

# Vestibular prostheses: The engineering and biomedical issues

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**Abstract.** Currently available data demonstrate the need for balance prostheses. Recent technological and biomedical advances now make it feasible to produce miniaturized sensors, signal processors, electric stimulators, and stimulating electrodes that are roughly analogous to a cochlear implant but which provide information about self motion, instead of sound. Many areas require work before balance prostheses become a reality. Some of these include: the development of a motion sensor array, the conversion of the sensed motion into physiologically meaningful information, the delivery of the transformed information to the CNS, the training of vestibular deficient individuals to use the prosthesis, and developing methods to evaluate the efficacy of the device. In this “white paper,” we consider these issues in the context of prototype baseline prosthetic devices.

**Keywords:** Balance, prosthetic devices, implant, sensory substitution, vibrotactile display

## 1. The need for a balance prosthesis

### 1.1. Overview

The inner ear’s vestibular system provides cues about self motion that help stabilize vision during movement. These cues also enable us to orient ourselves with respect to our surroundings, which helps us to stand and walk (Fig. 1). Each inner ear can sense in 3-D, angular motion and the sum of forces due to linear acceleration and gravity [110]. The central nervous system (CNS) can process these motion cues to estimate self motion in 6 degrees of freedom (dof): three an-

gular and three linear. When the inner ear, the neural pathways that connect it to the CNS, or the part of the CNS that processes self motion information malfunctions due to injury, disease, or to prolonged exposure to altered gravity, motion cues are lost or distorted. This lack of sensory information can result in dizziness, blurred vision, inability to orient correctly (including the ability to align with the vertical), and reduced ability to stand or walk, especially under difficult conditions. Some of these outcomes can have serious consequences, such as increasing the risk of falling. Because current treatments are not completely effective, there is a clear need for a prosthesis to help people with balance problems, including those recovering from ablative inner ear surgery, those with no vestibular inputs, and those in the elderly population who are prone to falls.

A recent analysis [47] of the National Health Interview Survey [73] reports that 6.2 million Americans

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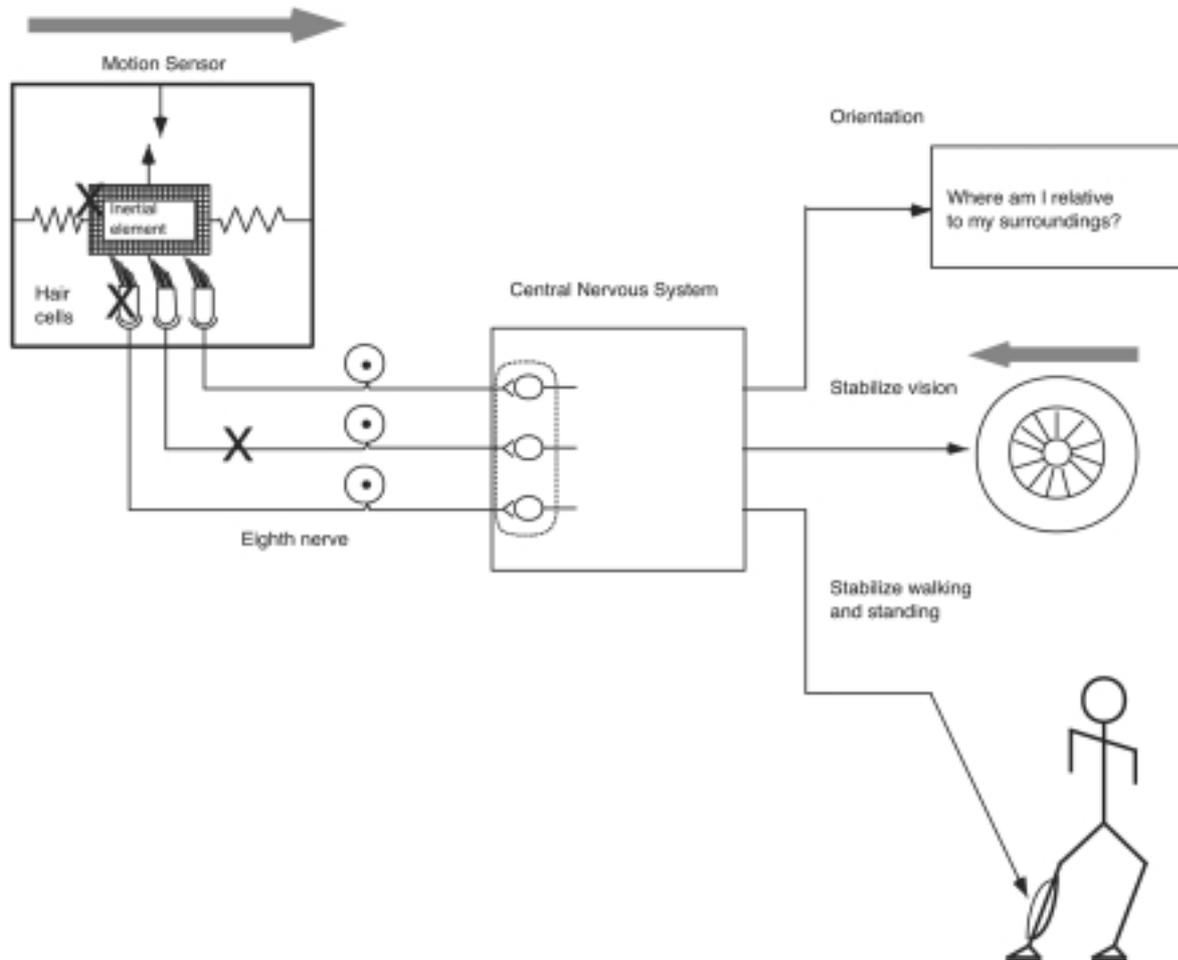


Fig. 1. Cartoon of vestibular function. The simplified motion sensor diagram shows an inertial element, a restoring element (represented by the two spring symbols) and the sensory hair cells whose motion is coupled to the inertial element. Motion of the subject in space, represented by the arrow at top left of figure, causes a displacement of the inertial element from its rest position (indicated by the two mis-aligned vertical arrows). This displacement hyperpolarizes or depolarizes the hair cells, which in turn modulate the spike activity of the first order vestibular afferents. Thus, motion information travels on the 8th nerve via Scarpa's Ganglion (shown by three cell bodies) to the vestibular nucleus (enclosed by dashed lines) in the central nervous system (CNS). The CNS integrates information necessary for: (1) spatial orientation, (2) stabilization vision (represented by the arrow which points in a direction that is compensatory to the sensed motion), and (3) maintaining postural control. Disease or injury can disrupt the peripheral three-link chain (inertial element, hair cells and nerve) of motion information, as represented by the X's. A prosthesis would restore lost motion information.

report chronic (3+ months) problems with dizziness or balance. To be conservative, if only 5% of them could benefit from some form of balance prosthesis, more than 300,000 devices would be needed. A survey of 9,198 community-dwelling, working age people randomly chosen from six large general medical practices found that 0.2% had dizziness severe enough to deserve treatment and were willing to submit to testing and rehabilitation [112]. It is not unreasonable to assume that this same population would at least be willing to consider the use of a balance aid. Some target groups that are likely to benefit from balance prosthe-

ses include: (1) Those with bilateral vestibular hypofunction who cannot adequately rely on motion cues from proprioception and vision during their activities of daily living, (2) Those with unilateral vestibular hypofunction whose central nervous systems have a tonic imbalance to which they cannot adjust, (3) Those with fluctuating vestibular function who cannot adapt to the fluctuations, (4) Those in the elderly population who are prone to fall. Since each of these target groups is a subset of a larger class (i.e., only a subset of patients with bilateral vestibular hypofunction will be viable prosthesis candidates), effective prosthesis deployment

will require careful patient selection. Selection of the appropriate kind of prosthesis for each application also will be necessary.

Both implantable and non-implantable prostheses are currently under consideration and will be discussed in detail later. By “implantable prosthesis” we specifically mean a prosthesis that delivers self-motion cues to the central nervous system (CNS) via implanted stimulator(s). This has a number of advantages over reliance upon non-vestibular sensory inputs or the reliance upon assistive devices such as canes. These advantages include: portability, intuitive operation, replacement of lost natural function, and the ability to work with existing CNS circuitry. However, risks such as possible diminished hearing as a side effect of implantation must be considered. Non-implantable prostheses are a less invasive means of providing some self-motion cues. They include stimulating the vestibular nerve via surface electrodes or by displaying self motion cues using “sensory substitution” (e.g., via vibrotactile stimulation of the skin or via electric currents applied to the tongue). Much of the technology to support a balance prosthesis has been developed or is being developed, but several key components, to be addressed later, remain. Some target populations will now be considered in more detail.

### *1.2. Target Group #1 Bilateral vestibular hypofunction patients who cannot adequately rely on motion cues from proprioception and vision during their activities of daily living*

Primary causes of bilateral vestibular hypofunction include: congenital anomalies, hereditary/genetic degenerative diseases, exposure to ototoxic drugs, disease or injury. The exact number of patients is not known. Gentamicin, one of the most common ototoxic antibiotics in wide general use, has a reported incidence of cochlear toxicity in 5–10% of cases [64,65,94]. We estimate that 10–20% of all Gentamicin-treated patients experience some degree of vestibular ototoxicity. Perhaps half of these cases will improve, while the other half will have chronic bilateral vestibular hypofunction. Community-dwelling patients over age 65 with bilateral vestibular hypofunction are more apt to fall than the general population [46]. Thus, there is an elevated risk of falls in this target group. While vestibular self-motion information is available to these patients, most, but not all, will adapt and can perform activities of daily living. For those who cannot adapt, one approach would be to restore self-motion information with CNS

input from an implantable vestibular prosthesis. Alternatively, a non-invasive prosthesis may provide a useful but reduced subset of self-motion information (e.g. body tilt relative to the vertical without rotational motion cues) but would avoid the risks associated with surgery. One study has shown that subjects with documented vestibular hypofunction who fall or have abnormal scores in the Sensory Organization Test portion of Computerized Dynamic Posturography without an aid can improve their scores or can even stand when a vibrotactile display of their anteroposterior body tilt is provided [56].

### *1.3. Target group #2: Unilateral vestibular hypofunction patients whose central nervous systems have a tonic imbalance to which they cannot adjust*

Primary causes of unilateral hypofunction include unilateral disease or injury of the peripheral or central vestibular system. Examples include viral vestibular neuritis or labyrinthitis, acoustic neuromas, chronic otitis media or mastoiditis, Ménière’s Disease, and temporal bone trauma. While the exact number of such patients is not known, estimates for Ménière’s Disease (MD), one of the major contributors to this target group, have been estimated for the US. at 38,000 to 115,000 new cases per year, with a total of 545,000 [75]. Patients with acoustic neuromas form another substantial fraction of unilateral patients. Acoustic neuroma surgery creates both a permanent, tonic imbalance (present target group) and a transient fluctuation (one rapid decrease in neuronal activity, discussed below) to which the central nervous adjust. Members of this target group have, on average, significant reduction of the long time constant of the vestibuloocular reflex (VOR), which degrades the sensitivity of their VOR at low frequencies. Based upon reported surgical cases, the incidence for acoustic neuromas varies world-wide from between 1–20 cases per million per year [48,99–101]. A study based on 24,245 MRI scans found 7 unsuspected acoustic neuromas per 10,000 or 0.7% [3], while studies based upon autopsy material suggest a slightly higher incidence of about 1% [12,25,55].

Based upon our clinical experience at a tertiary referral medical center, we estimate that between 5% and 10% of those with tonic imbalance are not able to adapt satisfactorily to it. Tonic imbalance due to asymmetric vestibular function may also degrade postural stability in some individuals [57], but the actual number affected is not yet known. Basic restoration of tonic balance

could be accomplished with an implantable device that provides a constant train of electric pulses to the endorgan, nerve, or vestibular nucleus on the side of the lesion. A more advanced approach would be to modulate the pulse train using self-motion cues from artificial head-mounted motion sensors. Another alternative is a non-invasive prosthesis that provides head or body tilt estimates to improve postural stability.

*1.4. Target group #3: Those with fluctuating or abruptly changing vestibular function who cannot adapt to the fluctuations*

Primary causes of fluctuating or abruptly changing vestibular function include early and middle stage MD patients, patients recovering from ablative surgery of the inner ear, and patients with viral attacks to the inner ear. One follow-up study of 141 patients who had acoustic neuroma surgery found that 45% reported balance problems, while 19% reported dizziness [2]. It is generally thought that a larger percentage of patients with fluctuations are unable to adapt, compared to the patients with a tonic imbalance. The goal for a prosthesis in this target group would be to provide a stimulus that would regulate the fluctuations. One simple device would consist of a stimulator that was turned on by the patient only when needed. An enhancement of this device would monitor the neuronal activity of the vestibular portion of the 8th nerve and turn the device on (and off) automatically. Another enhancement might be a feedback control system that monitored the neuronal activity in the vestibular part of the 8th nerve, and supplied a train of electric pulses to the nerve so that the overall activity level remained constant (see Section 4.2.1, “vestibular pacemaker”). Modulation of this signal with motion cues would not be as important as in cases of bilateral hypofunction, since motion cues would be available from the intact side. A non-invasive prosthesis to provide tilt estimates, while worth investigating, might not offer much benefit to this group of patients because it would have to compete with the confounding vestibular fluctuations. While vestibular adaptation exercises are reported to improve acute stage recovery from acoustic neuroma resection [45], the adaptive processes influenced by these exercises can be quite slow. The use of a balance prosthesis during the post-surgery period could promote more patient standing and walking activity, and thus hasten recovery.

*1.5. Target group #4: Those in the elderly population who are prone to fall*

In the elderly, the consequence of falling has been described as “an ominous sign” [51]. In a study of 311 nursing home residents, 74 of the 207 (35.7%) who fell died within one year compared to 13 (13.8%) deaths out of the 94 controls who did not fall. While not all falls in the elderly can be attributed to chronic problems of dizziness and balance, dizziness and balance problems are more prevalent (9.1%) in the geriatric sector of the US population compared to 1.9% for young adults and 3.7% for middle-aged adults. One reason may be due to decreased motion sensitivity. The number of vestibular hair cells is known to decrease significantly with age in humans [68]. It has been shown that elderly subjects have a decreased ability to rely on visual cues to maintain postural stability [63]. It has been hypothesized that vestibular disorders and dizziness may not develop until the nervous system is unable to compensate for the progressively decreasing function [63]. From US Census figures the total number of elderly in the US who are 65 years or older is 32,621,000 while 3,140,000 are 85 years or older. Thus, there is a large population at risk for serious injury. We are confident that it will be possible to reduce the number of elderly fallers by the use of a balance prosthesis. The appropriate sub-population would first need to be identified. A non-invasive balance aid that provided body tilt estimates useful for the control of postural stability might be an attractive alternative for this target population.

In summary, the data needed to make an accurate estimate of the number of patients who could actually use a balance prosthesis are incomplete. There are almost no experimental data to support or refute the notion that some kind of balance prosthesis could be beneficial to a substantial number of patients. The best available data clearly demonstrate that large populations exist who could potentially benefit from a balance prosthesis.

## **2. Feasibility and technology assessments**

### *2.1. Overview*

Over the past several years both technological and clinical advances make the implementation of a balance prosthesis possible. Small motion sensing elements ( $\sim 1.25 \text{ mm}^3$ ) and small digital signal processing circuits ( $< 0.5 \text{ cm}^3$ ) make it possible to produce the signals needed to drive implanted electrodes using packages

that are very small and lightweight. Clinical advances including testing and rehabilitation have made it possible to identify and provide such devices to patients who might need them. In this section, we examine the overall feasibility of a balance prosthesis, develop a reference, or baseline prosthesis model, and assess the technology as it applies to the reference model.

Although this is a new research area, results of basic research have provided some good reasons to believe that modern balance prostheses will work. Electrical stimulation of the vestibular system produces reflexive responses in both the vestibulo-ocular and the vestibulo-spinal pathways of normal subjects. The direction of these responses are correlated with the sensitive axis of the particular sense organ or nerve that is stimulated [19–22,39,40,62,95–98]. Studies of the degeneration process in humans indicate that loss of sensory vestibular hair cells is associated with some degeneration of vestibular nerve ganglion cells [89]. However, a significant number of nerve cells remain to respond to electrical stimulation. In addition, vestibular hair cell ablation experiments in animals show no change in the threshold to electrical stimulation of the remaining vestibular nerves compared to intact controls [52]. The remarkable ability of the nervous system to adapt to novel vestibular stimulation may allow it to compensate for less-than-ideal stimulus patterns. Examples include the adjustment of the sensitivity of the vestibular-ocular reflex in response to vision-reversing prisms [41], and across-axis VOR adaptation [32,80,81].

Clinical advances also contribute to the feasibility of balance prostheses. It is possible to evaluate dizzy patients objectively at a large number of clinical centers with a battery of tests. In addition, specialized balance system rehabilitation techniques have come into widespread use within the last decade. These advances enable balance prosthesis development in three ways: (1) they provide the means for subject selection by objective testing, (2) they allow for objective device evaluation during rehabilitation, and (3) they increase the likelihood that patient benefit from any given prosthesis design will be optimized.

## 2.2. Baseline prosthesis design

For purposes of discussion, we will assume a balance prosthesis design whose major elements are somewhat analogous to a cochlear implant prosthesis. These elements consist of signal detectors, signal conditioners, digital signal processors, an electric stimulator, and

stimulating electrodes. The motion detectors will be linear accelerometers and rotation sensors (e.g., angular rate sensors or angular accelerometers), possibly fabricated using micro-electrical-mechanical-systems (MEMS) technology. MEMS sensors typically need electronic circuitry to drive them, and all sensors with analog outputs require anti-alias filtering before they are digitized. This may be done using application-specific integrated circuits (ASICs). The conditioned analog signals will then be sampled and their motion information will be processed by one or more stimulus coding schemes using a microprocessor. These temporal patterns of logic will next be converted to currents by specialized stimulator circuits, which will probably be comprised of several components including ASICs. The baseline stimulus is a multiphasic charged-balanced train of pulses whose repetition rate is modulated by the processed motion signals (to be described later in more detail). A complete six degree of freedom device will need three angular and three linear motion sensors for inputs and therefore will need at least six independent electric nerve stimulation channels.

## 2.3. Micromechanical inertial instrumentation (motion sensors)

A generation ago, angular velocity was measured by rotating mass gyroscopes that occupied a volume of 10–20 in<sup>3</sup> and were driven by an electric motor or by a source of compressed air. Since then a gyroscope has been developed based upon the design of a tuning fork that does not require bearings [74]. This tuning fork design has subsequently been miniaturized, and can be manufactured on a tiny chip of silicon [42]. Linear accelerometers that work on the basis of an eccentric cantilevered beam have also been micro machined. A single micromechanical sensor element suitable for prosthesis use is less than 2 mm on a side or 1.25 mm<sup>3</sup>. Conventional packaging (including signal conditioning to produce an analog signal) typically increases this volume to about 850 mm<sup>3</sup>. Motion sensors can be classified into grades, according to use. Table 1 shows three grades of instruments (Navigational, Tactical, and Industrial/Automotive) and their maximum allowable errors [10,88,109]. The error itself consists of several components which include bias and change in sensitivity. Bias is an offset in sensor output when the input to the sensor is zero. Change in sensitivity is a change in the scale factor (sensor output units/sensor input units) of the sensor due, for example, to temperature.

Table 1  
Maximum allowable errors for three grades of motions sensors

| Sensor type          | Maximum error      |                    |                  |
|----------------------|--------------------|--------------------|------------------|
|                      | Navigational grade | Tactical grade     | Industrial grade |
| Rate gyroscope       | 0.01°/hr           | 1 to 10°/hr        | Ca. 60°/hr       |
| Linear accelerometer | 0.00001 g*         | 0.001 g to 0.005 g | >0.005 g         |

\*1 g = 9.8 M/s.

From human psychophysical experiments, the detection thresholds for linear acceleration [54] and angular rate/acceleration [11] are 0.005 g and 1 °/s respectively. It is thus reasonable to set the maximum allowable errors at or below threshold, which would require that tactical grade sensors be used for electric stimulation of the endorgans. If, instead, the goal is to control postural sway to within  $\pm 1^\circ$  using a sensory substitution device, the requirement would be to measure tilt to  $\pm 0.1^\circ$ , an order of magnitude better than normal human performance. It has been estimated that this requirement can also be met using tactical grade sensors, but only if the linear accelerometer instrumentation system actively compensates for changes in temperature [106].

#### 2.4. Application specific integrated circuits (ASICs)

ASIC's are semi-custom designed integrated circuit chips that typically provide the conditioning to connect external devices to microprocessors. They are usually created using computer aided design and consist of a large percentage of already-designed custom blocks. A typical ASIC for a MEMS sensor would provide an oscillator to drive a tuning fork gyroscope, a custom circuit to demodulate the sensor's output, and a custom circuit to low-pass filter the motion signal before it is digitized.

#### 2.5. Microprocessors

A microprocessor will form the crucial bridge between the sensed motion stimuli and the stimulation delivered to the nervous system. The requisite characteristics are not complex. The microprocessor must be fast enough to sample the motion sensors, carry out all required calculations (e.g., filtering, scaling, etc.), and control the stimulation of the nervous system. Its power consumption should not be excessive, and it should be relatively easy to program using a standard language. Microprocessor variants include the micro-controller and the digital signal processor (DSP). A micro-controller is an integrated system that uses one or more sensed signals to control one or more processes or devices. Thus, it typically includes analog-

to-digital inputs, digital outputs, programmable clocks, and memory. A digital signal processor (DSP) is a specialized high-performance microprocessor designed to operate in real time to perform such tasks as digital and which has a specific computer architecture suitable for common digital signal processing operations. DSP's are designed to be compatible with input-output devices like analog-to-digital converters.

We will estimate the processing speed required to implement the baseline prosthesis design. The maximum firing rate for a neuron is around 500 Hz, which translates to a 2 msec interval between successive neuronal firings. A substitute requires no more than 10 equally-spaced (0.2 msec) sub-intervals to accurately construct the shape of its electrical pulse. A desirable requirement is to be able to update the pulse shape at the 0.2 msec sub-interval (5 kHz per channel). The most complex processing of the input motion signals will probably involve intricate forms of filtering (e.g., Kalman filtering) to derive separate estimates of the direction of the gravity vertical and of linear acceleration from the linear inertial sensors. (This is done by using information from the angular sensors together with information from the linear ones [107]). We estimate that a maximum of 1000 machine cycles will be needed to implement the most complex algorithm (5 MHz per channel). Allowing for ten independent stimulus channels, a 50 MHz device would be required.

At least one digital signal processor (DSP) (Analog Devices ADSP 2183) has sufficiently high performance (52 MHz), low cubic volume ( $<0.5 \text{ cm}^3$ ), and low power (150 mW) to be suitable for use. Much of the software development for DSPs can be done using high level languages (C and C++) leading to a shorter development time. Thus, existing DSPs appear to be feasible for wearable balance prosthesis devices. If the design requirement for updating the stimulus pulse at the 0.2 msec sub-interval is relaxed, or fewer stimulation channels are needed, then a micro-controller could be used. A currently available 16 MHz device (Analog Devices ADuC812) includes an 8-channel, 12-Bit analog to digital converter, real-time clocks, digital I/O, 8 Kbytes of on-chip Flash memory, and 640 Bytes for data memory. It has a power requirement of about

75 mW and a cubic volume less than  $0.5 \text{ cm}^3$ . Software development can be done using C.

## 2.6. Electrode considerations and development

Electrodes act as the interface between the engineering device and the neurophysiological system. To reach the efficacy that we hope to achieve, it seems that the electrodes must be implanted, because the spatial resolution with skin electrodes is poor [43]. Implanted electrodes must be biocompatible, must demonstrate little corrosion or tissue damage, and must stimulate only target neurons. Cochlear implants, which share design constraints with vestibular prostheses due to the common physiological environment, use platinum/iridium electrodes with silicone insulation. Noble metals, like platinum, iridium, and rhodium are often used for electrodes because these materials are quite resistant to corrosion [84]. But even noble metals corrode, with the corrosion greatly accelerating when the charge delivery exceeds a limit specific to the material, electrode geometry, current waveform, etc. Platinum and its alloys with iridium are well-studied and among the most widely used electrode materials [84]. Theoretical analyses indicate that a platinum electrode can, without irreversibly damaging the electrode, deliver up to  $300 \text{ mC/cm}^2$  [16]. However, the practical limits for platinum determined from in vivo studies appear to be between  $25\text{--}75 \text{ mC/cm}^2$  [84].

Recently, silicon micro-electrodes have begun to be used for nervous system stimulation. These microelectrodes have several advantages over traditional electrodes. First, such stimulation micro-electrodes can include sites that are seeded with a noble metal like iridium prior to implantation. This seeding allows efficient current delivery and is accomplished by applying patterned electrical stimulation to the electrode in a chemical bath. Micro-electrodes can be mass-produced using standard techniques developed for digital silicon devices and can be made extremely small, which may make surgical insertion possible in locations not accessible to traditional electrodes (e.g., intra-neural insertion). Electrode insertion nearer the desired stimulation site may allow lower current levels [53], which will improve safety and simplify device design. Furthermore, more localized stimulation will allow the use of closely spaced stimulation sites, which may allow several independent stimulation channels to be applied fairly close to one another, stimulating separate sets of neurons within a single branch of the vestibular nerve. Finally, a single micro-electrode may be used for recording as

well as stimulation. This may provide opportunities to make localized recordings while also having the ability to decide upon the appropriate pattern of stimulation. This pattern will be dependent on the characteristics of the neurons near the electrode site. All of these characteristics make silicon micro-electrodes an attractive technology to consider as neural vestibular prostheses are developed.

## 2.7. Conclusions

Despite these encouraging advances, the development of balance prostheses raises many questions. From the engineering side: (1) Can the motion sensors be made small enough, yet still accurate? (2) Can the implanted components be made biocompatible? (3) Can the power consumption be made low enough? From the biomedical side, concerning stimulation with implantable electrodes: (4) What is the best stimulus waveform? (5) How should the stimulus be coded? (6) What sites should be stimulated? (7) What surgical approaches are possible to get to these sites? (8) How should animal models be used to help solve implantation problems? Other issues include: (9) Are there alternatives to implantable electrode devices? (10) How should the efficacy of prostheses be measured? (11) What are the safety and ethical considerations? These issues are addressed in the next two sections.

## 3. Major engineering issues to be addressed to achieve a practical prosthesis

### 3.1. Miniaturization of sensors and electronics

While it is conceptually possible to build a small, sensitive, 6 degree of freedom (dof) device and to process its signals so they can be used by the nervous system, much of the actual work remains to be done. While the micro-mechanical sensing elements themselves are small enough to implant (on the order of  $1\text{--}10 \text{ mm}^3$ ), the latest generation of laboratory-grade devices are too large to implant (about  $13 \text{ mm} \times 13 \text{ mm} \times 5 \text{ mm}$  or  $845 \text{ mm}^3$ ), but small enough to be mounted externally on the head. To provide 6 dof information, these individual motion sensors will be assembled into arrays. Micro-mechanical inertial instruments are typically misaligned 1 to 3 degrees with respect to their mounting surfaces, which produces a coupling error between axes of 2–5 percent. At this point it is not known whether these misalignments are acceptable for

balance prostheses. The instruments are also sensitive to temperature. These sensitivities must be known in order to correct the sensor signal as a function of temperature.

### 3.2. Biocompatible materials and sterilization procedures

All implanted materials must be biocompatible, preferably by using materials previously approved for other medical applications. For example, the electrodes and leads might be encased in biocompatible synthetic polymers, like silicone rubber or polyurethane [61]. Metallic cases (e.g., stainless steel or titanium) may also be applicable, since some metals are widely used clinically. Finally, many ceramics are used in various implants and may also be appropriate for use in a vestibular prosthesis.

Since sterilization procedures may affect the choice of materials, it is also important to briefly consider sterilization techniques. Heat sterilization and steam sterilization will likely destroy sensitive electronic components, and radiation sterilization often causes the deterioration of polymers. Therefore, these sterilization techniques are probably inappropriate for an implantable prosthesis. Gas sterilization seems appropriate since electronics are unaffected by gas sterilization and since most implant elements are unaffected by the procedure [61].

### 3.3. Power consumption and transmission

Power consumption is a significant technological concern for the development of a vestibular prosthesis. Sensors, microprocessors, and current sources all require power. Presently, the power of 150 mW required by one state-of-the-art MEMS sensor far exceeds the power required by other device components. The power of 15 mW required by the microprocessor (PIC 16F84-04) in current animal research use, while substantially less than that required for six sensors, is also significant. Solving these power problems will probably require advances on both the supply (e.g., batteries, power telemetry) and demand (e.g., low-power sensors and microprocessors) portions of the prosthesis.

For a clinical device, it seems likely that power may ultimately be provided across the skin using a radio-frequency transmitter and receiver. Even with this assumption, power delivery is likely to remain a significant problem, since individual motion sensors require much more power than the cochlear implant's mi-

crophone. In fact, for today's technology, the power consumption of a single tactical grade sensor is substantially greater than all other prosthesis components combined. Furthermore, at least 6 sensors (3 angular and 3 linear accelerometers) will be required to completely replace all information normally provided via the vestibular system. Therefore, it is safe to estimate that the power requirements for a vestibular prosthesis, using today's off-the-shelf technology, are roughly one order of magnitude greater than those of a cochlear implant. Fortunately, rapid improvements in power delivery technologies seem likely to meet these needs before a clinical device is developed.

## 4. Major biomedical issues to be addressed to achieve a practical prosthesis

### 4.1. Implanted nerve stimulation

Electrical stimulation must be chosen to maximize the efficacy of the implant while minimizing the magnitude of the current and the total charge delivery (i.e., current • time). Numerous scientific investigations have documented the effect of electrical stimulation on vestibular responses including single unit recordings [27,37], vestibulo-ocular reflexes [9,19], postural control [50,72], and conscious sensations of motion (i.e., vertigo and perceived self-motion or self-orientation) [26,83]. Both continuous (i.e., DC) and pulsatile electrical stimulation have previously been investigated.

Studies with DC stimulation showed that the firing rates of vestibular neurons can be increased or decreased depending upon the polarity of the current [4, 5,37,70]. This methodology is appealing because it allows us to reduce a neuron's firing rate below the resting discharge rate. However, DC currents preferentially influence the neurons having irregular spike interval statistics (irregular units) while having less of an influence on regular units; the sensitivity of the irregular units to electrical stimulation was, on average, 6 times greater than that of the regular units [37]. Since the majority of vestibular units are regular and since the importance of the regular units to adaptation has been demonstrated [14], it seems imprudent to disregard these units and electrically stimulate only the irregular units. Even more importantly, DC stimulation requires both higher peak current levels and much higher power (and total charge) delivery due to longer periods of activation. This enhances electrode dissolution and

neural damage. It may also make DC stimulation unfeasible for chronic stimulation provided via implanted electrodes like that required for a vestibular implant.

Investigations have shown that pulsatile electrical stimulation ( $\sim 100 \mu\text{A}$ ) of the ampullary nerves induces nystagmus parallel to the plane of the semicircular canal innervated by the stimulated nerve branch [19]. This mimics the natural response of the semicircular canals to rotation and shows that the spatial specificity associated with the canals is maintained with proper application of pulsatile, peripheral, electrical stimulation. The rate of applied current pulses was shown to influence the magnitude of the VOR, which is also consistent with the natural response of the vestibular system. Another study showed that low-level current pulses ( $< 60 \mu\text{A}$ ) excited the irregular units but caused little or no VOR response. As the current level was increased the more regular units were excited, and eye movement responses were observed [14]. Pulses, therefore, allow us to influence which neurons are recruited, via the peak current and pulse duration, and to determine the neural firing rate via the inter-pulse interval. The current levels required to elicit responses in the previous studies were in the range considered safe ( $< \sim 200 \mu\text{A}$ ). For short duration pulses, it can be shown that action potentials are initiated with the delivery of an approximately constant amount of charge [71]. Since studies have shown that the impedance of implanted electrodes varies with time [6,92], it will be important to carefully control charge delivery in order to achieve constant current stimulation [6,92]. The choice of current source stimulation also simplifies the task of charge balancing, which helps minimize electrode degradation [79, 84]. (Voltage sources cannot control the amount of charge delivery in the presence of variations in electrode impedance. This consideration outweighs the fact that voltage sources are simpler and more efficient than current sources.) Current sources are used for many implanted electrical stimulation devices, including cochlear prostheses [92].

#### 4.2. Sensory coding of information to be provided to CNS

Sensory coding should mimic the natural system in which there is ongoing, spontaneous, baseline, neural activity that is modulated by the motion detected by each endorgan. The rate-sensing semicircular canals act like lumped systems; the fibers innervating a semicircular canal are either excited or inhibited for a given angular motion input. However, the linear motion-

sensing otolith organs act like distributed systems; some nerve fibers are excited while others are inhibited for a given linear acceleration.

In nature, individual nerve fibers in a bundle carrying the same sensory information are not firing synchronously (as they might fire during pulsatile electric stimulation). It has been argued that information from these unsynchronized fibers is combined by the CNS to increase the signal-to-noise ratio of the ensemble to more than that of an individual nerve fiber. Furthermore, the nerve bundles from one vestibular endorgan carry both phasic (quickly changing) and tonic (slowly changing) information to the CNS [38]. Single unit recordings from the squirrel monkey show that the phasic units have a lower threshold to motion than the tonic ones.

It may not be possible to incorporate all these features in a prosthesis. One reasonable approach is to provide the most essential ones first. We describe a baseline electric stimulus (analogous to spontaneous activity) and four schemes to modulate it for coding (analogous to sensed motion). The baseline stimulus is a train of multi-phasic pulses (Fig. 2). It is presently used for both stimulation of the human cochlea and of the primate vestibular nerve (see section on nerve stimulation). Each pulse has four phases, three of which have a fixed interval (typically on the order of  $100 \mu\text{sec}$ ). To achieve charge balance the first and third phases have equal magnitudes but opposite signs, while the second and fourth phase have amplitudes of zero. The interval of the fourth phase is modulated using the schemes described below. Charge balance is maintained during modulation.

1. *Vestibular pacemaker*: Constant unmodulated stimulation of vestibular neurons might be used to override fluctuations that cause balance problems in patients (e.g., Ménière's Disease) who are unable to adapt to a constantly changing level of background activity. A variation of this application would be to measure the actual rate of neural activity in the vestibular nerve and adjust the amount of compensatory electrical stimulation to provide for a reduced amount of overall fluctuation. These schemes may have direct application as electric balance prostheses for patients with fluctuating balance problems. These schemes are not meant to provide information regarding motion.
2. *Simple modulation*: Modulate the baseline stimulus using a single degree-of-freedom (dof) rotation sensor designed to substitute for one semicir-

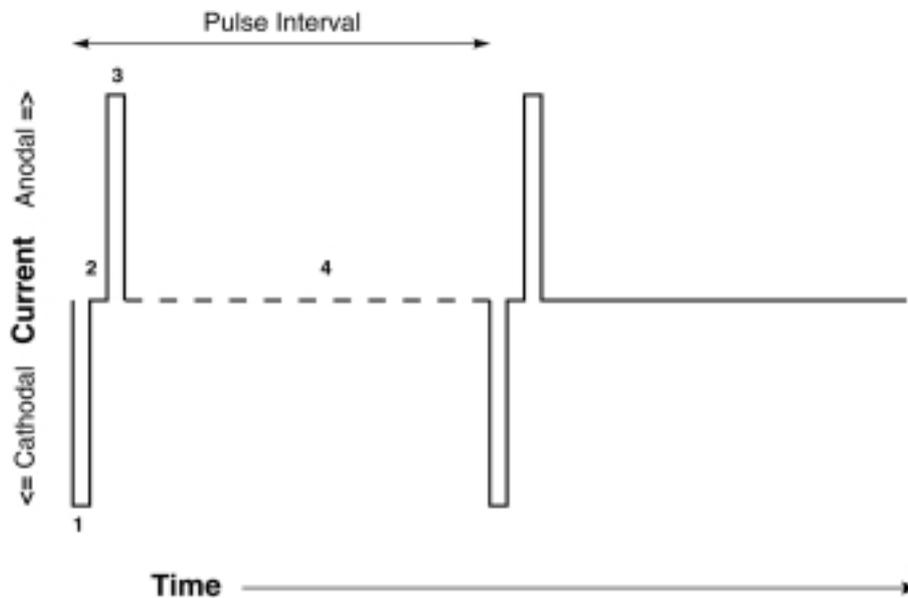


Fig. 2. Diagram of a baseline electric stimulus. It is a train of multi-phasic pulses. The horizontal line at the top of the figure shows one pulse interval (one complete cycle). Each pulse has four stimulus phases shown by numbers : (1) cathodic phase, (2) short zero current phase, (3) anodic phase, and (4) long zero current phase whose duration (represented by dashed line) is modulated by the motion stimulus. Because phases 1 and 3 are equal in duration and magnitude, but opposite in sign, the stimulus is charge balanced. Phases 1, 2, and 3 typically have durations of about  $100 \mu\text{s}$ . The duration of the fourth phase would vary between 20 and 2 ms as the stimulation rate varies between 50 and 500 Hz. Modulation does not affect charge balance since there is no current flow during phase 4.

cular canal. A single electric stimulation channel with one style of signal processing is used [39]. Processing could logically include elements for filtering and dynamic range amplitude compression. Dynamic range compression provides a higher gain signal for small input signals as compared to larger ones.

3. *Complex modulation*: We refer to methods which do not simultaneously drive all the responding fibers in a single vestibular nerve bundle as complex modulation. For example, it may be advantageous to selectively stimulate the phasic and tonic nerve fibers. Selective stimulation is feasible in this case because larger diameter (phasic) fibers have lower excitation thresholds to electric stimulation than the small diameter (tonic) ones.
4. *Direction-specific modulation*: Because the otolith organs act like distributed systems, linear acceleration in a specific 3-D direction will excite the sensory hair cells in some parts of the macula, inhibit them in other parts and fail to stimulate hair cells in still other parts of the macula. One way to provide direction-specific information is to use arrays of individual electrodes implanted in the macula itself or in its nerve fiber bundle. The signals from three linear accelerometers could

be combined to provide the appropriate signal to each electrode.

#### 4.3. Site of stimulation

##### 4.3.1. Effect of disease process upon site of stimulation

Cochlear implant research has shown that action potentials are triggered in auditory neurons when electric stimulation reaches their cell bodies in the spiral ganglion. Since the spiral ganglion of the cochlea is in close proximity to the scala tympani, intra-scalar electrodes are still close to their target nerve cell bodies and can stimulate them by direct current spread even if the peripheral nerve processes are degenerated. In the vestibular system, however, the endorgans are far removed from Scarpa's ganglion. If the peripheral processes have degenerated back to Scarpa's ganglion, there is no conduit for conduction of current to the cell bodies in Scarpa's ganglion. Thus, the only practical site for electric stimulation would be at the ganglion or central to it, rather than at the endorgans. Presently, we do not know what proportion of peripheral vestibular neuronal processes survive after loss of their hair cells nor for how long. It is conceivable that special histological processing techniques or special stains may in

the future provide a means to answer questions about neuronal degeneration in the vestibular system.

Since different disease processes affect the vestibular endorgans differently, it will be necessary to characterize the pathophysiology (and especially the status of peripheral neuronal processes) for a number of disease states and stages in order to predict what electrode locale is most likely to achieve effective stimulation. The main pathologies to be considered include: Ménière's disease, ototoxicity, temporal bone fracture, meningitis, idiopathic bilateral vestibular hypofunction, chronic disequilibrium of aging, vestibular neuronitis, and viral labyrinthitis.

In most quantitative vestibular otopathology studies to date, the focus has been on hair cell and, occasionally, ganglion cell counts. The complex geometry of the vestibular system and the convention of histologic sectioning in the mid-modiolar plane have precluded quantitative assessment of neuronal integrity of peripheral nerve processes. Recently, light microscopy using specialized Nomarski optics and graphic reconstruction techniques have been used to quantify the survival and distribution of hair cells in the vestibular endorgans, peripheral axons reaching the endorgans, and ganglion cells in Scarpa's ganglion [67]. This type of histopathologic correlation is directly analogous to the work of Schuknecht and others in defining the histopathology of the peripheral auditory system [90]. Isolated reports of vestibular histopathology have occasionally appeared in the literature, but a broader, more systematic, quantitative survey is necessary. Recent studies in normal human temporal bones have shown a linear age-related decline in hair cell and Scarpa's ganglion cell counts [68, 104]. In Ménière's disease, there is an accelerated loss of type II hair cells from the vestibular organs, but no difference from normal aging in the type I hair cells and in Scarpa's ganglion [103]. Aminoglycoside ototoxicity exhibits a drug-specific effect on hair cell degeneration [102]. The most common aminoglycoside to cause vestibulopathy is Gentamicin, but there are as yet no reports of quantitative analysis of post-mortem temporal bones from such cases.

Our interpretation based on present data is as follows. After hair cell insult, the peripheral bipolar dendrites will initially remain intact. Over time, however, they will tend to "die back" to Scarpa's ganglion. For most pathologies, approximately 50% of vestibular ganglion cells will survive long term [102,103]. There is some evidence from experiments in cats that electrical stimulation after deafening the ear with an ototoxic drug promotes survival of the spiral ganglion cells [59]. If

the human vestibular nerve responds in a similar way to electric stimulation, and if the stimulation can start soon enough after a vestibular insult, then long term electric stimulation of the nerve fiber bundles is feasible. If not, then Scarpa's ganglion may be the preferred site of implantation.

#### 4.3.2. Unilateral versus bilateral stimulation

While "normal" vestibular function relies upon "push-pull" sensory inputs from both ears, subjects with only one functional labyrinth are generally able to function very well. Motion that excites a hair cell will produce an increase above the background activity in the firing of the afferent neuron connected to it. Motion that inhibits the hair cell will likewise produce a decrease of firing to below the background activity rate. It is this ability to "up-modulate" and to "down-modulate" that allows acceptable performance from just one functional labyrinth. For a unilateral implant to deliver acceptable performance, it too must be able to deliver both excitatory (up-modulated) and inhibitory (down-modulated) signals to the CNS.

Stimulation in the range of roughly 100 to 400 Hz might entrain the activity of the vestibular neurons. In this case, the only signal going to the CNS is from the stimulator, since by definition entrainment abolishes the spontaneous component. Neural entrainment has been studied for the senses of audition, vibration, and vision [1,60,82,93,105]. There are no known studies of entrainment of vestibular nerve activity, but the related topic of phase-locking in vestibular afferents has been studied [66,76,111,113]. Thus, there is presently not enough information available to say if entrainment of vestibular first order neurons is practical or desirable, but there is some preliminary evidence showing that animals can respond and adapt to electric stimulation in a single ear, with the stimulation rate modulated upward and downward with respect to an elevated resting stimulation rate [39,40,62].

#### 4.4. Surgical approaches for implantable prosthesis electrodes

All three semicircular canal ampullae, both otolith organs, both vestibular nerves, and Scarpa's ganglion are potential candidate sites for implantation of stimulation electrodes. There are three overriding principles which will govern electrode placement: (1) the electrode should be placed as close as possible to the stim- ulable neural tissue (endorgan, neurons, or ganglion cells) in order to optimize specificity of vestibular neu-

rons to be stimulated; (2) hearing should be preserved; and (3) surgical risk should be minimized. In practice, these three principles may be in competition. In an ear whose peripheral vestibular neuronal processes are intact, implantation of electrodes adjacent to the endorgans would suit principle #1, optimizing specificity of stimulation. If, however, the electrode is positioned outside the endosteum of the semicircular canal, current spread may lessen the signal actually reaching the vestibular neurons, and if the electrode is inserted through the endosteum into the ampulla of a semicircular canal, it is likely to deafen the ear. In a hearing ear, electrodes could be placed directly on Scarpa's ganglion to get them closer to the stimutable neural elements (principle #1) and spare hearing (principle #2), but there would probably be a loss of specificity of stimulation and there would certainly be higher surgical risk due to the intracranial locale of the operation.

A combination of serially sectioned human temporal bone slides, 3-D imaging technology and surgical dissections in human temporal bones can logically be combined to define practical approaches to electrode placement. This information must be combined with data on endorgan/neuronal survival to plan electrode placement for patients with specific diagnoses. We believe that an animal model experiment that used surgical approaches identical to ones proposed for human experiments and that was successful in "semi-chronic" experiments would provide strong support for human procedures. We consider three implantation approaches starting with the most peripheral and least invasive.

#### 4.4.1. Implantation near the ampullae

The ampullated ends of all three semicircular canals are readily accessible via surgery through the mastoid bone behind the external ear. Electrodes could be applied to the bony otic capsule surrounding the ampullae to stimulate the peripheral processes of the ampullary nerves. However, the electric impedance of bone may preclude this option. If so, the bone can be thinned to expose the underlying endosteum, a more conductive tissue. This approach is attractive, at least initially, to see what can be affected using the least invasive surgical methods. Current applied here would spread more or less uniformly along the lining of the semicircular canals and some current would thereby reach the ampullary nerves. In deaf ears, it would be possible to pass electrodes through the endosteum and labyrinthine fluid spaces to the ampullae or maculae ("intralabyrinthine placement") to assure closest proximity of the electrodes to stimutable neural elements.

#### 4.4.2. Implantation of individual nerve bundles

Implantation of individual nerve bundles supplying the vestibular periphery represents an attractive intermediate method for targeted electric stimulation of a single endorgan's nerve supply. There are currently no human surgeries that isolate individual vestibular nerves within the temporal bone peripheral to the internal auditory canal. Such isolation, however, may be feasible. A method for isolating and sectioning the posterior ampullary nerve has been described for treatment of benign paroxysmal positional vertigo [33]. A surgical approach to the vestibular nerve branches without damaging the respective endorgan has been described for the squirrel monkey [49]. Semicircular canal plugging can be done in humans without damage to the labyrinthine contents [77,78]. It should be possible to implant the peripheral nerve branches by slightly modifying the approach used for human canal plugging so that the nerve branches are accessible as demonstrated by the squirrel monkey experiments.

One or more C-shaped electrodes could be placed to partially surround the nerve fibers as they course through the trabecular structure, but would not be supported by or touch the fragile fibers themselves. The nerve fiber bundle subserving the horizontal canal would be the easiest to study in terms of testing with sinusoidal vertical axis rotation and recording the responses of the horizontal eye movements. But the proximity of the horizontal and anterior canal fiber bundles raises issues of electric "cross-talk." This consideration, together with relative ease of access suggests that the posterior ampullary nerve, with its relatively longer course and with its separation from the other two canal nerve bundles, might be a better place to start. This is despite the added complication of comparing the responses to electric and physiologic stimuli when testing the posterior canal.

#### 4.4.3. Implantation of Scarpa's ganglion

Because of the spatial organization of the five vestibular receptors, the implanted electrodes must have the capability of presenting the brain with analogous spatial information. It has been demonstrated anatomically that the spatial organization of the vestibular receptors is preserved in Scarpa's ganglion [87]. There are three surgical approaches to Scarpa's ganglion within the internal auditory canal: via the mastoid and bony labyrinth ("translabyrinthine approach"), by opening the roof of the internal auditory canal in the floor of the middle cranial fossa ("middle fossa approach"), and by opening the poste-

rior wall of the internal auditory canal in the posterior cranial fossa (“suboccipital” or “retrosigmoid approach”). Both translabyrinthine and posterior fossa approaches provide excellent exposure to the internal auditory canal and both the superior and inferior divisions of Scarpa’s ganglion. The middle fossa approach provides a more limited exposure of the inferior portion of Scarpa’s ganglion and increases risk of facial nerve injury. The translabyrinthine approach cannot be performed if hearing conservation is desired. A microelectrode array designed with this preservation of organization in mind could be placed near or into the ganglion. After a recovery period, the electrode array would be partially “tuned” by stimulating individual electrode elements and measuring perceived motion and/or the resulting eye movement responses. This stimulation procedure would help differentiate whether the response was due to a linear or angular based endorgan.

#### 4.5. Initial and follow-up tuning of implant to individual user

The electrical stimulation parameters (current level, pulse width, etc.) will be determined using procedures similar to those used for cochlear implant patients [15]. One possible difference is that instead of relying only upon perceptual feedback, it will also be possible to measure the VOR responses induced by electrical stimulation. Since actual tuning protocols will be developed only when much greater understanding is available, we will simply briefly outline some of the relevant issues in this section. Peak current levels for each active electrode will need to be investigated. Responses will probably be measured as the peak current level is increased. Subjects and technicians will be vigilantly looking for facial twitching, electrically evoked “sounds”, and pain. This procedure will be repeated for each stimulation site. The characteristics of the eye movements (and/or perception) will be recorded assuming pulsatile stimulation, once the current levels are determined, a brief characterization of the responses should be obtained as a function of stimulation frequency. Armed with this information for each individual electrode, an initial “tuning” of the prosthesis should be feasible. However, since the adaptability of the nervous system to incoming sensory information is widely known, such a tuning procedure may need to be repeated regularly, especially during the first months of stimulation.

#### 4.6. Development of appropriate animal models

Mammalian species seem likely to be the primary animal models used to develop and investigate vestibular prostheses for several reasons. First, despite the contributions of non-mammalian species to our understanding of vestibular physiology, the peripheral geometry and function of most mammalian vestibular endorgans is most similar to that of humans. Second, a more detailed understanding of vestibular behavioral responses exists for mammalian species than for non-mammalian species. In animal studies, the vestibulo-ocular reflex (VOR) is likely to be a primary objective measurement used to quantify prosthesis efficacy, though evoked potentials, neural recordings, vestibulo-spinal reflexes and other measures will also be crucial. The angular VOR is the controlled reflexive response of the eyes that helps stabilize images on the retina during head movements. Primate species appear to be a good match because of the breadth knowledge of both central and peripheral vestibular function in primates, but other foveate mammals (e.g., cat) may also be appropriate. Non-foveate mammals are also likely to be appropriate for many investigations. For example, rodents (e.g., guinea pigs or chinchillas) might be appropriate for studies of electrode design, demonstrating the safety of chronic electrical stimulation, and preliminary development of surgical procedures. In our own animal studies, we have decided to proceed using both squirrel monkeys [62], because of our experience with this species and the detailed knowledge of both central and peripheral aspects of the vestibular system [28–31, 35,36], and guinea pigs [39,40].

#### 4.7. Non-implantable approaches

Not everyone may want, or need, an implantable prosthesis. It therefore seems reasonable to consider less invasive devices that use externally applied stimulation. Several candidate devices exist or are in development.

##### 4.7.1. Vibrotactile display of physiologically meaningful information

A balance aid has been designed to estimate a subject’s body tilt using 6 dof motion sensors mounted on the small of the back, and display the magnitude and direction of the tilt estimate with a 3 row by 16 column array of tactile vibrators mounted on the subject’s torso. Rows are used to display body tilt magnitude. Presently, a vibrator mounted on the lowest row is acti-

vated when a minimum tilt threshold is exceeded. Tilt greater than a second, higher threshold activates a vibrator in the middle row, and so on. Columns are used to display body tilt direction ( $22.5^\circ$  resolution) [107]. A simplified (2 dof) research device [106] has recently been shown to significantly assist vestibulopathic subjects during simple postural control tasks [56, 108]. Dynamic tactile displays [23] have been demonstrated successfully as both auditory and visual prostheses [13]. Moreover, much has been learned about properties of the skin that can be used in building a tactile display [18,58].

A commercially available sensory substitution hearing prosthesis uses an array of two or more small ( $24\text{ mm} \times 19\text{ mm} \times 10\text{ mm}$ ) tactile vibrators that are typically applied to the arm. These electro-mechanical devices are driven by a 250–400 Hz oscillator whose signal is modulated by sound that is picked up via a microphone worn by the user. The vibrator units have been designed for low power application and have been approved for human use by the Food and Drug Administration. To create a balance prosthesis, one could use the signal of small motion detectors that measure the motion of subjects to modulate the oscillator signals.

Vibrotactile displays have also been demonstrated in aviation [17,34,85]. The US Navy is developing a device to evaluate the use of tactile cues to provide situational awareness information to aircraft pilots. Their tactile cue device uses externally measured angular and linear motions that are fed from the aircraft's inertial navigation system into a 3-D vibrotactile display (a vest worn by the pilot). In roughly one hour of training, experienced Navy pilots were able to perform acrobatic maneuvers like loops or barrel rolls and return to stable, level flight while completely blindfolded [86]. In contrast, blindfolded pilots with normal vestibular function are unable to perform simple tasks like maintaining a standard 3-minute turn in which the aircraft makes a  $360^\circ$  circular turn in a horizontal plane in 180s. Similarly, blindfolded Army helicopter pilots using the tactile cue device can take control of the aircraft after it has been put into an unstable orientation and can return it to stable, level flight. These tasks present a higher degree of difficulty than that encountered in tasks of active daily living. Thus, it is reasonable to expect that in a short amount of training time, willing subjects having little or no vestibular function can learn to improve tasks of active daily living.

#### 4.7.2. Electric stimulation without near proximity to the 8th nerve

Externally applied low-frequency galvanic stimulation is another method of providing an alternate sensory input. We distinguish this from high-frequency galvanic stimulation of the 8th nerve via an electrode that touches or is in very close proximity to the nerve. Galvanic stimulation has been applied transdermally to the temporal bone by Collins and his collaborators in order to stimulate the vestibular apparatus [91]. There is some evidence that low-frequency galvanic stimulation may be stimulating the hair cell epithelia [69]. Because of this, it may not be effective in vestibulopathies that kill the hair cells or affect their ability to release transmitter substance. We believe this evidence to be refuted in favor of findings from galvanic stimulation studies in vestibulopathic patients who presumably have abnormal hair cells, which report elevated responses compared to normals [9,24].

Galvanic stimulation has also been used on the skin of the torso and to stimulate the tongue [8]. An array of electrodes on the tongue has recently shown promising preliminary body, head, and eye stabilization results [7]. One disadvantage of using the tongue is that talking or eating may interfere with the delivery of the galvanic input.

We believe that non-implantable approaches have a potential advantage of helping a significant patient subpopulation in a fairly short development time (perhaps 3–5 years), without having to wait for the time required to develop implants. In addition, their use could provide the beginning for an objective balance prosthesis evaluation process based on performance measures currently in use by the balance rehabilitation community. Development of these objective performance measures will drive the field by using a standardized evaluation approach. This will be necessary for the widespread acceptance of both implantable and non-implantable prosthetic balance devices.

#### 4.8. Evaluation of prosthesis efficacy

An appropriate outcome analysis of vestibular prostheses may be broadly defined as the ability of the vestibular deficient patient to use information provided by the prosthetic device to accomplish a vestibular-dependent task successfully. A preoperative test battery should be used to provide the baseline or reference data for the outcome analysis. Decisions must therefore be made as to what is an acceptable anticipated "yield" in these patients. In order to make such de-

cisions, the following minimal objective data will be needed: (1) vestibular function tests, (2) tests of visual and proprioceptive function, (3) test of vestibular, visual and proprioceptive (somatosensory) interaction, (4) preoperative tests of vestibular neuronal survival, (5) tests of cognitive function (appropriate neuropsychological test battery), (6) objective evaluation of attempted vestibular rehabilitation, and (7) tests of hearing function.

#### 4.9. Safety, ethical considerations and FDA approval

The efficacy of the prosthesis must also consider issues of safety to the user. These include: biocompatibility [44], operational lifetime of device (failure data), current spread, and undesirable side-effects (e.g., motion sickness, vertigo, postural instability, disrupted vision, and the risk of hearing loss). Development of an implantable neural vestibular prosthesis must be accomplished incrementally and within accepted ethical standards and with institutional review board (IRB) approval. It is our understanding that the legal requirements for human experimentation, including surgery, are met by IRB approval. Informed consent on the part of the subject is one ethical standard. The risk to the subject must be carefully assessed and clearly explained to the subject, to the satisfaction of the IRB.

One logical way to approach implantation is to start with the least risky procedures. This agrees with the principle presented in the section on surgical approaches (4.4). We believe this to be stimulation which does not require its own surgical procedure. Initial testing of vestibular electric stimulation can be performed by non-invasive application of surface electrodes within the cavity in the temporal bone that was previously created during a mastoidectomy operation or via a chronic tympanic membrane perforation. This procedure has passed IRB approval. This testing is not very invasive and can be done without anesthesia (which might suppress the reflexive and psychophysical responses), but there is a thin layer of insulating bone between the electrode and the nerve which impedes stimulation. Since the facial nerve lies close to the 8th nerve, there is a chance of stimulating it, therefore producing unpleasant sensations. Intra-operative stimulation can be performed as an acute experiment during tympanomastoid surgery using extralabyrinthine stimulation, or can be performed at intralabyrinthine sites during surgical labyrinthectomy for intractable Ménière's disease. Because this procedure is similar to routine acute electric stimulation during 8th nerve resection and "piggy back-

s" onto a needed surgical procedure, we believe it to be of low additional risk. Since the surgical procedure itself normally requires a deep general anesthesia, the patient is unable to report any sensations, and reflexive responses may be suppressed.

To overcome the disadvantages introduced by general anesthesia, and to provide more time to investigate electric stimulation responses than is available during an acute experiment it might be possible to use "pull-out" electrodes implanted into the ear during necessary tympanomastoid surgery. These electrodes would be allowed to heal in place for 2–4 weeks, and then stimulated electrically. Within a few days of stimulating the electrodes, they would be pulled out through the skin. In order to meet the ethical standard of informed consent, the risks associated with the pull-out electrode would need to be fully evaluated. Evaluation could involve studies in animal models. When prototype implantable electrodes are fabricated and stimulation parameters are adequately characterized, long-term or permanent implantation could then be performed. Due to the sophisticated fabrication technology required to make implants and the substantial administrative and regulatory constraints necessary to achieve FDA approval of an implantable device, we believe that some sort of industrial participation will be a virtual necessity.

## 5. Summary and conclusions

As presented in the overview, there are now statistical data from a national database about people with dizziness disabilities which are available for analysis [47, 73]. These statistics pool all causes of dizziness and, unfortunately, cannot be broken down into specific disease categories.

Among the four target groups (bilateral vestibular hypofunction, unilateral vestibular hypofunction, fluctuating vestibular function, elderly fallers) that we considered for prostheses, it is not currently possible to make a completely quantitative estimate of either the incidence of the contributing diseases or of the fraction in a target population that would actually benefit from a prosthesis. Thus, we have used a combination of quantitative and qualitative (clinical judgement) information. Despite this limitation, we believe these evaluations argue strongly that balance prostheses are needed.

Creating a simple mock-up for a prosthesis allows one to make a road map of what is required for a func-

tional prototype. The tactical grade of micromechanical inertial instrumentation needed to detect movement thresholds and to estimate tilt accurately is currently in limited production, but has been licensed for commercial manufacture. Techniques for making customized electronic circuitry to support the motion sensors and to drive stimulators have been developed. Current microprocessors are powerful enough for prostheses applications. Single stimulation electrodes similar to the ones we expect will be needed are in existence, and arrays of electrodes are being developed.

Motion sensors are currently small enough for a wearable device, but not for implantation. Total implantation is theoretically possible if the instrument size shrinks to be slightly larger than the present sensor element size. We can find no extraordinary problems with biocompatibility, unless some new material is needed. Sensor power consumption is too high, and must be reduced. There are good preliminary responses to pulsatile stimulation with charges that appear to be within acceptable limits for neural material and electrodes. A planned first approach on how to code the motion information to drive electric stimulators is in place. For various diseases, stimulation sites are well defined, but the issue of unilateral versus bilateral stimulation remains to be settled. A principle-based strategy of surgical approaches has been developed but remains to be implemented.

For non-implantable balance prostheses, a proof-of-principle experiment for vibrotactile display of sway in vestibulopathic patients has given positive results. Transdermal galvanic stimulation has been clearly shown to influence postural sway in normal subjects. Galvanic stimulation of the tongue showed promising pilot results on one vestibulopathic subject.

Finally, brief guidelines have been developed for evaluating balance prostheses. An ethical approach to implantation that starts with the lowest risk procedures has also been established.

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