

# Energetic assessment of trunk postural modifications induced by a wearable audio-biofeedback system

D. Giansanti<sup>a,\*</sup>, M. Dozza<sup>b</sup>, L. Chiari<sup>b</sup>, G. Maccioni<sup>a,\*</sup>, A. Cappello<sup>b</sup>

<sup>a</sup> *Technology and Health Department, The Italian National Institute of Health, Viale Regina Elena 299, 00161 Roma, Italy*

<sup>b</sup> *Department of Electronics, Computer Science and Systems, Alma Mater Studiorum, Università di Bologna, Viale Risorgimento 2, Bologna, Italy*

Received 9 February 2007; received in revised form 8 April 2008; accepted 9 April 2008

---

## Abstract

This paper investigates the trunk postural modifications induced by a wearable device which assesses the trunk sway and provides biofeedback information through sonification of trunk kinematics. The device is based on an inertial wearable sensing unit including three mono-axial accelerometers and three rate gyroscopes embedded and mounted orthogonally. The biofeedback device was tested on nine healthy subjects during quiet stance in different conditions of sensory limitation eyes closed on solid surface, eyes open on foam cushion surface, eyes closed on foam cushion surface. Five trials were performed for each condition; the order of the trials was randomized. The results reported in this paper show how subjects reduced their rotational kinetic energy by using the biofeedback information and how this reduction was related to the limitation of sensory information.

© 2008 IPEM. Published by Elsevier Ltd. All rights reserved.

**Keywords:** Inertial sensor; Auditory biofeedback; Balance; Postural control; Prosthesis; Rotational kinetic energy

---

## 1. Introduction

A complex interplay of feedback and feed-forward control ensures the natural ability of the human body to maintain an upright stance and to stabilize during movements [1]. A weak or lacking contribution from sensory inputs, and/or neuronal pathways, and/or muscle actuators results in postural instability and increased risk of falling, which is one of the major causes of morbidity in an elderly population.

One approach to improving balance, which has been widely used in physical therapy and rehabilitation, involves feeding back to the CNS supplementary environmental information about body motion. This supplemental information may come from a therapist, laboratory equipments, or artificial sensors [2]. Biofeedback systems for postural control are aimed at providing additional sensory information to supplement the natural sensory information and improve human

balance. Since the experimentation of biofeedback systems for postural control began, tactile and audio biofeedback have received much less attention than the visual biofeedback. Nevertheless, in the last few years, interest in tactile and audio-biofeedback systems for postural control has been renewed [3,4], partially due to advances in technology for real-time processing and movement sensing and to new trends in wireless wearable devices that can be worn during daily activities. In 2001, Wall et al. [3] developed a device able to provide tactile feedback of trunk tilt by vibrating tactors that the subjects wore around their trunk. This study showed how vibrotactile feedback might improve balance performance of healthy subjects and the possible usefulness and validity of this system as a prosthesis for people with pathologies that impair balance. Audio-biofeedback (ABF) experimentation was recently carried out by Chiari et al. [4] and Hegeman et al. [5] who developed audio BF devices able to encode trunk movement information into a sound.

In particular, Chiari et al. [4,6] showed, using a force platform, that subjects improved balance taking advantage of the ABF and that this improvement was greater the more

---

\* Corresponding authors. Tel.: +39 06 49902701; fax: +39 06 49387079.

E-mail addresses: [daniele.giansanti@ieee.org](mailto:daniele.giansanti@ieee.org) (D. Giansanti), [giovanni.maccioni@ieee.org](mailto:giovanni.maccioni@ieee.org) (G. Maccioni).

that balance was challenged by absent or unreliable sensory cues. Other studies showed how this ABF improved stance stability of participants with bilateral vestibular loss by increasing the amount of their postural corrections and suggested that such increase in stability was not at the expense of leg muscular activity, which remained almost unchanged [7], but rather, ABF increased the amount of feedback control exerted by the CNS for maintaining balance. Accelerometers (ACCs) and/or rate-gyroscopes (GYROs) have been successfully investigated by several authors for mobility monitoring [8], fall-detection [9–11], and for measuring balance control [12,13]; only recently they have been also used for activating vibrotactile or ABF biofeedback devices [3–5]. Up to now ACCs and GYROs have not been used for an energetic investigation of the trunk posture behind the success of the proposed ABF device. The aim of this paper is to assess the energetic consequences of improved stance stability induced by the ABF wearable device presented in Ref. [4] using the kinematic variables directly provided by the inertial measurement unit (IMU) assembling ACCs and GYROs as described in Ref. [14].

## 2. Materials and methods

The customized ABF device measures trunk kinematics by an IMU and provides biofeedback information through sonification of linear accelerations, as described below.

### 2.1. Inertial measurement unit

The IMU incorporates three uni-axial ACCs (3031-Euro Sensors, UK) and three GYROs (Gyrostar ENC-03J-Murata, Japan), assembled together and oriented according to an orthogonal reference frame. The acceleration and angular velocity signals are then smoothed by means of Sallen-Key active low-pass filters with a Butterworth response, amplified, and calibrated. Signal processing and calibration parameters have been optimized by means of a simulation procedure based on a Levenberg-Marquardt optimization [8]. The cut-off frequency was set at 14 Hz and the gain at  $G = 10$ . The IMU (case included) is very small ( $4 \text{ cm} \times 5 \text{ cm} \times 2 \text{ cm}$ ) and light-weight enough (180 g) for clinical applications. The development and validation of the IMU are described in detail in Ref. [14]. Using the IMU we measured the trunk movements in terms of rotations around the axes of an orthogonal frame. We aimed at mounting the sensor as close as possible to the body centre of mass (COM). Since we are investigating here static posture tests the sensor was installed on the subject's back, taking as a reference the subject's navel, at the height of L5. ACCs signals are used for the initial alignment of the IMU and then to drive the ABF. The actual body segment acceleration  $A(a_x, a_y, a_z)$  and angular velocity  $\Omega(\omega_x, \omega_y, \omega_z)$  vectors were obtained using the calibration procedure described in Ref. [9]. The segment orientation is determined by the orientation matrix  $\mathbf{R}$  of the local frame with respect to

Table 1  
Characteristics of the six sensor channels

Parameter	Accelerometer channel	Rate-gyroscope channel
Range	2 g ( $\pm$ g)	180 deg/s ( $\pm$ 90 deg/s)
Cross-talk	$<10^{-6}$ g	$<10^{-4}$ deg/s
Non-linearity	$<\pm 5 \times 10^{-2}\%$ full scale	$<\pm 5 \times 10^{-2}\%$ full scale
Accuracy	$10^{-1}\%$ full scale	$10^{-1}\%$ full scale
Hysteresis	$<5 \times 10^{-2}\%$ full scale	$<5 \times 10^{-2}\%$ full scale
Over all resolution	$8 \times 10^{-5}$ g	$2 \times 10^{-2}$ deg/s

an inertial frame, which is calculated by solving the following differential matrix-equation (1) and then obtaining the three orientation angles expressed by means of nautical angles ( $\theta$  is the pitch angle,  $\varphi$  is the roll angle,  $\psi$  is the yaw angle):

$$\frac{d\mathbf{R}}{dt} = \begin{bmatrix} 0 & -\omega_z & \omega_y \\ \omega_z & 0 & -\omega_x \\ -\omega_y & \omega_x & 0 \end{bmatrix} \cdot \mathbf{R}(\theta, \varphi, \psi) \quad (1)$$

Table 1 shows the characteristics of the six channels after calibration.

Fig. 1 shows some basic details of the IMU with the service unit.

### 2.2. Audio-biofeedback data processing

The general aim is to map linear accelerations in the antero-posterior (AP) and medial-lateral (ML) directions provided by the IMU into a stereo sound, modulated in frequency and amplitude, and adjustable in balance. The two horizontal acceleration outputs from the IMU were acquired using a DAQ board (NI-6024E, National Instruments, Austin, TX), and were real-time processed on a Toshiba laptop computer (CPU: Intel Celeron 2.0 GHz) running Matlab with the Data Acquisition Toolbox (Mathworks, Natick, MA) in order to generate the ABF. The sound was updated with a 20 Hz refresh rate, meaning that the process is intrinsically delayed by  $1/20$  s. Preliminary trials, conducted using the more complex DSP-based system dsPIC33F (Microchip, USA, capable of further minimizing the refresh rate), showed that a higher refresh rate did not show improvements in the results; therefore, felt confident on the adequacy of the proposed solution. Obviously, the laptop also recorded the complete 3D linear and angular trunk kinematics for off-line analyses. After digital processing in the laptop, the DAQ board converted the digital, audio, and output signal into a binaural synthetic feedback signal flowing through a common audio amplifier (Fostex PH-5, Japan) into headphones (Philips SBC HP-140, The Netherlands) worn by the subject.

### 2.3. The audio-biofeedback mapping

Details of the algorithm for ABF sound generation are provided in Refs. [4,20,21]. Here we report a brief description for the sake of clarity. The design of the ABF sound representation was intended for display to the user of spatial

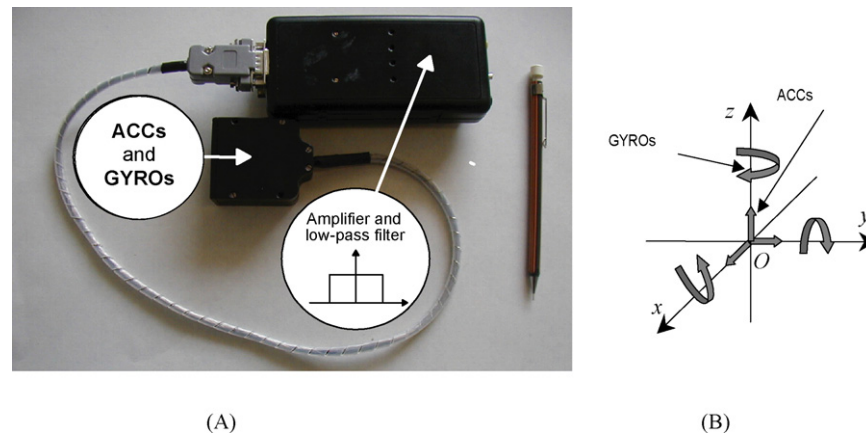


Fig. 1. (A) Photograph of major components of the wearable unit (IMU and service unit): data storing and transmission box, including signal-conditioning circuitry (top); sensor box (bottom). (B) sensitive axis of the six sensors.

information about trunk horizontal movements. The linear accelerations in the antero-posterior (AP) and medial-lateral (ML) directions provided by the sensor unit are mapped into a stereo sound modulated in frequency and amplitude, and adjustable in balance.

The right and left output channels are independently modulated. The panels of Fig. 2(A)–(D) show the coding functions chosen for the feedback sound generation. As seen in Fig. 2(A) and (C), the larger the absolute value of the AP or ML acceleration, the higher the volume of the sound. Fig. 2(B) shows the relationship between sound pitch and AP acceleration; positive accelerations (corresponding to forward movements) increase frequency, while negative AP accelerations (corresponding to backward movements)

decrease frequency. In regards to the ML direction, Fig. 2(D) shows that an acceleration pointing to the left or right of the subject induces a volume increase in the corresponding channel to the detriment of the contralateral channel. In this way, the user can recognize lateral accelerations sensed by the wearable sensor by listening to the balance between the two audio channels.

In order to avoid an overload of information that may be possibly cryptic or even misleading, the ABF coding takes into account the existence of a region around the natural posture where a small spontaneous sway can always be observed even in healthy subjects with all sensory cues available. This reflects the stabilization movements, active while balancing, via small, ballistic-like, throw and catch move-

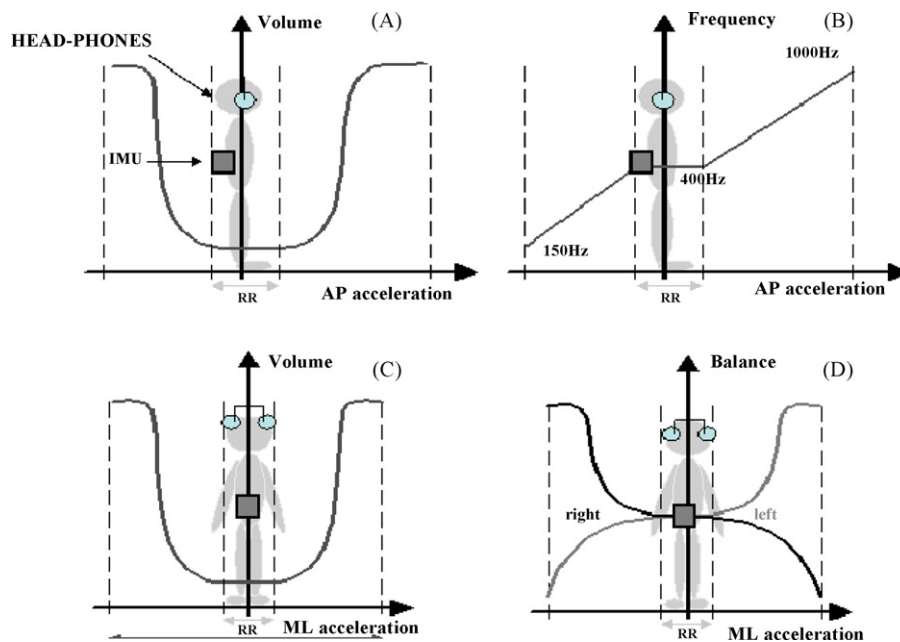


Fig. 2. (A and B) Volume and frequency modulation functions based on AP movements. (C and D) Volume and stereo balance modulation functions based on ML movements.

ments which are provided by the posture control system [14]. Hence, in quiet standing, balance is usually maintained in a regime of small accelerations over a range of angles and not just at one angle. This means that, when planning the sound display, one may think of a small but finite region where sound could be constant and comfortable to inform the user he is inside his regular sway region. We refer to this as the reference region (RR) since it becomes the target of any feedback instruction. The reference region, expressed in terms of AP and ML accelerations, represents the threshold for providing ABF information, as seen from the curves in Fig. 2.

When the user finds himself in the RR, he can hear a pure tone at  $f_0 = 400$  Hz with the lowest volume in both of the channels. This choice was dictated by the functioning of the human auditory system. It is well known that subjects can easily recognize high and low frequencies if they have a reference sound to compare with. This means that subjects use the static sound, provided in the RR, as a reference to better understand the ABF sound as soon as they leave the RR region.

The size of the RR is subject-specific and is defined as a function of the subject's height. In particular, we used an inverted pendulum model and assumed, as a threshold, the acceleration which keeps the vertical projection of the COM within  $\pm 1^\circ$  of sway from the natural posture [13]. Since forward sway is usually larger than in the other directions, we used the value obtained from the model to set the anterior threshold, and used a coefficient of 2/3 to obtain the posterior, left, and right thresholds from it.

#### 2.4. Off-line biomechanical analyses

The segment orientation is determined by the orientation matrix  $\mathbf{R}$  of the local frame with respect to an inertial frame, which is calculated by solving the differential matrix-equation (1) described above and then obtaining the three orientation angles expressed by means of nautical angles.

We also estimated the squared angular velocity module,  $|\dot{\Omega}|^2 = \dot{\omega}_x^2 + \dot{\omega}_y^2 + \dot{\omega}_z^2$ . After observing that the rotational kinetic energy (RKE) of the trunk is proportional to  $|\dot{\Omega}|^2$ ,  $\text{RKE} = (1/2) \dot{\Omega} \mathbf{I} \dot{\Omega}^T$ , where  $\mathbf{I}$  is the inertia tensor, we computed the percentage changes in kinetic energy:

$$\Delta \text{KE}_i \% = \frac{\text{RKE}_i - \text{RKE}_{i-\text{ABF}}}{\text{RKE}_i} \% = 1 - \frac{|\dot{\Omega}_{i-\text{ABF}}|^2}{|\dot{\Omega}_i|^2} \% \quad (2)$$

with  $i = \text{EC}, \text{EOF}, \text{ECF}$ , in order to estimate the energetic changes due to the use of the ABF device.

In Ref. [4] we had demonstrated using the signals from a force-platform that subjects using Biofeedback balanced according the so-called *ankle strategy*. This is the basis for the approach described in the following, based on the inverted pendulum model. Fig. 3 shows the block diagram of the ABF system.

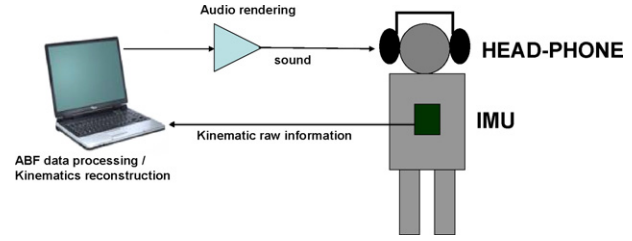


Fig. 3. Block diagram of the ABF system.

### 3. Protocol and results

#### 3.1. Experimental protocol

Nine healthy subjects performed this experiment. Age: mean 55 years, range 33–71 years, height: mean 167 cm, range 151–180 cm, weight: mean 73 kg, range 65–86 kg. The rights of the participants were guaranteed according to the Declaration of Helsinki. Quiet standing sway of the subjects was recorded during 50-s trials in six different conditions: eyes closed on solid surface (EC), eyes open on foam cushion surface (EOF), eyes closed on foam cushion surface (ECF), EC with ABF (EC–ABF), EOF with ABF (EOF–ABF), and ECF with ABF (ECF–ABF). Five trials were performed for each condition; the order of the trials was randomized. The foam used in the cushion had the following characteristics: indentation force deflection at 25%: 116N, tensile strength: 125 kN/m<sup>2</sup>, elongation: 109%, when temperature is 72 °F and relative humidity is 50%, thickness 10 cm. During the trials Malleoli were 2-cm apart, the feet were 15° extra flexed.

#### 3.2. Biomechanical outcome

Paired *t*-tests with Bonferroni correction were performed to determine the effect of ABF on the changes in angular sway and kinetic energy variables.

Using ABF, all subjects significantly reduced pitch, roll and angular velocity in all conditions tested ( $p < 0.05$ ). Fig. 4 shows the raw data from a representative subject in the ECF condition with and without ABF. The largest pitch and roll amplitude reduction was observed when subject used ABF in the ECF condition. The second largest pitch and roll amplitude reduction was observed when subject used ABF in the EOF condition. The smallest pitch and roll amplitude reduction was observed when subject used ABF in the eyes closed condition.

The mean average percentage reduction occurred in pitch and roll angles when subjects used ABF in the three conditions tested is shown in Fig. 5(A). Such a decrease in angular sway of course reflects in a substantial saving of trunk rotational kinetic energy, as shown in Fig. 5(B). RKE was reduced by ABF in all subjects in all the three conditions tested ( $p < 0.05$ ). As expected, the energy saving showed the same trend across test conditions as observed in angular sway, with the largest saving in ECF.



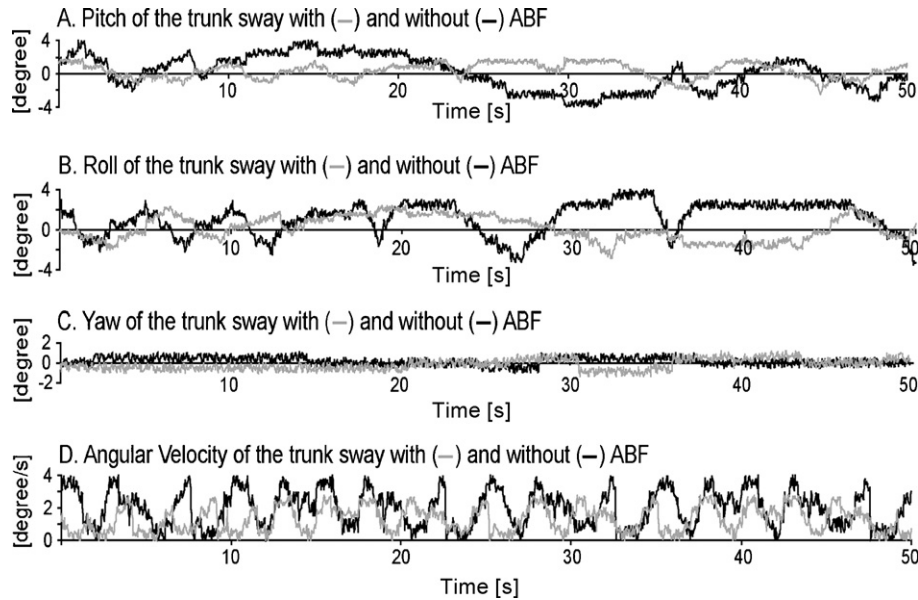


Fig. 4. (A–C) Pitch, roll and yaw angular displacement with and without ABF in one representative trial in the eyes closed on foam condition. (D) Angular velocity modulus with and without ABF in one trial in the eyes closed on foam condition.

### 3.3. Multisegmental analysis

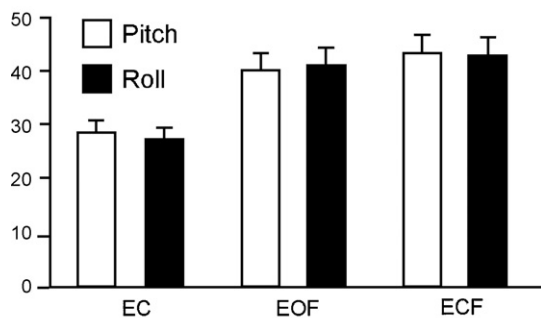
The modelling approach described so far was based on the assumption that balance is maintained by a pure *ankle strategy* [4]. This was the basis for the determination of the RKE on the one-segment-inverted pendulum model. To

Table 2

Segmental model reconstructed by means of optoelectronic equipment

	Chain of segments	Number of segments
1	Ankle–head	1-segm
2	Ankle–hip–head	2-segm
3	Ankle–knee–hip–head	3-segm
4	Ankle–knee–hip–neck–head	4-segm

(A) Angular Sway Percentage Reduction with ABF



(B) RKE Percentage Reduction with ABF

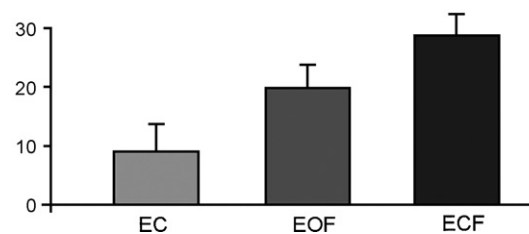


Fig. 5. (A) Mean angular percentage reduction between trials with and without ABF in the three conditions tested. Error bars represent standard errors. (B) Mean energy ratio percentage reduction between trials with and without ABF in the three conditions tested. Error bars represent standard errors.

investigate model adequacy, we repeated the experiment with a Vicon (Vicon, USA) optoelectronic system. The markers were affixed in order to monitor the human body and obtain a segmental reconstruction (by means of relevant software) according to the conditions described in Table 2. Table 3 shows the error in the calculation of percentage changes in trunk kinetic energy,  $\Delta KE_i\%$  when using the single segment model compared to the multi-segmental ones (2/4) during the quiet stance conditions examined in this protocol. We used Dunnett's test to investigate the statistical significance. This test is preferable when comparisons are performed only with one group versus all other groups. It is also useful to protect the analysis from Type-I error. Table 4 reports the statistical significance obtained by means of the Dunnett's test, that was always higher than 99.5%.

Table 3

Percentage error in the estimation of  $\Delta KE_i\%$  when using the single-segment model instead of 2-to-4 segments multi-segmental models

	1-segm vs.		
	2-segm	3-segm	4-segm
Mean error	0.503	0.584	0.612
Maximal error	0.557	0.646	0.677
Standard deviation	0.032	0.037	0.041

Table 4  
Statistical significance of comparison assessed by means of the Dunnett's test

1-segm vs.	Significance
2-segm	99.89
3-segm	99.82
4-segm	99.53

## 4. Discussion and conclusion

### 4.1. Clinical outcome of the methodology

This paper investigated trunk postural modifications induced by a wearable device which assesses trunk sway and provides ABF information through sonification of trunk kinematics kinematics (ACCs). The wearable device is based on an IMU unit including three mono-axial accelerometers and three rate gyroscopes embedded and mounted orthogonally. The biofeedback device was tested on nine healthy subjects during quiet stance under different conditions of sensory limitation. For each condition tested, the IMU of the ABF device hereby introduced permitted the assessment of the trunk angular sway in pitch, roll and yaw directions from which the squared angular velocity module,  $|\dot{\Omega}|^2$ , and the resulting kinetic energy percentage change,  $\Delta KE_i\%$ , could be calculated in the three sensory conditions  $i = EC, EOF, ECF$ . It was found that the more the subjects' balance was challenged by absent or unreliable sensory cues the more ABF was effective in reducing  $\Delta KE_i\%$  and pitch and roll amplitude of subjects' sway. This result demonstrates how, using ABF the energy necessary to control sway decreased and how in the condition which requires the most energy expenditure (ECF), ABF is particularly effective in reducing energy consumption. ABF has already been proved to increase postural corrections by augmenting feedback control of posture [7]. This result, combined with the previous about energy saving, suggests that, using ABF, subjects can save mechanical energy by increasing feedback control of posture. In other words, subjects may be able to trade a higher active control of posture for a lower mechanical energy expenditure. As a consequence, devices, such as the ABF used in this paper, may be particularly suitable for elderly people. In fact, the more people age the more (1) sensory information is reduced [16–18], and (2) muscular energy decreases over time [19]. ABF may be useful to enable elderly subjects to save muscular energy by compensating for their lack of sensory information. As side result the proposed methodology for the energetic investigation based on the RKE percentage reduction due to the biofeedback ABF also opens a new strategy for investigating the effectiveness of several biofeedback methods and coding (visual, tactile, ABF).

### 4.2. Acceptance of the audio-biofeedback-system and possible future scenario as a routine methodology

The information provided to the subject by the ABF system was very easy to understand since nobody had a problem

learning how to use the new information and 1 min of training before starting the experiment was enough. Furthermore, listening to subjects' impression, the audio feedback seems easier to learn than other biofeedback codings they were exposed to in the past (e.g. electro- or mechano-tactile feedback). In fact, it may be easier and more intuitive for the subjects to interpret the link between the audio modulation chosen here and self body movement than to link body movements with a spatially, frequency, or intensity coded tactile stimulation somewhere in the body. The results obtained from the experiments are very encouraging because they show an improvement in balance with a decreasing of the energy expenditure. Although subject attention and stiffness could contribute to improving balance, there is evidence that the bigger contribution is due to the ABF system. It should be acknowledged that ABF initially obliges the user to pay continuous attention to the sound so it limits the possibility for the subject to use ABF and, at the same time, to use hearing for communication. Still, we have preliminary evidences that ABF acts both as a source of information and as a tuning fork, permitting the users, over time, to possibly recalibrate their internal models and becoming able to reproduce the convenient strategy to keep the balance improvement also once ABF is no longer available. This means the acoustic feedback can be discontinuously used for training and then removed. So ABF could be used for training the subject to exploit at best the residual sensing capacity. Furthermore ABF simplicity and usefulness, open interesting scenarios for future applications in clinical and rehabilitation medicine as a routine methodology for promoting mobility and treating balance disorders.

### 4.3. Future developments

We selected normal hearing subjects for this study. However, the perception of sound parameters (*volume*, *pitch*, and *balance*) is not obviously the same across subjects and, mostly, in subjects with partial hearing deficits as in the elderly. A further improvement of the methodology could then include a subject-specific tuning of *volume*, *pitch*, and *balance* to reach in a some manner a hearing normalization/standardization. In order to reach this further objective, we are investigating the use of specific equipment currently used to determine so-called *hearing functions*. This will allow the determination of specific hearing calibration functions to use in the ABF system.

## References

- [1] Massion J. Postural control system. *Curr Opin Neurobiol* 1994;4:877–87.
- [2] Wall III C, Weinberg MS. Balance prostheses for postural control. *IEEE Eng Med Biol Mag* 2003;22(2):84–90.
- [3] Wall III C, Weinberg MS, Schmidt PB, Krebs DE. Balance prosthesis based on micromechanical sensors using vibrotactile feedback of tilt. *IEEE Trans Biomed Eng* 2001;48(10):1153–61.

- [4] Chiari L, Dozza M, Cappello A, Horak FB, Macellari V, Giansanti D. Audio-biofeedback for balance improvement: an accelerometry-based system. *IEEE Trans Biomed Eng* Dec. 2005;52(12):2108–11.
- [5] Hegeman J, Honegger F, Kupper M, Allum JH. The balance control of bilateral peripheral vestibular loss subjects and its improvement with auditory prosthetic feedback. *J Vestib Res* 2005;15(2):109–17.
- [6] Dozza M, Chiari L, Horak FB. Audio-biofeedback improves balance in patients with bilateral vestibular loss. *Arch Phys Med Rehabil* 2005;86(7):1401–3.
- [7] Dozza M, Chiari L, Chan B, Rocchi L, Horak FB, Cappello A. Influence of a portable audio-biofeedback device on structural properties of postural sway. *J Neuroeng Rehabil* 2005;2:13.
- [8] Lyons GM, Culhane KM, Hilton D, Grace PA, Lyons DA. Description of an accelerometer-based mobility monitoring technique. *Med Eng Phys* 2005;27(6):497–504.
- [9] Bourke AK, O'Brien JV, Lyons GM. Evaluation of a threshold-based tri-axial accelerometer fall detection algorithm. *Gait Posture* 2007;26(2):194–9 [Epub November 13, 2006].
- [10] Bourke AK, Lyons GM. A threshold based fall detection algorithm using a bi-axial gyroscope sensor. *Med Eng Phys* January 10, 2007 [Epub ahead of print].
- [11] Nyan MN, Tay FEH, Tan AWY, Seah KHW. Distinguishing fall activities from normal activities by angular rate characteristics and high-speed camera characterisation. *Med Eng Phys* 2006;28(8):9–842 [Epub January 6, 2006].
- [12] Moe-Nilssen R, Helbostad JL. Trunk accelerometry as a measure of balance control during quiet standing. *Gait Posture* 2002;16(1):60–8.
- [13] Mayagoitia RE, Lotters JC, Veltink PH, Hermens H. Standing balance evaluation using a triaxial accelerometer. *Gait Posture* 2002;16:55–9.
- [14] Giansanti D, Maccioni G, Macellari V. The development and test of a device for the reconstruction of 3-D position and orientation by means of a kinematic sensor assembly with rate gyroscopes and accelerometers. *IEEE Trans Biomed Eng* 2005;52(7):1271–7.
- [16] Peterka RJ, Black FO. Age-related changes in human posture control: motor coordination tests. *J Vestib Res* 1990;1(1):87–96.
- [17] Enrietto JA, Jacobson KM, Baloh RW. Aging effects on auditory and vestibular responses: a longitudinal study. *Am J Otolaryngol* 1999;20(6):371–8.
- [18] Kuo AD, Speers RA, Peterka RJ, Horak FB. Effect of altered sensory conditions on multivariate descriptors of human postural sway. *Exp Brain Res* 1998;122(2):185–95.
- [19] Kappeler L, Epelbaum J. Biological aspects of longevity and ageing. *Rev Epidemiol* 2005;53(3):235–41.