# **Chapter 3 Form Follows Function: Bridging Neuroscience and Architecture**

Eve A. Edelstein and Eduardo Macagno

## 3.1 Introduction

"Primum non nocere", the guiding principle of medicine credited to Hippocrates, emphatically asks that we first do no harm; our architectural principles must serve the same goal. Yet, too often the form and function of architectural environments neglect to take into account the influence of the built setting on human responses and indeed, on human health itself. How can we assess this influence in an objective, consistent manner? Can we predict what this influence in the early stages of design and before the structure is built? An emerging discipline, one that bridges neuroscience and architecture, is beginning to provide more rigorous methodologies and a growing number of research reports that explores the interaction between brain, body, building, and the environment.

Neuroscience encompasses a range of disciplines that study the multiple functions of our brains, and how these functions change from birth to death and are affected by disease. Our brains survey our environments through multiple sensory organs and generate appropriate behaviors, conscious and unconscious. Neuroscientific research reveals how dynamic and plastic our brains are, and informs us about how different our capacities to respond to our environments are as children and as adults, and how exposure to environmental conditions influence such capacities. Coupled with this new knowledge are advances in several technologies for measurement of human brain responses to external stimuli that can provide architects with the tools to perform more

E.A. Edelstein (🖂)

Innovative Design Science, Academy of Neuroscience for Architecture, San Diego, CA, USA e-mail: neuroarchitecture@gmail.com

E. Macagno University of California San Diego La Jolla, Academy of Neuroscience for Architecture San Diego, CA, USA e-mail: emacagno@ucsd.edu

Fig. 3.1 An immersive 3D virtual reality CAVE allows viewers to navigate through full-scale building models while their movement and physiological responses are synchronously monitored



objective studies, indeed to quantify how their built products engage and affect the human mind and body. The products of such studies are beginning to inform sustainable guidelines and enhance human health and function within the built environment.

It is often suggested that the complexity of architecture makes impossible the reduction of the human interaction with built settings to measurable parts. However, scientific studies combined with rigorous social and cultural observations can be applied to architectural evaluations to yield greater analytic power. For example, it is now possible to measure the electrical activity of the brain with a wearable multielectrode array that can transmit data wirelessly to a computer, leaving the subject of study relatively unencumbered and free to move in space. Together with parallel physiological measurements obtained with eye movement, heart rate, and skin conductivity sensors, the sum of the gathered data can yield critical information about attention, stress, learning, mental state, etc., that can be analyzed with respect to the audiovisual and physical inputs that are being perceived. These human monitoring techniques joined with advanced auditory and visual virtual reality (VR) environments can provide a means to test designs and to acquire objective evidence for evaluating a priori and a posteriori the influence of architecture in human terms (Fig. 3.1).

## 3.2 Neuroscientific Methods

In the domain of architecture, a scientifically derived "neuro-architectural" hypothesis may be used to articulate a testable idea about how a specific feature of design may influence psychological or physiological processes that may in turn be associated with measurable changes that reveal the impact of the built environment on human health.

Historically, architectural research relied on philosophical constructs or analysis of behavior patterns in order to relate human responses to design. Psychological studies using subjective methods, such as surveys or interviews, have also been used to test such relationships; however, these methods rely on the subject's understanding or ability to articulate why they respond to a design element in a particular way. In contrast, neuroscientific investigations offer a higher degree of objectivity, providing a number of additional tools that can measure both conscious and subconscious responses without the need to interrupt and perhaps bias the subject. Nor do researchers interfere with the results themselves by asking subjects to think about how or why they respond as they do. This is especially important when studying those unable to understand or verbalize their perceptual and emotional responses due to their age, limited abilities, or medical conditions. As demographic changes in the elder population indicate an increasing prevalence of dementia and the use of improved diagnostic tools identifies larger percentages of children with developmental disabilities such as autism spectrum disorder, considerations of the diversity of user characteristics are increasingly important.

With the inclusion of people with a broad range of abilities in all architectural settings, healthcare, educational, institutional, and residential facilities should be designed to support the heterogeneous and dynamically changing nature of the brain's response to the environment. Particular attention is needed in the design of healthcare facilities where complex cognitive tasks are performed under duress, while serving the most fragile in great need of care. While sustainable guidelines are increasingly incorporating objectives directed at improving both human and environmental outcomes, in healthcare facilities, the overwhelming focus of sustainable design must be on the human impact of built spaces.

The confluence between healthy design and sustainable design is most notable in recent developments of sustainable guidelines for healthcare institutions by institutions such as BREEAM for Health, LEED<sup>®</sup> for Healthcare, AIA Facilities Guidelines Institute, the Joint Commission, and the Global Health and Safety Initiative, among others. International guidelines for health and safety are increasingly focused on minimizing harm resulting from the extreme conditions, materials, and procedures required to provide care. These initiatives reflect the urgent need to continue to investigate the effectiveness of sustainable strategies that seek to improve clinical outcomes in medical and all environments, and to reduce the risk of diseases and disorders related to pollutants, toxins, and infectious agents from air, water, and physical contact that have been incorporated in sustainable guidelines to date [1].

This chapter provides examples of how emerging technologies and scientific methods may be applied to neuro-architectural studies, exploring three elements of the physical environment (sound, location, and light) that are within the scope of the architects, and have measurable impact on both human outcomes and sustainable objectives. Neuroscientific data offers the means to advance and validate novel additional guidelines, which now can be continually updated based upon measurable evidence. It is critical that best practices and protocols based upon incomplete data inform, rather than prescribe, design rules, and allow architecture to respond as new medical and neuroscientific data are revealed [2]. In this context, objective measurement of the neural, psychological, and cognitive impact of the built environment becomes feasible and is indeed necessary.

### 3.3 Neuroscientific Evidence

The human brain is the most complex organ in our bodies, comprising 100 billion neurons of many different types, arrayed in dozens of domains with their own unique architectures and patterns of synaptic connections. Electrical and chemical signals Fig. 3.2 A 256 electrode array records electroencephalographic (EEG) responses from cortical brain components



course continuously through the brain, parsing, analyzing, and storing incoming information from sensory organs that respond to both the external environment (light, sound, smell, taste, touch, temperature, and position relative to gravity) and internal parameters (temperature, chemical concentrations, oxygen tension, and blood pressure). The brain generates motor and chemical responses that are adaptive for maintenance, survival, procreation, and meaningful experiences that create memory, consciousness, a sense of self, and history. The field of neuroscience explores the breadth of these input signals and the corresponding outputs that underlie unconscious and conscious thought, physiological, emotional, and aesthetic responses.

Highly refined and powerful new tools allow the monitoring of the chemical and electrical signals that are responsible for these properties. For example, functional magnetic resonance imaging (fMRI) allows us to peer into the recruitment of different domains of the brain in perception and decision making while undergoing sensory stimuli that evoke memories and desires. The use of high-definition electroencephalography (HD-EEG) allows for real-time recording of patterns of electrical activity that subserve attention and cognition in way-finding and path selection in a hospital environment, as described in experiments such as those discussed below. EEG methods offer an advantage by revealing the immediate response of neural signals in microsecond time frames as subjects move within and among distinct experimental conditions. Biochemical assays of perspiration currently allow the rapid determination of neurohormonal responses to stressful environments, such as those found in healthcare facilities. Electrocardiography (ECG or EKG) allows the measurement of heart rate variability (HRV) that is driven by the autonomic nervous system in order to modulate stress and relaxation in response to light and other environmental changes. In sum, we can now measure what our brains are doing, rather than make an educated guess from a verbal exchange or a psychosocial survey of behavior (Fig. 3.2).

#### 3.4 Our Brains Are Dynamic Structures

When we design a building, we need to take into account the age and health status of the people who will use it, as much as we incorporate criteria for the physical performance and sustainability of the facility and local environmental conditions. At birth, the brain is still quite immature, and it will take over 20 years for the maturation The StarCAVE is a five-sided virtual reality room created by 15 back-projection screens that enclose multiple viewers in a space 3 m in diameter by 3.5 m in height. Projectors create 3D stereo, 20/40 vision resolution of over 68 million pixels – 34 million per eye – distributed over the walls and floor. The viewer interacts with the virtual images using a 3D joystick and a head tracking infrared sensor system that registers the subject's location and orientation in space, and moves 3D visual fields according to their point of view. The viewer's head and joystick locations are logged over time, dynamically tracking their first-person perspective, position, and interactions with the virtual setting [3].

A novel computer-aided design software (CAVECAD<sup>TM</sup>) has been developed that has the capability of altering dynamically the VR environment while subjects stand within the VR model itself [4]. This approach eliminates the traditional step of creating a 3D model at a desktop computer, before bringing it into a virtual environment, thus allowing for much shorter turnaround times when changes to the model are to be made. Therefore, a number of design concepts and use cases can be tested while logging subject responses to specific changes in controlled experimental paradigms, and without necessitating the building of or change to mock-ups before further testing proceeds. In addition, Collaborative-CAVE software allows the same virtual model to be projected in many CAVE environments distributed in different global locations, with participants at each site able to control their own movement through the model, while the other teams' viewports move in synchrony. We expect this to become a valuable tool for the architectural profession to design and evaluate complex designs in full-scale and ultrahigh quality visualizations. In addition, experts, clinicians, and clients are collaborating to use this virtual reality design laboratory to evaluate operational use and programmatic functions within the VR models.

In order to measure the neurological and associated psychophysiological and behavioral responses to design, the immersive and interactive capabilities of the VR environment are augmented with simultaneous monitoring of the subject's responses to enable a new class of controlled experiments to test design before the first brick is laid. These advances contribute to the mobility and simplicity of objectively recording the subject's experience along with continuous brain and ocular activity while in 3D virtual reality mockups, and in due course, in real architectural environments. Broad-band data emanating from the brain and body are recorded using a newly developed and tested customized noncontact biopotential sensing and logging device that can detect and collect electroencephalographic (EEG) brain waves, in addition to detecting electrical activities that measure eye movement (electrooculography - EOG), cardiovascular (electro-cardiography - ECG), and muscular potentials (electro-myography - EMG). Unobtrusive sensors pick up the body's electrical potentials without conductive contact to the skin and can be mounted over hair or over clothing without gel or other skin preparation. Other versions of the sensor make use of dry-contact sensors as well as conductive fabric to integrate sensing into apparel worn by the user. The EEG/EOG system directly interfaces with the StarCAVE computing platform and transmits digitize waveforms through a Bluetooth communication link that is synchronized with CAVE data, tracking the location, head position, and reaction time of the viewer as she moves within the 3D

model. A real-time "bio-cursor" uses EOG synchronized with VR head tracking to reveal attention to specific elements in the virtual environment, detecting gaze and micro-movements (saccades) in three dimensions [5].

These technological breakthroughs and the evidence they can reveal hold the promise of the means to validate data that may inform and expand sustainable guidelines that serve human and environmental health.

### 3.6 Neuro-architectural Research

Discussion of our recent research describes emerging technologies that provide the means to predict, test, and validate how physical features within the scope of architectural designs, such as sound, location, and light, may inform and enhance both human and environmental health. Such controlled laboratory-based studies form the foundation for future research that uses wireless, sensor-based technologies in actual built settings, to gain deeper understanding of the impact of architectural conditions and environmental exposure on human and sustainable outcomes.

#### 3.6.1 Sound as an Environmental Stressor

The field of acoustics provides a useful example of the intersection of neuroscience and architecture, as it consolidates knowledge of the physical propagation of sound with understanding of the human response to speech, background sounds, and the impact of unwanted noise. Noise is a well-recognized environmental stressor that puts all users at risk. Beyond acoustic guidelines already considered in sustainable programs, ongoing research reveals that unwanted noise, at intensity levels below those known to cause noise-induced hearing loss, may disturb immune, cardiovascular, endocrine, sleep, emotional, and cognitive responses [6]. Even low sound levels, if unwanted, competing or disturbing, may be associated with diminished speech intelligibility, lowered cognition, and lack of rest, along with increased stress responses [7]. The Environmental Expert Council found a consistent trend toward an increased cardiovascular risk if the daytime noise levels exceed 65 dB(A) [8]. Chronic stress reactions, such as cortisol disturbances, have been observed in children with long-term low-frequency traffic noise exposure averaged at less than 55 dB(A) [9].

The influence of unwanted noise on human health is of greatest importance in healthcare settings where diminished speech intelligibility, cognitive function, and stress status may directly impact the quality of care and healing processes. Edelstein et al. (2008) logged continuous sound levels in emergency and intensive care units and found average levels ranging from 75 to 85 Leq dB(A), with impulse levels from 85 to 100 dB(A), peaking at 120 dB(A) during shift change [10]. Averaged sound pressure levels in intensive care units were up to 10 times greater than conversational speech. Indeed, recent findings show that background noise levels in

healthcare environments have been steadily increasing over the past 50 years, with no single facility operating within the sound levels recommended by the World Health Organization [11].

The acoustic profile of healthcare spaces may introduce direct and measurable risks of doing harm if ambient noises mask the perception of body sounds [12]. Neuroscientific and clinical studies clearly demonstrate that competing sounds or noise, wanted or unwanted, mask perception and attention to speech and sound signals [13]. Clinical studies confirm that diagnostic accuracy by means of stethoscope auscultation is diminished in flight or ambulances [14]. However, there is a scarcity of research into diagnostic accuracy during masking from ambient HVAC, clinical or equipment sounds within architectural settings. Of equal concern is the risk that elevated sound levels from competing alarms, equipment, conversations, and mechanical systems may interfere with speech intelligibility, and be a factor in "look-alike-sound-alike" medication errors [15].

Although sustainable guidelines increasingly call for acoustic design that reduces unwanted noise, and an "Integrated Project Team" approach that includes acoustic consultants on the design team, most acoustic modeling systems currently available have greatest predictive accuracy for large theatre and concert spaces, yet low accuracy for small spaces such as patient rooms or emergency bays.

To advance understanding of these vital issues, the research team at UCSD created a virtual sound simulation environment to enable architects and users to see *and hear* in advance the consequences of design choices. CAVE and Sound Labs technologies were integrated to create SoniCAVE<sup>™</sup> in which ultrahigh definition recordings and sound simulations of real environments are merged with ultrahigh resolution, full-scale visualizations. Emerging software-controlled audio rendering environments are being developed to create accurate, predictive auditory scenes, derived from computer-aided design models, photographic images, objects, avatars, "real-world" audio samples, and design materials databases, leveraging spatial auralization and 3D scientific visualization to evaluate entirely new contexts. These new developments provide virtual reality environments in which users and architects may predict and measure neurological, cognitive, stress, and performance measures as their teams interact in realistic healthcare scenarios.

Immersive 3D VR "sound-scenes" are used to investigate the impact of acoustical design elements on speech perception and cognitive error, using simulations and recordings of actual clinical conversations, equipment alarms, and mechanicals sound. Demonstrations using spatially-distributed multiple sound sources reveal how discrimination of heart sounds, recordings of medication orders, and "sound-alike" pharmaceuticals are made indistinguishable when masked by realistic clinical sounds [16]. This is clearly an area that requires far greater attention and experimentation. Emerging techniques for sound abatement while making critical sounds available in specific locations and directions (e.g., reducing sound reaching the patient while allowing patient sounds to reach the nurse) need to be validated in terms of stress and cognition in order to inform sustainable acoustic design in all architectural contexts, where communication and relaxation have direct impact on outcomes (Fig. 3.3).

**Fig. 3.4** The EEG waveforms shown on the laptop are compared in order to investigate different responses as subjects navigate through spaces with and without wayfinding cues



These early results indicated a progressively subtle use of visual cues as subjects navigated the ambiguous space. In the case where obvious cue were not presented, subjects looked for any distinguishing features that might indicate location, including shadows around doors, or patterned finishes. This suggests a continuum of cue effectiveness dependent on the surrounding context and the opportunity to repeatedly search for cues. This technology is expected to become a valuable tool to create virtual reality mockups in which wayfinding systems can be tested at the scale of a building or an urban environment and inform sustainable objectives that promote walking and exercise, and the reduction of reliance on transportation systems that use nonrenewable fuels or create pollutants.

Design for effective navigation has value beyond circulation and cognitive mapping strategies. McCarthy (2004) reported that in one hospital, 4,500 h each year were spent by staff giving directions to lost patients, with an associated cost equivalent of \$220,000 per annum [21]. In addition to the reduction of stress or anxiety so often experienced when one feels lost, the consequence of ineffective wayfinding design may have more severe consequences, and may even prove fatal during infectious epidemics, should the separation between clean and contaminated spaces be compromised.

It is also proposed that neuroscientific methodologies and emerging technologies will serve investigation of the most effective navigation cues, in multiple modalities, for people with a range of abilities and disabilities, including those associated with dementia, Alzheimer's disease, and other dementias or with other disorders that interfere with memory formation.

## 3.6.3 The Influence of Light on Human Health and Function

A long history of research, dating to ancient texts and reports from the beginning of the seventeenth century, reveals that exposure to light has significant impact on human outcomes [22]. Advances in research into the brain's neural "clock", located in the supra-chiasmatic nucleus and associated pineal and endocrine systems, reveal multiple oscillatory systems that modulate human responses to changing light patterns. The solar cycle of daylight and darkness over approximately 24 h is the primary stimulus that synchronizes biological and behavioral rhythms in response to daily (circadian) and seasonal (circannual) variations in light. For example, diurnal

and nocturnal fluctuations in melatonin modulates sleep and wakefulness, while elevated cortisol levels in the morning prime the body for activity, and lower cortisol levels at night encourage relaxation. Recent discoveries of special photoreceptive ganglion cells in the retina reveal how slowly changing light regulates a complex system of neural hormone responses to synchronize psycho-physiological responses with the time of day [23, 24]. Recent studies indicate that the cones, previously thought to function solely as vision receptors, also play a role in eliciting such non-visual responses, in certain conditions [25].

Short-term electrical light exposure also influences human responses, and if excessive, may comprise an environmental health risk. Edelstein et al. [26] demonstrated that heart rate variability, a well-established indicator of health risk, morbidity, and mortality [27] was highly significantly different during memory task performance during brief exposure (less than 15 m) to red, bright white, and dark conditions. Whereas many studies have focused on the influence of blue and bright white light of melatonin responses, this experiment demonstrated that red light regulated cardiac responses, with appropriate HRV relaxation during rest and activation during the memory task. In contrast, bright white light with a blue peak was associated with constant heart rate activation throughout the experiment [28]. In a parallel study, brainwaves recorded via a 256 electrode EEG array tended to be different during red versus bright white light conditions in a single subject self-control study [29]. Other studies reveal that green light also stimulates circadian responses under certain conditions [30]. It should be noted that the influence of "full spectrum" electrical lighting, which has a limited number of spectral peaks within the range of visible light, has yet to be established [31].

Research suggests that the dynamic manipulation of light and darkness may impose some risk to mental and physical health. For example, epidemiological studies suggest that cancer rates in night-shift workers, including flight crew, factory workers and nurses, may be related to an abnormal pattern of light–dark exposure [32, 33]. Low levels of lighting during the day have been associated with mental health status, including seasonal affective disorder and longer recovery times for mental health patients [34]. Diminished cognitive function has also been associated with inadequate lighting, such that pharmaceutical medication error rates have been correlated with seasonal reduction in light [35].

Most sustainable programs include guidelines that access to daylight. For example, rating systems such as LEED® encourage access to daylight in "regularly occupied areas" with 90% of "inpatient staff and public areas" required to have design and materials that provide both daylight and natural views [36]. Design recommendations include the solar orientation of buildings, control of light pollution, and innovative electrical lighting [37].

However, an approach that gives credit to the proportion of space with daylight, rather than crediting adjustable lighting systems that provide for individual needs, is unlikely to address the range of human conditions, and the dynamically changing nature of functions that take place in architectural settings. While ongoing neuroscientific research will continue to reveal the parameters of light and dark that best serve human outcomes, the natural pattern and spectrum of solar light should continue to inspire and guide lighting for human health [38].

#### 3.7 Conclusions

Much has been made of the development and implementation of standard criteria that measure the performance of a building in relation to the physical environment. Designers, architects, and builders strive to achieve the highest level of certification from regional or international sustainable ranking programs to demonstrate excellence in concern for the environments in which they build. A similar concern and aspiration needs to be developed for building performance with respect to user benefits. The approach we have discussed, using contemporary high technology to measure user responses to the buildings in which they work, live, learn, and seek better health, parallels the green initiative and puts concern for the user on a par with concern for the physical environment. Recent developments in sensor technology and wireless communication provide a means to implement wearable monitoring devices that leave the subject both unencumbered and able to move both within virtual and real built environments. These advances allow the possibility of recording real-time neurological and physiological data from human subjects while testing how they respond to stimuli.

The general premise that looks to the natural environment as the "gold-standard" for healthy architectural and ecological design has guided sustainable programs to date. In relation to this metric, it is of great importance that rigorous research continues to inform sustainable guidelines that seek to assess and minimize the risks from exposure to pollutants or infectious agents in air, water, and materials. Beyond reduction in exposure to neurotoxins, pollutants, and harmful by-products of the building profession and industrial processes, the fusion of architectural, scientific, and medical knowledge can accelerate the development of sustainable objectives that enhance human experience, performance, and health outcomes.

Architects and their clients are increasingly asking for rigorous and trustworthy data to support their design decisions. We suggest that the application of new approaches created at the interface between neuroscience and architecture will be the best source for the "evidence" in evidence-based design. Such evidence, from multidisciplinary studies of human development, neurology, physiology, and psychology that assess the impact of the environment on human health and wellbeing, should complement parallel studies of the reverse influence, that of humans on their environments. Ultimately, our goal must be to implement guidelines for sustaining and enhancing human health that serve the range of human needs from birth to death, and for the most fragile as well as the most gifted.

Acknowledgements The Neuroscience Design team acknowledges Calit2 and UCSD for supporting the projects described here including the contributions of Gert Cauwenberghs, Michael Chi, Nicholas Echols, Joachim Gossmann, Peter Otto, Jurgen Schulze, Cory Stevenson, Toshiro Yamada, and Lelin Zhang, Thomas DeFanti and Ramesh Roa. We also acknowledge Randy Peterson and Alvaro Velasquez for use of their models, and a generous gift in support of the project from HMC Architects.

## References

- 1. Guenther R. (2009) Sustainable architecture for health: a mindset shift. HERD. 2009 Summer;2(4):3–9. http://www.ncbi.nlm.nih.gov/pubmed/21165839. Accessed 30 Jan 2011.
- Edelstein EA, Hill H (2008) Evidence for sustainable design that benefits human health and performance. City Center Development Corps Best Practices in Urban Sustainability Award. http://www.ccdc.com/media-and-publications/news/archived-news-2008. Accessed 30 Jan 2011.
- DeFanti, T.A., Dawe, G., Sandin, D.J., Schulze, J.P., Otto, P., Girado, J., Kuester, F., Smarr, L., Rao, R., "The StarCAVE, A third-generation CAVE and virtual reality OptIPortal," Future generation computer systems/The international journal of grid computing: Theory, methods and applications, Elsevier B.V. 25(2):169–178. DOI: 10.1016/j.future.2008.07.015
- 4. Zhang, L., Chi, Y.M., Edelstein, E.A., Schulze, J., Gramann, K., Velasquez, A., Cauwenberghs, G., and Macagno, E. (2010). Wireless Physiological Monitoring and Ocular Tracking: 3D Calibration in a Fully-Immersive Virtual Health Care Environment. 32nd Annual International Conference of theIEEE Engineering in Medicine and Biology Society. http://www.isn.ucsd. edu/pubs/embc10\_eog.pdf. Accessed 1 February 2011.
- 5. Ibid. Zhang et al. (2010).
- Selander J, Bluhm G, Theorell T, Pershagen G, Babisch W, Seiffert I, Houthuijs D, Breugelmans O, Vigna-Taglianti F, Antoniotti MC, Velonakis E, Davou E, Dudley ML, Järup L; HYENA Consortium. Saliva cortisol and exposure to aircraft noise in six European countries. Environ Health Perspect. 2009 Nov;117(11):1713–7. Epub 2009 Jul 20. http://www.ncbi.nlm.nih.gov/ pubmed/20049122. Accessed 30 Jan 2011.
- Ising H, Braun C (2000) Acute and chronic endocrine effects of noise: Review of the research conducted at the Institute for Water, Soil and Air Hygiene. Noise Health. (7):7–24. http://www. ncbi.nlm.nih.gov/pubmed/12689468. Accessed 1 February 2011.
- Ising H, Kruppa B (2004) Health effects caused by noise: Evidence in the literature from the past 25 years. Noise Health. 6:22:5–13. http://www.ncbi.nlm.nih.gov/pubmed/15070524. Accessed 30 Jan 2011.
- Ising H, Ising M (2002) Chronic cortisol increases in the first half of the night caused by road traffic noise. Noise Health. 4:16:13–21. http://www.ncbi.nlm.nih.gov/pubmed/12537837
- Edelstein, E. A., McCoy, L. Wilson, S. Stephens, K., The Mind, Body, and the Healing Environment: Sustaining a Measureable Balance. Planetree Annual Conference. October 21, 2008. Chicago, IL.
- Busch-Vishniac IJ, West JE, Barnhill C, Hunter T, Orellana D, Chivukula R. (2005) Noise levels in Johns Hopkins Hospital. J Acoust Soc Am. 2005 Dec;118(6):3629–45. http://www. ncbi.nlm.nih.gov/pubmed/16419808. Accessed 1 February 2011.
- Zun LS, Downey L. (2005) The effect of noise in the emergency department. Acad Emerg Med. 2005 Jul;12(7):663–6. http://www.ncbi.nlm.nih.gov/pubmed/15995101. Accessed 1 February 2011.
- 13. Edelstein-Williams, EA. (2000) Clinical Applications of Otoacoustic Emissions in the Assessment of Olivocochlear Dysfunction. Ph.D. Thesis. University College London.
- 14. Tourtier JP, Fontaine E, Coste S, Ramsang S, Schiano P, Viaggi M, Libert N, Durand X, Chargari C, Borne M. (2010) In flight auscultation: comparison of electronic and conventional stethoscopes. Am J Emerg Med. 2010 Jul 30 [Epub ahead of print]. http://www.ncbi.nlm.nih. gov/pubmed/20674225. Accessed 1 February 2011.

- James KL, Barlow D, McArtney R, Hiom S, Roberts D, Whittlesea C. (2009) Incidence, type and causes of dispensing errors: a review of the literature. Int J Pharm Pract. 2009 Feb 17(1):9–30. http://www.ncbi.nlm.nih.gov/pubmed/20218026. Accessed 1 February 2011.
- Edelstein, E. A., Sound Advice: How Environmental Audits Reveal Urgent Drivers to Modify the Acoustic Profile in Healthcare Settings. Healthcare Design Conference. November 15, 2010. Las Vegas, NV.
- O'Keefe, J., & Dostrovsky, J. (1971). The hippocampus as a spatial map. Preliminary evidence from unit activity in the freely-moving rat. *Brain Res*, 34(1), 171–175. http://www.ncbi.nlm. nih.gov/pubmed/5124915. Accessed 1 February 2011.
- McNaughton, B. L., Battaglia, F. P., Jensen, O., Moser, E. I., & Moser, M. B. (2006). Path integration and the neural basis of the 'cognitive map'. *Nat Rev Neurosci*, 7(8), 663–678. http://www.ncbi.nlm.nih.gov/pubmed/16858394. Accessed 30 Jan 2011.
- Aguirre, G. K., & D'Esposito, M. (1999). Topographical disorientation: a synthesis and taxonomy. *Brain*, 122, 1613–1628. http://www.ncbi.nlm.nih.gov/pubmed/10468502. Accessed 30 Jan 2011.
- 20. Edelstein, E. A., Gramann, K., Schulze, J., Shamlo, N. B., van Erp, E., Vankov, A. Makeig, S., Wolszon, L., Macagno, E. Neural Responses during Navigation and Wayfinding in the Virtual Aided Design Laboratory Brain Dynamics of Re-Orientation in Architecturally Ambiguous Space. In SFB/TR 8 Report No. *Report Series of the Transregional Collaborative Research Center SFB/TR 8 Spatial Cognition*. Haq, S., Hölscher, C., Torgrude, S. (Eds.) 2008 (p35–41). http://www.calit2.net/~jschulze/publications/Edelstein2008.pdf Accessed 30 Jan 2011.
- McCarthy M (2004) Healthy design. Lancet. 2004 Jul 31-Aug 6;364(9432):405-6. http://www.ncbi.nlm.nih.gov/pubmed/15290839. Accessed 1 February 2011.
- 22. Lemmer B (2009) Discoveries of rhythms in human biological functions: a historical review. Chronobiol Int. 26:6:1019–68. http://www.ncbi.nlm.nih.gov/pubmed/19731105. Accessed 30 Jan 2011.
- Brainard GC, Hanifin JP, Greeson JM, Byrne B, Glickman G, Gerner E, Rollag MD. (2001) Action spectrum for melatonin regulation in humans: evidence for a novel circadian photoreceptor. J Neurosci. 21(16):6405–12. http://www.ncbi.nlm.nih.gov/pubmed/11487664. Accessed 30 Jan 2011.
- 24. Thapan K, Arendt J, Skene DJ (2001) An action spectrum for melatonin suppression: evidence for a novel non-rod, non-cone photoreceptor system in humans. J Physiol. 15:535:261–7. http://www.ncbi.nlm.nih.gov/pubmed/11507175. Accessed 30 Jan 2011.
- 25. Gooley JJ, Rajaratnam SM, Brainard GC, Kronauer RE, Czeisler CA, Lockley SW. (2010) Spectral Responses of the Human Circadian System Depend on the Irradiance and Duration of Exposure to Light. Sci Transl Med 12 May 2010 2:31ra33. DOI:10.1126.
- 26. Edelstein EA, Ellis RJ, Sollers III JJ, Thayer JF (2007) The effects of lighting on autonomic control of the heart. Society for Psychophysiological Research Proceedings. 60:108. http://www.sprweb.org/meeting/past\_mtng/2007/07SPRFinalb.pdf. Accessed 30 Jan 2011.
- Thayer JF, R.D. Lane (2007). The role of vagal function in the risk for cardiovascular disease and mortality. Biol Psychol 74(2):224–42. http://www.ncbi.nlm.nih.gov/pubmed/17182165. Accessed 30 Jan 2011.
- Edelstein, E.A. Influence of Architectural Lighting on Health. *InformeDesign*, Epub. 2009, 7(2):1–5. http://www.informedesign.org/\_news/april\_v07r-pr.2.pdf. Accessed 30 Jan 2011.
- 29. Chong, G. H., Brandt, R. M., Cranz, G. Denton B. P., Doctors, S. I., Edelstein, E. A., Mangel, R. S., Martin, W. M. (2008) AIA College of Fellows 2005 Latrobe Fellowship: Developing an Evidence-Based Design Model that Measures Human Response: A Pilot Study of a Collaborative, Trans-Disciplinary Model in a Healthcare Setting. American Institute of Architects, Washington, D.C. http://www.aia.org/groups/aia/documents/pdf/aiab082986.pdf. Accessed 30 Jan 2011.
- 30. Gooley JJ, Rajaratnam SM, Brainard GC, Kronauer RE, Czeisler CA, Lockley SW (2010) Spectral Responses of the Human Circadian System Depend on the Irradiance and Duration of Exposure to Light. Sci Transl Med 12 May 2010 2:31ra33. DOI:10.1126.

- McColl SL, Veitch JA (2001) Full spectrum fluorescent lighting: a review of its effects on physiology and health. Psychol Med. 31:949–964. http://www.ncbi.nlm.nih.gov/pubmed/ 11513381. Accessed 30 Jan 2011.
- Schernhammer ES, Thompson CA (2010) Light at night and health: the perils of rotating shift work. Occup Environ Med. http://www.ncbi.nlm.nih.gov/pubmed/20921271. Accessed 30 Jan 2011. http://oem.bmj.com/content/early/2010/10/04/oem.2010.058222.long.
- 33. Stevens RG, Blask DE, Brainard GC, Hansen J, Lockley SW, Provencio I, Rea MS, Reinlib L (2007) Meeting report: the role of environmental lighting and circadian disruption in cancer and other diseases. Environ Health Perspect. 115:9:1357–62. http://www.ncbi.nlm.nih.gov/pubmed/17805428. Accessed 30 Jan 2011.
- Beauchemin KM, Hays P (1996) Sunny hospital rooms expedite recovery from severe and refractory depressions. J Affective Disord 40:49–51. http://www.ncbi.nlm.nih.gov/ pubmed/8882914. Accessed 30 Jan 2011.
- Buchanan TL, Barker KN, Gibson JT, Jiang BC, Pearson RE. Illumination and errors in dispensing. Am J Hosp Pharm 1991; 48(10)2137–45. http://www.ncbi.nlm.nih.gov/ pubmed/1781468. Accessed 30 Jan 2011.
- 36. U.S. Green Building Council® (2009) LEED for Healthcare. Professional Report. http://www. usgbc.org/ShowFile.aspx?DocumentID=8257. Accessed 30 Jan 2011.
- 37. Edelstein EA, Hill H (2008) Evidence for sustainable design that benefits human health and performance. City Center Development Corps Best Practices in Urban Sustainability Award. http://www.ccdc.com/media-and-publications/news/archived-news-2008/594-ccdc-newsccdc-announces-winners-for-urban-sustainability-papers.html. Accessed 30 Jan 2011.
- Edelstein EA. (2007) The effects of colour and light. World Health Design. 2: 57–61. http:// www.worldhealthdesign.com/The-Effects-Of-Colour-And-Light.aspx. Accessed 30 Jan 2001.