Chapter 2

Experimental setup and methodology

This chapter presents a global and detailed view of the data used in the following chapters, as well as the conditions in which it was acquired. In order to maintain each chapter self-contained, the following chapters repeat, whenever necessary, the relevant portions of the information contained in the present chapter. However, this chapter presents a global view that is not found elsewhere in this text.

Data analyzed and discussed in the present work was essentially obtained in the framework of the study entitled “Sleep and respiration in microgravity”. The principal investigator of this study was John B. West, and Ann R. Elliott, G. Kim Prisk and Manuel Paiva were co-investigators. The National Aeronautics and Space Administration (NASA) and European Space Agency (ESA) supported this study and scheduled it to fly on the space shuttle, namely on a specific flight dedicated to the study of the brain. This mission was entitled *Neurolab*, and citing NASA ([1]), its intended goal was “(...) to study basic research questions and to increase the understanding of the mechanisms responsible for neurological and behavioral changes in space.”

As mentioned in the previous chapter, sleep and sleep quality has been a constant concern during space-flight and poor sleep quality is a common complaint upon return to earth, though the causes of sleep disruptions remain unknown. The aim of the study “Sleep and respiration in microgravity” was to determine if sleep disordered breathing or other respiratory related factor were linked to the reported poor sleep quality during space-flight.

In the framework of this study, cardiac, respiratory and sleep related parameters were recorded continuously during sleep before, during and after two space shuttle flights. Respiratory and cardiac signals during sleep, and the corresponding sleep stage, constitute the main source of data used in the following chapters for the study of the influence of gravity on respiration and cardio-respiratory interactions.

Results concerning the sleep component of this study, namely the impact of gravity on sleep-disordered breathing, were published in [2]. The experimental protocol included day-time experiments on the same subjects, focusing on the determination of the respiratory response to hypoxia and hypercapnia ([3]), as well as day-time heart rate variability ([4]).

The experiment reported here was part of a larger set of experiments, concerning sleep in space. Thus the present work also benefitted from the work and results of parallel experiments, namely the work of the team of prof. Czeisler, who studied sleep, performance,

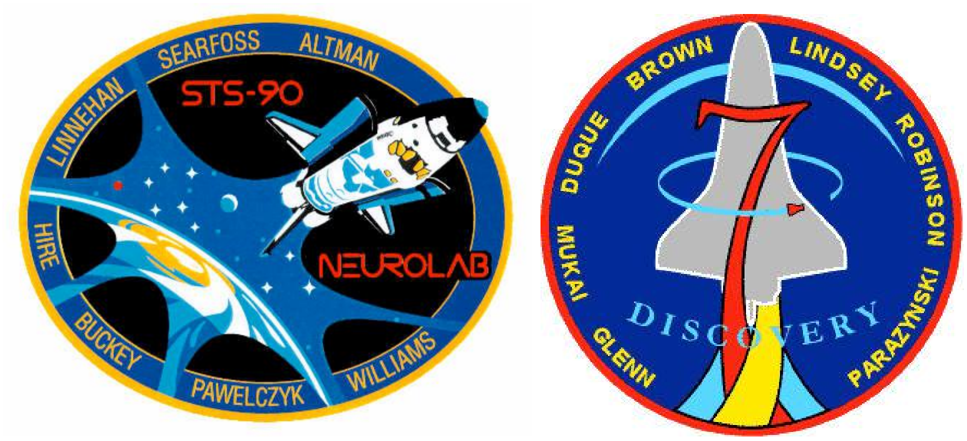

Figure 2.1: Neurolab (left) and STS-95 (right) mission patches.

circadian rhythms and light-dark cycles in the same subjects ([5]). Sleep stage scoring used in the current work was performed by this team.

2.1 Space flights, subjects and recording sessions

Space flights The experiment “Sleep and breathing in microgravity” monitored the sleep of 6 human subjects before, during and after two space shuttle flights. Four subjects flew on space shuttle Columbia during STS-90 Neurolab, a 17 day mission launched on April 17th, 1998 (figure 2.1, left). During this mission the shuttle flew with the ESA built Spacelab module on its bay, allowing for an additional pressurized volume where experiments on human and animal physiology were performed.

Two additional subjects flew later the same year on a 10 day mission on-board space shuttle Discovery during mission STS-95 (figure 2.1, right), launched on October 29th, 1998. This mission took onboard 77 years old John Glenn, making him the oldest man having flown in space to this day. Discovery flew with a different pressurized module on its bay, called Spacehab.

The experimental protocol was approved by the Institutional Review Board of NASA Johnson Space Center, the University of California San Diego and the Brigham and Women’s Hospital. The subjects provided written informed consent before performing the protocol.

Astronaut John Glenn was himself a subject of this experience, though data relative to this subject was not analyzed in the present work. As Glenn himself writes in his autobiography “Older people often sleep poorly , and so do astronauts in space (...)” ([6]). However, having one single data point of the oldest astronaut, quite far apart from the average age of the group studied, would hardly allow to draw sound scientific conclusions. Moreover, Glenn did not perform the entire protocol, again citing Glenn’s autobiography ([6]), “It was one small part of the sleep experiments [testing melatonin as a sleep inducing drug in space], (...) among a long list of exclusionary criteria in this (...) study was one that precluded my participation.” .

Subjects Five astronauts aged 37 to 46 years, 1 woman and 4 men, were thus retained in the present study. Table 2.1 presents the average antropometric data of the subjects.

All subjects met NASA health criteria for flight assignment, and reported no sleep disorders. Three of the subjects underwent clinical polysomnography (two subjects were recorded twice, the third only once), confirming the reported absence of sleep disorders ([5]).

All subjects were non-smokers and had a normal respiratory function (FVC and FEV_1 within the predicted normal range). Subjects refrained from consuming caffeine or alcohol in the 12h preceding each recording. Subjects were also asked to refrain from the use of hypnotic drugs for the duration of the study. As part of a computerized sleep log, astronauts were asked to report any use of sleep medication. Only one such event was reported, with one astronaut reporting taking *"zolpidem"* during a sleep episode when no polysomnographic recording was scheduled. *Zolpidem* is a hypnotic drug that binds to the benzodiazepine receptors, potentiating the inhibitory neurotransmitter GABA; this class of hypnotics has both a fast action (15 minutes) and a very short half-live (less than 3 hours).

	Mean	±	SD	
Age	41.0	±	2.7	years
Height	181	±	13	cm
Weight	79	±	14	kg
BMI	24	±	1.6	kg/m^2

Table 2.1: Average and standard deviation of age, height, weight and body mass index (BMI) of the subjects retained for analysis.

Data collection calendar A total of 77 entire night polysomnographic recordings (PSGs) were retained for analysis, each lasting approximately 8h; 42 were recorded pre-flight, 20 in-flight and 15 post-flight; 13 to 16 PSGs were recorded for each subject, 9 pre-flight (6 only for the subject flying on STS - 95), 4 in-flight, and 3 post-flight. Table 2.2 presents the data collection calendar for each subject.

Pre-flight recordings were performed in batches of 2 consecutive nights, roughly 3 months, 2 months, 1 month before take off, and in 3 consecutive nights roughly one week prior to flight. This last pre-flight recording did not take place for STS - 95. The first two recordings for each subject were considered as habituation nights, and were discarded from the analysis.

In-flight, recordings were limited to 2 subjects per night - a limitation imposed by the equipment available in the space shuttle - and took place for each subject in two pairs of consecutive nights. The first pair of recording sessions took place early during the flight, and the second was performed roughly one week later. During STS - 95, as it was a shorter flight, only 1 day separated the first and second pair of sleep recordings.

Post-flight data collection took place on day 1, 3 and 4 after landing (corresponding to the second, fourth and fifth sleep episode after return to earth). All subjects followed the same calendar post-flight, with the first sleep recording taking place roughly 36 hours after landing.

All pre and post-flight recordings were performed in NASA's Johnson Space Center's crew quarters, or in a local hotel (for STS-95 only). In-flight recordings took place in the shuttle mid-deck, which was equipped with four sleep compartments. Each sleep compartment contained a sleeping bag/liner, a light and a ventilation inlet and outlet. These

Subject	Pre-flight									In-flight				Post-flight		
	(*Launch*−)									(Flight Day)				(*Return*+)		
A	-102	-101	-73	-72	-45	-44	-7	-6	-5	3	4	12	13	1	3	4
B	-102	-101	-73	-72	-45	-44	-7	-6	-5	3	4	12	13	1	3	4
C	-102	-101	-73	-72	-45	-44	-7	-6	-5	5	6	14	15	1	3	4
D	-102	-101	-73	-72	-45	-44	-7	-6	-5	5	6	14	15	1	3	4
E	-77	-76	-50	-49	-38	-37				4	5	7	8	1	3	4

Table 2.2: Data collection calendar, in days. Pre-flight corresponds to days before launch (Launch −), in-flight to days spent in space (Flight Day) and post-flight to days after return to earth (Return +). Subjects A-D flew on Neurolab while subject E flew on STS-95.

compartments are 2 m long, 0.75 m high, and wide enough for one, and can be seen in figures 2.4, 2.5 (left panel) and 2.6. The sleep compartments provide a private sleeping space for the subjects, isolating them from the 90 minute light-darkness cycle of the shuttle's orbit, from noise and activity of the rest of the crew. The sleep compartments, as small as they might seem, constitute a real comfort for astronauts (one astronaut reported that he slept on "his" compartment only in the four nights when recordings were scheduled, for it was taken by the commander in the remaining nights).

Recordings on the ground were performed from around 11 pm to 7 am local time, except on the first Neurolab post-flight recording, where sleep started 1 h earlier upon crew's request due to fatigue. In space, the same time-table was kept. The two missions were single shift missions, all subject having the same scheduled bedtime.

Launch and landing constraints imposed a slightly different day length in space; in both Neurolab and STS - 95, the space day was shorter than 24 hr, 20 min shorter in Neurolab, and 35 min shorter in the case of STS - 95. Therefore, the sleep onset in space was shifted earlier by 20 min / flight day for Neurolab, 35 min / flight day for STS - 95. This is done routinely in human space flights, to assure that on the day of reentry the sleep-wake cycles are timed appropriately for optimal astronaut's performance. Figure 2.2 presents the scheduled sleep-wake cycle for one astronaut from one week prior to take off to day four after return. The shorter than 24h scheduled sleep-wake rhythmicity during the flight is clearly visible in this representation.

A light sensor incorporated in the overall recording system allowed the determination of the exact moment of lights off, and the moment when they are turned back on.

Cabin atmosphere during flight are normoxic (760 mm Hg, 21% O_2) with a slightly increased level of CO_2 (roughly 0.4%).

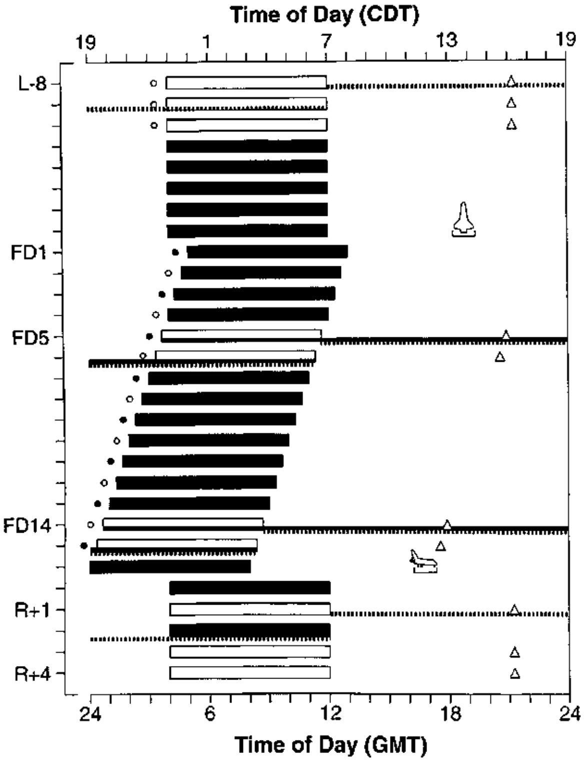

Figure 2.2: Schema presenting the experimental schedule and the scheduled sleep-wake cycles in the week before flight (L-), during the length of the mission (FD), and upon return to earth (R), for one subject flying on STS-90 Neurolab mission. Scheduled sleep episodes are indicated by the white or black bars, white bars corresponding to nights in which polysomnographic recordings took place. Additional measurements, not presented in the figure, were performed roughly three months, two months and one month prior to flight. Launch day (FD1) ends with the first sleep episode in space, later than what was scheduled in the previous days, and in the consecutive flight days, the sleep is scheduled earlier every day by 20 minutes. Open and closed circles indicate respectively placebo or melatonin intake, open triangles refer to neurobehavioral performance tests, and dashed horizontal lines indicate days when urine was collected. Solid horizontal lines correspond to days when this subject's body temperature was also recorded continuously, using the ingestible temperature sensor. Symbols for take-off and landing are easily recognizable. The top and bottom x-axis indicate time of day in two different time zones: Central Daylight Time (CDT, top, time zone encompassing Houston, where astronauts are based) and Greenwich Mean Time (GMT, bottom). Figure from [5]. The shorter than 24h imposed sleep-wake schedule is visible in the "earlier to bed" trend present during flight.

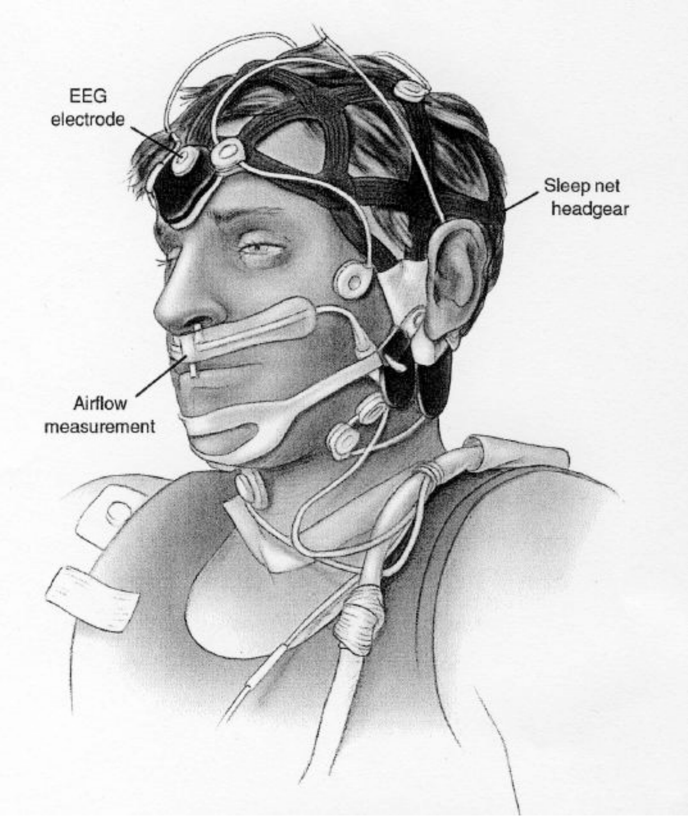

Figure 2.3: Schematic view of the sleep net, with EEG electrodes, EOG and chin EMG electrodes. The three-pronged thermistor is also indicated. Illustration from [7].

2.2 Polysomnography and sleep stage scoring

Studying sleep in space imposes constraints far from those common in a sleep laboratory. The most relevant constraints for space bounded equipment concern power consumption, weight, the space it occupies, and the astronaut time required for operation. A portable digital sleep system was developed for this study. The entire hardware is thoroughly described in [8].

2.2.1 Polysomnography hardware and signal preconditioning

Polysomnographic data was digitally recorded using a portable recorder (Vitaport-2, Temec Instruments B.V., The Netherlands), using a sleep monitoring system developed for this specific experiment. The system consisted of a custom fitted sleep cap, custom fitted respiratory plethysmography body suit, a cable harness, and an impedance meter. The impedance meter was used to verify each electrode in the sleep cap prior to recording. A computerized signal-quality assessment system (described in [9]) was also developed for this experiment, using a laptop computer and an interface to access signal quality prior to sleep onset. Using this expert system during and after instrumentation, but before sleep, all physiological signals were visually controlled and the software assisted astronauts in troubleshooting eventual problems.

The same system and procedures were used in all pre, in and post-flight recordings. In-flight instrumentation was performed by a second astronaut (figure 2.7) while on-ground instrumentation was performed by technicians. Prior to flight, astronauts were trained extensively in the application of sensors, the use of the equipment and the quality control of the recorded signals.

Recorded signals The following signals were recorded:

- 4 Electroencephalogram (EEG) channels, namely O1/A2, O2/A1, C3/A2 and C4/A1, recorded with a sampling frequency of 128 Hz;
- Left and right electro-oculogram (EOG), sampled at 64 Hz;
- 3 chin electromyogram (EMG) channels, mesuring activity of the chin muscles, sampled at 128 Hz;
- Nasal and oral flow, using a three-pronged thermistor placed in the upper lips, signal sampled at 32 Hz;
- Abdominal and thoracic motion, acquired using Respiratory Inductive Plethysmography (RIP), sampled at 32 Hz;
- Snoring was recorded using a microphone;
- Arterial oxygen saturation ($S_{a_{O_2}}$), sampled at 1Hz, recorded through a pulse oximeter;
- Lead II electrocardiogram (ECG), sampled at 256 Hz;
- Light intensity, recorded at 1 sample per second using a light sensor;
- An “event marker channel” allowed the subject to mark specific events.

All signals were recorded using the fore-mentioned Vitagraph recorder. The recorder sampled the brain’s electrical activity using an electroencephalogram (EEG), recorded eye movements by electro-oculogram (EOG, left and right, placed in the outer canthus), and registered muscular activity around the chin, using an electromyogram (EMG).

The portable recorder’s main components were a 12 bit analog-to-digital (ADC) converter, supporting electronics, batteries, and PCMCIA bay compatible with flash memory card. The recorder fitted in a 4x9x15 cm box and was able to operate for 10h on 4 AA batteries, saving data on a removable 85 Mb flash memory.

EEG, EMG and EOG electrodes were implemented on an elastic lattice cap, a modified sleep net (e-Net, Physiometrix, MA, USA), that used disposable sensors (Hydrobot Biosensors, Physiometrix, MA, USA). Head and face electrode placing was simplified by the integration in a lattice cap secured on the head by a chin and neck strap. An illustration of the sleep net is presented in figure 2.3, and photos of astronauts wearing the cap are presented in figures 2.5 and 2.7.

Sleep nets were individually tailored for each participant for comfort and reproducibility of electrode placement. Electrode placement followed the international 10-20 system, with two reference electrodes behind the ears, one forehead ground electrode, two EOG electrodes, four chin EMG electrodes and four EEG electrodes (in positions C3, C4, O1 and O2). Electroencephalogram (EEG) channels O1/A2, O2/A1, C3/A2 and C4/A1 were recorded.

On top of these signals, in two of the in-flight recording sessions, subjects were also instrumented with a continuous core body temperature sensor, consisting of an ingestive pill (CorTemp 100 sensor, HTI Technologies, Florida, USA), and a belt receiver recording the signals emitted by the pill (Personal Electronics Devices, MA, USA). Core body temperature was sampled once every 15 s.

Urinary cortisol concentration was also measured in 24h sequences, two of these daily measurements taking place in space (figure 2.2). Core body temperature and free cortisol concentration allowed to determine whether the subject's internal circadian cycles remained synchronized or not with the imposed rest-activity schedule. Both core body temperature and cortisol have strong circadian rhythms, and are routinely used to track changes between the internal and the imposed circadian rhythm.

An activity monitor (Mini-motion logger, Ambulatory Monitoring, Inc., NY, USA), used in the non-dominant wrist, recorded wrist activity. Actigraphy is a simple reliable method of estimating total sleep time, and allowed to verify compliance with the imposed sleep schedule in nights where no PSG recording was performed. The wrist activity monitor can be seen in figures 2.4 and 2.5.

Light intensity was recorded throughout the missions (Actillume light recorded, Ambulatory monitoring Inc, NY, USA) in three different locations: the shuttle's flight-deck, the mid-deck and in the Spacelab (Neurolab) and the Spacehab (STS - 95). Light intensity was sampled once per minute.

Polysomnographic signal preconditioning EEG signals were low-pass filtered at 70 Hz, and high-pass filtered with a time constant of 0.33 s, then sampled at 256 Hz. To this time series a moving average filter with a cutoff frequency of 64 Hz was then applied, and each EEG channel was stored at 128 Hz.

EOG channels were low-pass filtered at 35 Hz, and high-pass filtered with a time constant of 1 s, and then sampled. Software in the recording device applied a moving average filter, with a cutoff frequency of 32 Hz, and saved the results at a 64 Hz sampling rate.

Chin EMG signals were low-pass filtered at 100 Hz, high-pass filtered with a time constant of 0.015 s, and stored in the Flash memory at 128 Hz.

2.2.2 Sleep stage scoring

EEG recordings, together with two EOG channels (left and right) and two facial EMG signals, were used for sleep stage scoring, according to the standard criteria of Rechtschaffen and Kales ([10]). Sleep scoring using 30-second epochs was performed for prior publication ([5],[7]) and our analysis were based on those scorings.

Six sleep stages were considered: Non-REM sleep stages 1, 2, 3 and 4 (from lighter sleep to deeper sleep), REM sleep, and windows when the subject is awake.

For the analysis presented in this work, sleep stages were grouped into 4 classes: *Light Sleep*, including NREM sleep stages 1 and 2; *Deep Sleep*, sleep stages 3 and 4; *REM* sleep (no distinction was made between tonic REM and phasic episodes); and *Awake*. Events in the awake state were retained only when happening in periods of darkness. This was done in order to avoid standing periods, periods of movement, activity, etc, prior to lights out.

Subjective sleep quality, performance and neurobehavioral assessment After every sleep period, astronauts answered a computer based survey (or a paper equivalent) on subjective sleep quality, causes of sleep disruption and eventual use of medication.

Figure 2.4: Astronaut John Glenn in Discovery's mid-deck, ready to go to sleep. He is wearing all instrumentation of the sleep study, namely the sleep net (detailed photo below), and the custom-fitted two-piece lycra body suit, containing the rib cage and abdominal RIP sensors. On his finger one can see the pulse oximeter, and on the wrist a wrist activity monitor. All sensors are connected to the recorder, seen here on the astronaut's belly, by a single cable. Behind are the 4 sleep compartments where subjects slept (Photo NASA). In his autobiography ([6]), John Glenn describes the night of this photo as follows: "Night four of the mission saw me (...) rigged up in our head nets and instrumented vest. The twenty-one leads from the apparatus fed into boxes we wore on our waists, where the information was recorded for later analysis. We repeated everything the next night. (...) Sleeping with the elaborate head net and vest turned out to be easier on orbit than on the ground, where the electrode leads were uncomfortable. Imagine sleeping with a dozen buttons over half an inch thick stuck on your head that you feel every time you roll over. Weightlessness removed the irritating pressure. (...) On nights 7 and 8 (...) I put the sleep nets and vests on again for two more sets of readings."

On the afternoons following a PSG recording, astronauts' attention, reaction time, cognitive throughput and memory were tested. A battery of tests was used to quantify these parameters, namely a psychomotor vigilance task, a two-digits addition task, and a probed recall memory test. Astronauts were also asked to perform a subjective auto assessment of their own performance and effort.

Sleepiness and mood were probed using the Karolinska sleepiness scale, and a visual analog scaler test, as well as psychomotor tracking task.

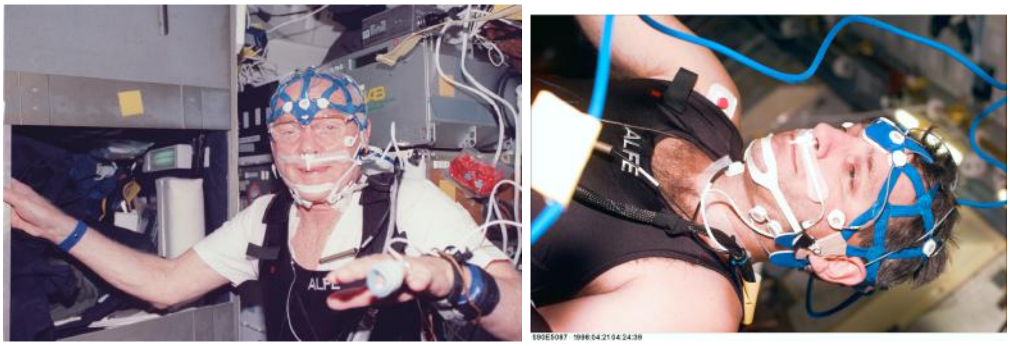

Figure 2.5: Left: astronaut John Glenn (STS-95), right: Richard M. Linnehan (STS-90 Neurolab), both wearing the sleep net, containing the EEG electrodes, and also instrumented with EOG and chin EMG electrodes. The thermistor recording nasal and oral flow is also clearly visible, and the event marker push button can be seen floating. The shoulder straps on the lycra body suit allow to compensate for the increase in length of the spine that occurs in microgravity, maintaining RIP body position constant (Photos NASA).

2.3 Respiratory and cardiac signals

2.3.1 Respiratory data

In addition to the electro-physiological recordings allowing the determination of sleep stage, other signals were recorded. Respiratory related measurements include nasal/oral flow (three-pronged thermistor adhered to the upper lip, EdenTec Corporation, Eden Prairie, MN, sampled at 32 Hz), rib cage and abdominal motion (respiratory inductive plethysmography, 32 Hz), snoring sounds (a microphone was placed at the level of the larynx and it included a light intensity detector), arterial pulse oximetry, determining arterial oxygen saturation (Ohmeda Flex-probe, Ohmeda Medical Inc., Columbia, MD, placed on the left ring finger), as well as an event marker channel. No body position sensor was present.

Most of the previous sensors were integrated into a custom-fitted two-piece (vest and short) lycra body suit (Blackbottoms, Salt Lake City, UT, USA). The two-piece body suit can be seen in figure 2.4. Rib cage and abdominal wires for the inductance plethysmography were sewn into the body suit, with the chest band at the level of the nipples and the abdominal band over the umbilicus. In microgravity the spine lengthens; therefore, changing the length of the suit was required to place the sensors at the desired position. The custom fitted respiratory plethysmograph body suit allowed, by adjusting shoulder straps, to adjust its size, thus to maintain proper location of each plethysmographic band in every gravity condition. Vest and shorts were attached together by velcro strips to ensure proper location of the bands at all times.

Calibration The relative gain between thoracic and abdominal respiratory signals was determined by performing an isovolume maneuver prior to sleep onset. Each isovolume maneuver was visually identified in the respiratory signals and analyzed for the determination of relative abdominal and thoracic gain. No absolute calibration of volume was performed. The signal obtained from the weighted sum of thoracic and abdominal respiratory movements corresponds thus to respiratory volume measured in arbitrary units (a.u.).

Figure 2.6: Astronaut Scott F. Parazynski prepares to withdraw a blood sample from astronaut John Glenn, who is partially in the sleep compartment, wearing the lycra body suit used to record respiratory movements during sleep (Photo NASA).

Figure 2.7: Detail of the instrumentation procedure in space. In this photo payload specialist Jay C. Buckey, Jr. (right) helps astronaut Richard M. Linnehan with a sleep cap during the Neurolab mission (Photo NASA).

Because there was no absolute volume calibration, volume variables are expressed in arbitrary units and are therefore not directly comparable from one night to the next. As comparison in absolute terms is not possible, volume was normalized. The volume of the *Awake* class was taken as reference. Respiratory volumes are then expressed as a percentage of their *awake* values.

2.3.2 Cardiac signal

Cardiac electrical activity was recorded by performing a two lead electrocardiogram, in the lead II configuration. ECG was recorded at 256 Hz. From the ECG recording, the instantaneous heart rate was determined using a cross correlation algorithm matching each portion of the signal with a pre-determined individual QRS template. The R-peak detection algorithm is described in [11].

2.4 Data analysis

Data recorded on the Vitaport's memory was visualized on a Macintosh computer, using TEMECs Vitagraph software package (TEMEC Instruments B.V., The Netherlands), and exported in ASCII format. These files were then imported into Matlab (the Mathworks Inc., MA, USA). All subsequent analysis presented in this work were performed in Matlab. The same environment was used for development of new analyzing algorithms.

Data from the first pair of sleep recordings, 90 days prior to flight, was excluded from the data analysis, in order to eliminate possible effects of the adaptation to the sleep instrumentation. One in-flight recording for subject B (corresponding to flight day 4) was excluded from the present analysis for technical reasons.

The signal from the light sensor was used to determine the moments of lights out and the moments when they were turned back on. The analysis was restricted to periods of darkness. Periods presenting large body movements and other artifacts were also removed from the analysis.

Subjects performing this experiment participated in a simultaneous experiment, studying the effectiveness of melatonin as a hypnotic for use in space-flight. 0.3 mg of melatonin were administered in a double blind manner (melatonin, placebo on alternate nights) 30 min prior to sleep onset on four pre-flight recordings and prior to each in-flight sleep episode. Melatonin was not administered post-flight.

Following the results of [12], [2] and [5], melatonin and placebo recordings were indistinguishable in every variable studied, except for the number of awakenings. Thus, for the purpose of the presented analyses, no distinction was made between melatonin and placebo nights.

Bibliography

[1] NASA Space Shuttle Mission Archive on STS-90 Neurolab. http://science.ksc.nasa.gov/shuttle/missions/sts-90/mission-sts-90.html, February 2001.

[2] A.R. Elliott, S.A. Shea, D.-J. Dijk, J.K. Wyatt, E. Riel, D.F. Neri, C.A. Czeisler, J.B. West, and G. Kim Prisk. Microgravity reduces sleep-disordered breathing in humans. *Am J Respir Crit Care Med*, 164(3):478–485, 2001.

[3] G.K. Prisk, A.R. Elliott, and J.B. West. Sustained microgravity reduces the human ventilatory response to hypoxia but not to hypercapnia. *J Appl Physiol*, 88(4):1421–1430, 2000.

[4] P-F. Migeotte, G. Kim Prisk, and M. Paiva. Microgravity alters respiratory sinus arrhythmia and short-term heart rate variability in humans. *Am J Physiol Heart Circ Physiol*, 284(6):H1995–2006, 2003.

[5] D.-J. Dijk, D. F. Neri, J. K. Wyatt, J. M. Ronda, E. Riel, A. Ritz-De Cecco, R. J. Hughes, A. R. Elliott, G. K. Prisk, J. B. West, and C. A. Czeisler. Sleep, performance, circadian rhythms, and light-dark cycles during two space shuttle flights. *Am J Physiol Regul Integr Comp Physiol*, 281(5):R1647–1664, 2001.

[6] J. Glenn and N. Taylor. *John Glenn: A Memoir.* Bantam, 2000.

[7] D.-J. Dijk, D.F. Neri, J.K. Wyatt, J.M. Ronda, E. Riel, A. Ritz-De Cecco, R. J. Hughes, and C.A. Czeisler. *The Neurolab Spacelab Mission: Neuroscience Research in Space*, chapter Sleep, circadian rhythms, and performance during space shuttle missions, pages 211–221. Number SP-2003-535. NASA, Houston, Texas, 2003.

[8] D.-J. Dijk, J.C. Buckey Jr., D.F. Neri, J.K. Wyatt, J.M. Ronda, E. Riel, G.K. Prisk, J.B. West, and C.A. Czeisler. *The Neurolab Spacelab Mission: Neuroscience Research in Space*, chapter Portable sleep monitoring system, pages 249–251. Number SP-2003-535. NASA, Houston, Texas, 2003.

[9] G. Callini, S. M. Essig, D. Heher, and L. R. Young. Effectiveness of an expert system for astronaut assistance on a sleep experiment. *Aviat Space Environ Med*, 71(10):1023–1032, 2000.

[10] A. Rechtcschaffen and A. Kales. *A manual of standardized terminology, techniques and scoring system for sleep stages of human subjetcs*, volume 204. National Institute of Health Publ., 1968.

[11] P.F. Migeotte. *Heart rate variability - Applications in microgravity.* PhD thesis, Université Libre de Bruxelles, 2003.

[12] G.K. Prisk, A.R. Elliott, M. Paiva, and J.B. West. *The Neurolab Spacelab Mission: Neuroscience Research in Space*, chapter Sleep and respiration in microgravity, pages 223–232. Number SP-2003-535. NASA, Houston, Texas, 2003.