean Temperature (Celsius)

FIG. 4B

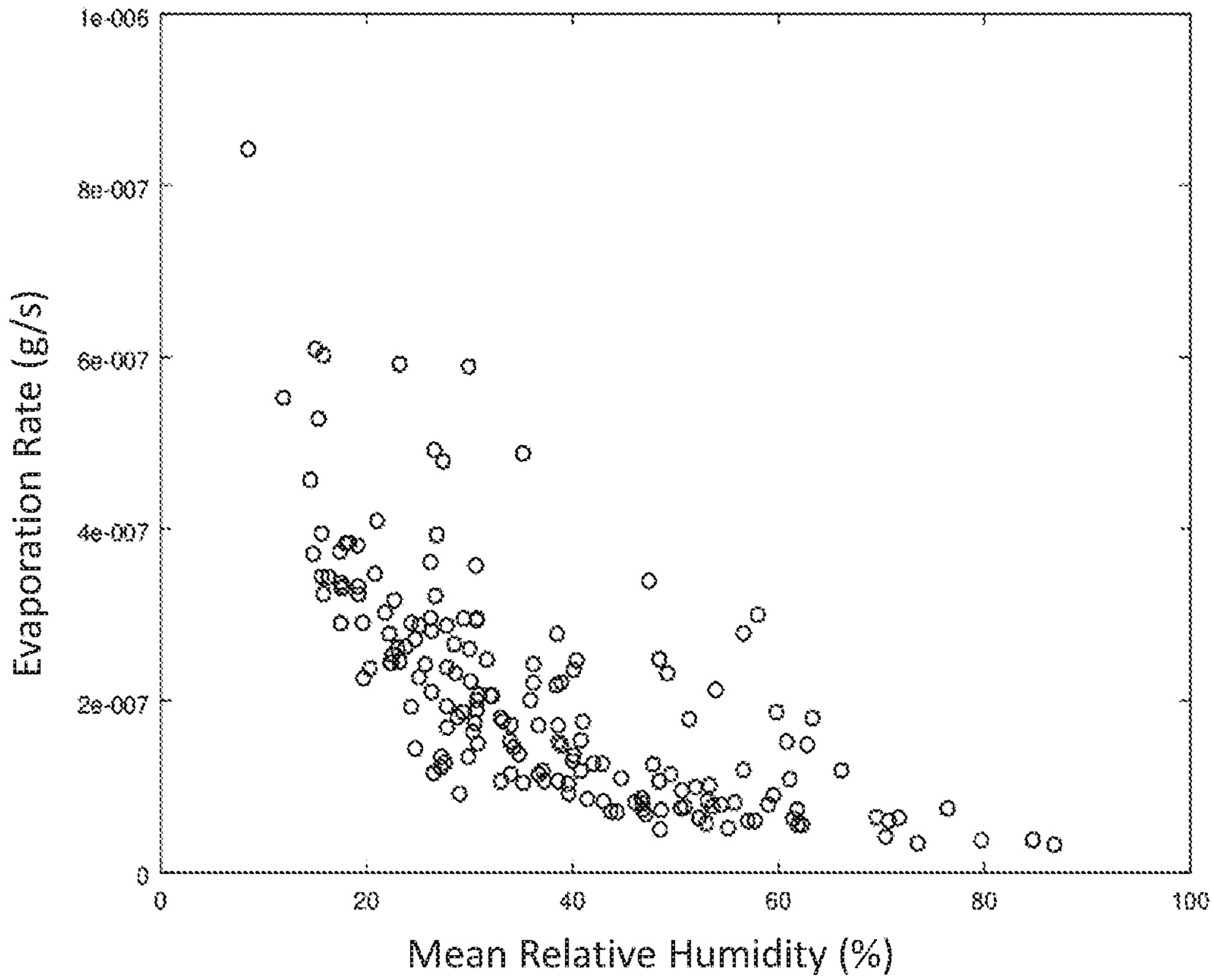
1e-006
8e-007
6e-007
4e-007
2e-007
0
Evaporation Rate (g/s)
0
20
40
60
80
100
Mean Relative Humidity (%)

FIG. 4C

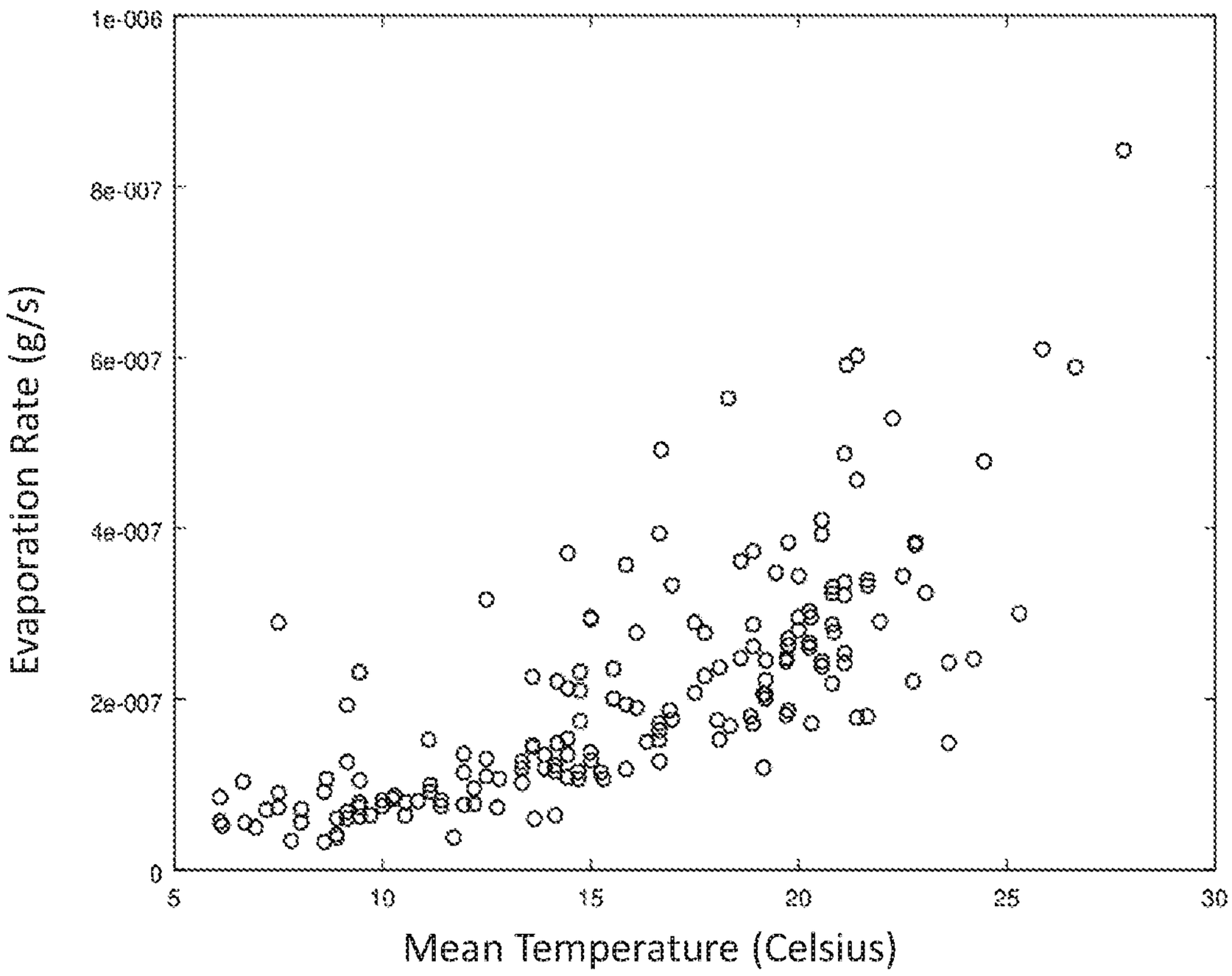
1e-006
8e-007
6e-007
4e-007
2e-007
0
Evaporation Rate (g/s)
5
10
15
20
25
30
Mean Temperature (Celsius)

FIG. 4D

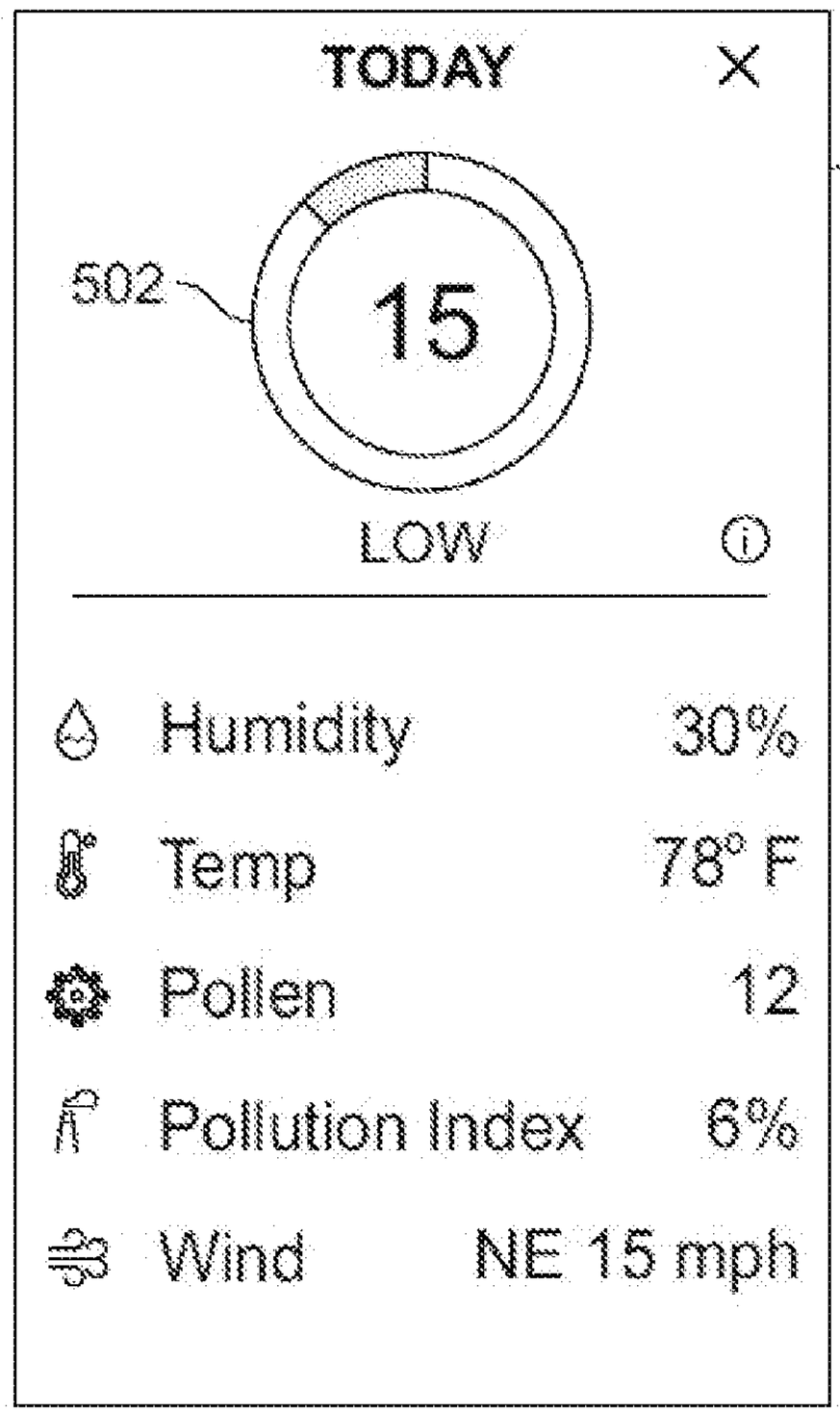
TODAY
502
15
LOW
500
Humidity 30%
Temp 78° F
Pollen 12
Pollution Index 6%
Wind NE 15 mph

FIG. 5A

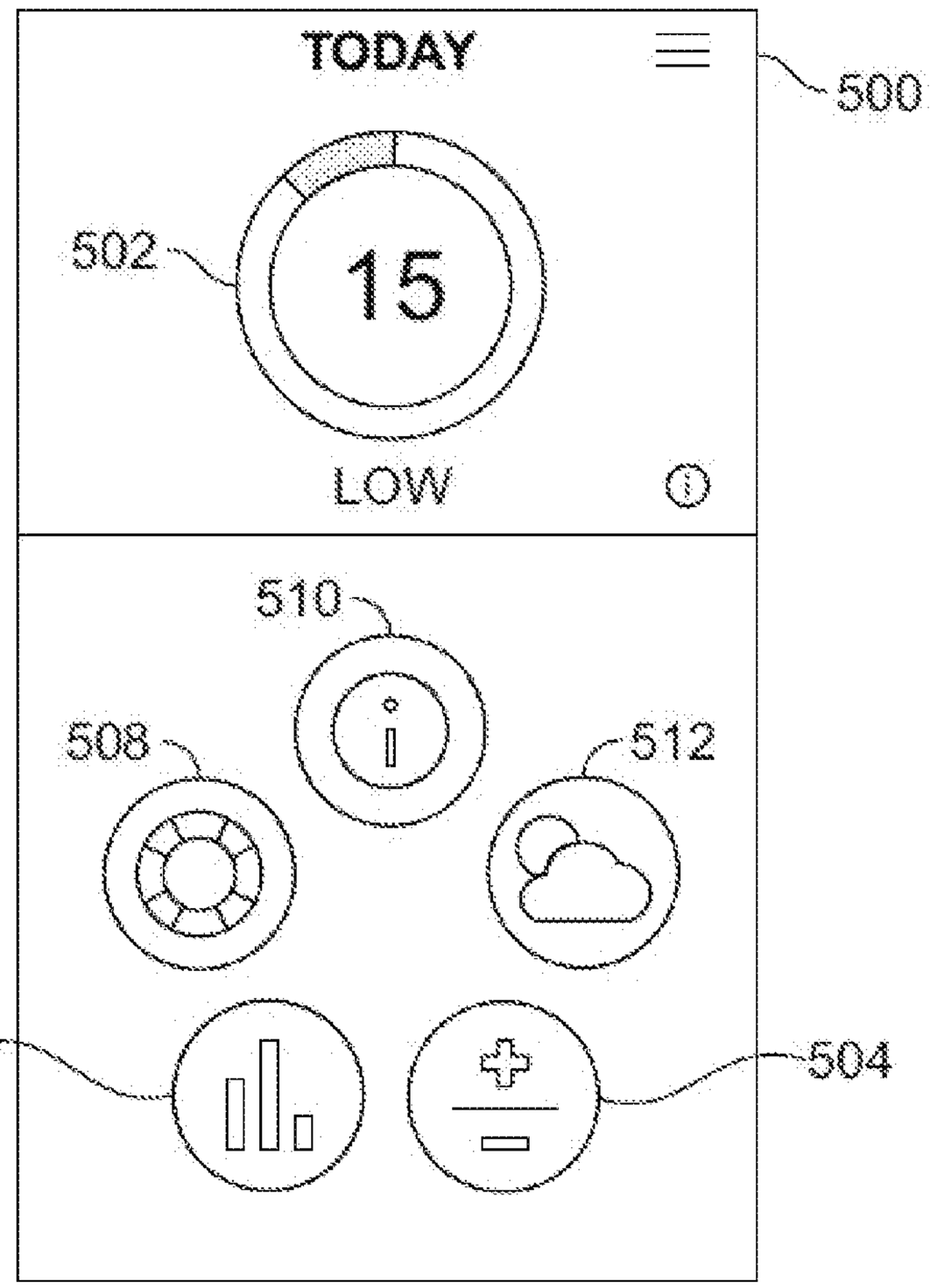
TODAY
502
15
LOW
500
510
508
512
506
504

FIG. 5B

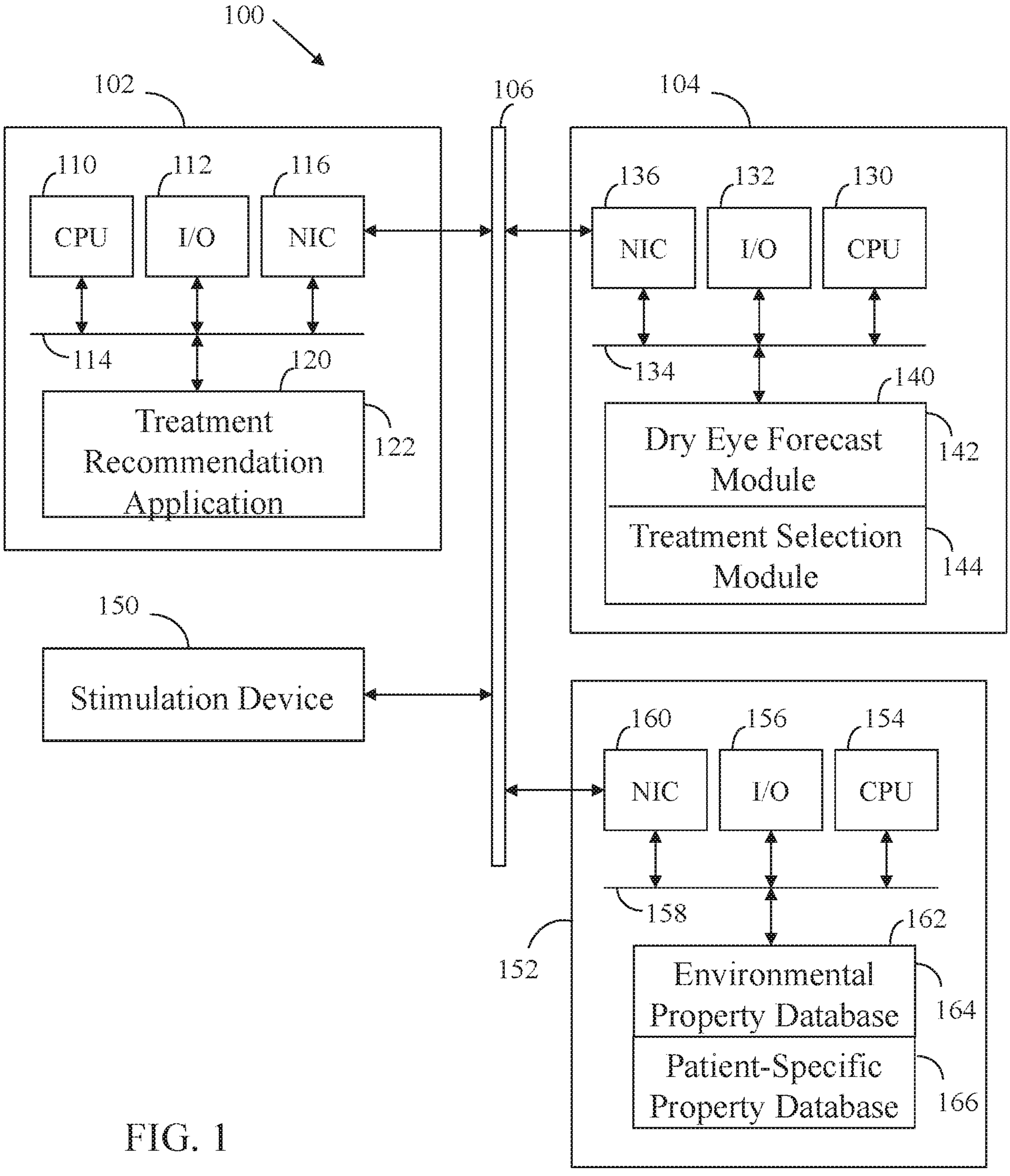
100
102
106
104
110
112
116
CPU
I/O
NIC
114
120
Treatment Recommendation Application
122
136
132
130
NIC
I/O
CPU
134
140
Dry Eye Forecast Module
142
Treatment Selection Module
144
150
Stimulation Device
160
156
154
NIC
I/O
CPU
158
162
152
Environmental Property Database
164
Patient-Specific Property Database
166

FIG. 1