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# Refinement, Validation and Application of a Machine Learning Method For Estimating Physical Activity And Sedentary Behavior in Free-Living People

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# REFINEMENT, VALIDATION AND APPLICATION OF A MACHINE LEARNING METHOD FOR ESTIMATING PHYSICAL ACTIVITY AND SEDENTARY BEHAVIOR IN FREE-LIVING PEOPLE

A Dissertation Presented

by

KATE LYDEN

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## ABSTRACT

### REFINEMENT, VALIDATION AND APPLICATION OF A MACHINE LEARNING METHOD FOR ESTIMATING PHYSICAL ACTIVITY AND SEDENTARY BEHAVIOR IN FREE-LIVING PEOPLE

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There is limited knowledge of the dose-response relationship between physical activity (PA), sedentary behavior (SB) and health. Poor measures of free-living PA and SB exposure are major contributing factors to these knowledge gaps. The overall objective of this dissertation was to address these issues by refining, validating and applying a machine-learning methodology for measuring PA and SB for use in free-living people. By combining neural networks and decision tree analyses we developed a method better suited for use in free-living people. Our new method is called the sojourn method and it estimates PA and SB from a single hip mounted accelerometer.

Study 1 validated two versions of this method: sojourn-1x (soj-1x) and sojourn-3x (soj-3x). Soj-1x uses data from a vertical accelerometer sensor, while soj-3x uses r data from the vertical, anterior-posterior and medial-lateral accelerometer sensors. Seven participants were directly observed in the free-living environment for ten consecutive hours on three separate occasions. PA and SB estimated from soj-1x, soj-3x and a neural network previously calibrated in the laboratory (lab-nnet) were compared to direct observation. Compared to the lab-nnet, soj-1x and soj-3x improved estimates of MET-

hours (lab-nnet: bias (95% CI) = 5.4 (4.6-6.2), rMSE = 5.4 (4.6-6.2), soj-1x: bias = 0.3 (-0.2-0.9), rMSE = 1.0 (0.6-1.3), soj-3x: bias = 0.5 (-0.1-1.1), rMSE = 1.1 (0.7-1.5)) and minutes in different intensity categories (lab-nnet: rMSE range = 10.2 (vigorous) – 55.0 (light), soj-1x: rMSE range = 4.0 (MVPA) – 50.1 (sedentary), soj-3x: rMSE range = 7.8 (MVPA) – 27.8 (light)). Soj-1x and soj-3x also produced accurate estimates of qualifying minutes, qualifying bouts, breaks from sedentary time and break-rate.

Study 2 evaluated the sensitivity of soj-1x and soj-3x to detect change in habitual activity. Thirteen participants completed three, seven day conditions: sedentary, moderately active and very active. Soj-1x and soj-3x were sensitive to change in MET-hours (mean (95% CI): soj-1x: sedentary = 19.8 (19.0-20.7), moderately active = 22.7 (22.0-23.4), very active = 27.0 (25.8-28.2), soj-3x: sedentary = 18.2 (17.7-18.8), moderately active = 22.3 (21.6-23.1), very active = 27.6 (26.4-28.7)) and time in different intensity categories.

Study 3 applied soj-3x to a free-living intervention to elucidate the effects of increased sedentary behavior on markers of cardiometabolic health. Eleven participants completed seven days of an active condition followed by seven days of an inactive condition. Insulin action significantly decreased 17% (5.4-30.2), while total cholesterol, LDL and HDL did not change from the active to inactive condition. This dissertation used novel methods to improve PA and SB estimation in a free-living environment and to improve our understanding of the physiologic response to increased free-living SB. These methods ultimately have the potential to broaden our understanding of how PA and SB dose are linked to health.

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# CHAPTER I

# INTRODUCTION

## Statement of the Problem

There is a clear association between physical activity (PA) and a reduced risk for cardiovascular disease (CVD), diabetes, obesity, metabolic syndrome and some types of cancer (16). Recent research has emerged indicating sedentary behavior (SB) may also play a key role in determining an individual's health. However, as outlined in the recent **Physical Activity Guidelines Advisory Committee Report (PAGAC)**, there is a gap in our understanding of the exact dose-response relationship between PA and specific health outcomes (16). The report also emphasized the need to expand sedentary behavior research and to better understand its specific effects on health (16). These knowledge gaps can be directly attributed to the lack of a valid tool to measure activity across the full spectrum of behavior. To accurately estimate the characteristics of physical activity and sedentary behavior that influence chronic disease or chronic disease risk factors, valid measurement tools are required.

### Objective Measurement of Free-Living Physical Activity and Sedentary Behavior

Accelerometer sensors are popular devices to objectively measure activity. They can collect movement patterns for prolonged periods of time (e.g. weeks) with minimal subject burden and the data can be transformed into estimates of time spent in intensities of PA (e.g. light, moderate, vigorous) and point estimates of energy expenditure (EE) (e.g. 3 METs). Linear regression was initially used to model the relationship between accelerometer output (counts) and EE (32, 76, 100). This approach was well received by the scientific community and produces relatively accurate estimates of EE when applied to locomotion activities (18, 63, 87). However, this linearity is valid only within a single activity type and when applied to activities that require non-rhythmic movement (e.g. intermittent lifestyle activities) the linear relationship breaks down and inaccurate estimates result (12, 18, 47, 63, 73, 87). In an effort to address these limitations, researchers expanded the linear regression model (LRM) in several ways: 1) adding multiple sensors (e.g. accelerometers on the ankle and wrist), 2) including a physiological parameter (e.g. heart rate), and 3) using activity specific equations (e.g. locomotion or lifestyle). Despite these advances and recent advances in motion sensor technology, accelerometers have yet to realize their potential to produce accurate estimates of EE across a range of activity types and intensities.

More sophisticated machine learning techniques have emerged as possible analytic alternatives to simple regression. Machine learning approaches are adaptive modeling techniques that predict outputs based on known properties learned from training data (66). They are inherently more flexible than simple linear regressions in that they don't assume a simple linear between the input features (counts$\cdot$min$^{-1}$) and prediction (METs). Our group has developed a machine learning approach that uses an artificial neural network (lab-nnet) to estimate METs (97). The lab-nnet method improved MET estimates compared to traditional regressions and was successful at identifying activities as sedentary, locomotion, lifestyle, or vigorous sport (97). It has also been shown to be valid when applied to data from an independent sample (31).

This method however, was developed and validated in a laboratory setting, and preliminary observations suggest its performance significantly declines when applied to accelerometer output from free-living people. We have refined our lab-nnet to be more appropriate for free-living applications. Our new method is called the sojourn method, and it is a hybrid machine learning technique that combines artificial neural networks with a decision tree analysis. The sojourn method uses three steps to measure physical activity and sedentary behavior in free-living settings. Using simple parameters from the acceleration signal the sojourn method: 1) identifies bouts of activity and inactivity, 2) assigns non-physical activity MET values to inactivity bouts and 3) applies the original lab-nnet to estimate METs for activity bouts.

### Sedentary Behavior

Sedentary behaviors are defined as seated or reclining behaviors that require low levels of energy expenditure (e.g. < 1.5 METs) (81). Habitual sedentary behavior (sometimes called inactivity) primarily consists of sitting/lying activities, with short intermittent bouts of light intensity activity. Due to an increasingly sedentary population (71) and the realization that even regular exercisers spend large portions of their day in sedentary behaviors (38, 106), the value of accumulating light intensity activity and decreasing sedentary time for health has emerged (105). Epidemiological evidence also indicates SB, independent of PA, is positively associated with all-cause and cause-specific mortality (24, 55). Thus, it has been suggested that sedentary behaviors (e.g. sitting) stimulate and/or inhibit physiologic mechanisms responsible for regulating disease risk factors (e.g. high blood pressure, insulin resistance, elevated triglycerides and cholesterol) (37, 38). However, the available data are primarily observational and often rely on crude, subjective measures of SB. Additionally, measures of SB usually do not account for the non-sitting, light intensity activities that are frequently the main source of

EE in habitually sedentary individual. As a result, it is very difficult to translate observational data to comprehensive public health recommendations that can be applied to typical free-living people.

Several laboratory-based studies have attempted to elucidate the effects of sedentary behavior on specific physiologic responses by experimentally manipulating sitting time. However, sedentary behaviors are ubiquitous and spontaneous, making them very difficult to study in a laboratory. For example, in a typical free-living environment, individuals perform many bouts of sitting throughout the day. Some bouts are very brief, mixed with bouts of standing and/or ambulation. Alternatively, individuals may sit for hours at a time, breaking from sitting only to perform basic hygiene. Observational studies indicate breaks in sitting may be important covariates moderating the effects of SB (15, 42, 44). However, previous experimental manipulations of SB disregard natural breaks and rely on highly artificial laboratory conditions (e.g. prolonged bed rest in humans (74); hind-limb immobilization in rodents (6, 7)), restricting any type of ambulation for hours to days at a time. Such conditions are not representative of true free-living sedentary behavior, but are exaggerated bouts of extreme inactivity. In a free-living environment, even the most sedentary (but otherwise healthy) individuals take breaks from sitting.

It has been recognized that there is a need to more effectively study the relationship between SB and health, but because SB is typically unplanned and makes up such a large portion of the day, it is very difficult to prescribe and monitor a bout of SB that reflects typical behavior. Thus, to truly understand the relationship between SB and health, it is ideal that it be studied in the context in which it typically appears. Research should not only address the act of sitting, but also the range of activities that collectively represent the typical habitual behavior of a sedentary individual, including bouts of sitting, ambulatory breaks from sitting, and small amounts of light intensity activity. These are distinct activities with meaningful independent effects, but together they make up "sedentary behavior." By studying SB in this context, we are in a unique position to understand the potentially important interactions of all components of SB and ultimately to translate research evidence to relevant public health recommendations.

## Objectives and Significance

The main goal of this dissertation was to validate the sojourn method for assessing free-living PA and SB and to apply it during seven days of increased SB to elucidate the effects of multiple components of SB on cardiometabolic health.

**Study 1 examined the validity of the lab-nnet and two versions of the sojourn method (soj-1x and soj-3x) to assess free-living physical activity and sedentary behavior.** Using direct observation as the criterion measure, the validity of the methods to estimate MET-hours and time spent in different physical activity intensity categories was determined. Study 1 provides two novel machine-learning methods that use a single commercially available accelerometer and an open source statistical environment to improve the estimation of free-living PA and SB.

**Study 2 evaluated the sensitivity of soj-1x and soj-3x to detect change in EE within an individual.** We applied the algorithms to three behavior pattern conditions in a free-living setting: sedentary, moderately active, and very active. These data provide evidence soj-1x and soj-3x can be applied in population surveillance of physical activity and in PA and SB interventions to detect changes in these three behavior patterns.

**Study 3 applied the soj-3x algorithm to elucidate the effects of increased free-living sedentary behavior on markers of cardiometabolic health**. Using soj-3x we measured detailed components of free-living PA and SB and evaluated the effects of increased sedentary behavior on insulin action and fasting lipid markers. These data provide some of the first experimental evidence that increased free-living sedentary behavior is detrimental to markers of health.

# CHAPTER II

# REVIEW OF LITERATURE

## Estimating Physical Activity and Sedentary Behavior with Accelerometers

Accurately ESTIMATING PHYSICAL ACTIVITY (PA) and sedentary behavior (SB) is difficult. Large-scale epidemiological studies, field-based research and clinical trials have traditionally relied on participant testimony in the form of questionnaires, self-report diaries and interviews. These subjective methods are often inaccurate, with individuals tending to over-report time spent in PA (90). The inherent limitations of subjective methods have led researchers to focus on objective measurement techniques, mostly in the form of wearable devices. Such devices often measure one or more physiologic variables (e.g. heart rate, heat flux) and relate it to physical activity and/or energy expenditure.

Accelerometers have emerged as the device of choice to estimate free living PA because of their minimal subject and researcher burden, versatility, and relative cost efficiency. The use of accelerometers to estimate PA is based on the premise that vertical acceleration can be related to energy expenditure. Calibration studies use simultaneous recordings of accelerometer output (counts) and energy expenditure (EE) (measured via indirect calorimetry), to model the relationship between vertical acceleration and EE. Traditionally, models used simple or multiple regression to predict point estimates of EE, or to classify an activity as sedentary, light, moderate or vigorous intensity.

Accelerometers and their corresponding data processing methods have been well received by the scientific community. This is due in part to their relative ease of use, and their substantial improvement over subjective methods. However, recent validation studies indicate simple and multiple prediction models are not valid across a range of activity types and intensities (18, 63, 87). Recent advances in motion sensor technology allows for the collection and storage of much more data than previously possible. As a result, researchers have begun to explore the use of more sophisticated data processing techniques (e.g. machine-learning). The following review will outline the evolution of accelerometer EE prediction techniques starting with Freedson et al. (32), and addressing the subsequent progression of limitations that have evolved along with each generation of new prediction models.

**In the Beginning**

In 1998, Freedson et al. (32) were among the first exercise physiologists to use accelerometers to estimate PA and estimate EE. It was a relatively simple calibration study in which 25 males (mean ± SD age = 24.8 ± 4.2 yr., mass = 71.8 ± 7.9 kg, height = 177.6 ± 6.7 cm) and 25 females (age = 22.9 ± 3.8 yr., mass = 63.0 ± 7.5 kg, height = 166.1 ± 6.3 cm) completed 1 running (9.7 $km\cdot hr^{-1}$) and 2 walking speeds (4.8 and 6.4 $km\cdot hr^{-1}$) on the treadmill. Participants performed each treadmill speed for 6 consecutive minutes while wearing an ActiGraph accelerometer (model 7164) on their right hip and having their energy expenditure measured using indirect calorimetry. Both accelerometer and indirect calorimetry data were processed as minute-by-minute averages. The data indicated there is a linear relationship (r=0.88) between $counts\cdot min^{-1}$ and METs, and thus a simple linear regression model was developed to predict point estimates of EE. Count cut-points were also established to classify activity as light (< 3 METs), moderate (3-5.99 METs), vigorous (6-8.99 METs) and very vigorous (≥ 9 METs) intensity activity.

Freedson et al. (32) concluded these cut-points could be used to establish time spent in various activity intensities and thus used to assess both quality and quantity of free-living activity and its relation to health outcomes.

This novel approach to measuring PA and estimating EE was well received, but several limitations in the calibration process were identified, including a relatively small sample not representative of the population and the use of only three treadmill activities to establish the relationship between counts and EE. Hendelman et al. (47) suggested there is a different count-EE relationship for non-locomotion activities. In this study, researchers applied a linear regression model developed on locomotion activities to a data set of combined locomotion and non-locomotion activities. It was clear the linear relationship was weakened when non-locomotion activities were added to the model (locomotion activities $r = 0.77$; locomotion + non-locomotion activities $r = 0.59$). These data indicate models developed using locomotion activities only (such as the Freedson model) are limited in their generalizability to normal free-living conditions in which individuals perform a wide range of locomotion and non-locomotion activities. Additionally, several recent reviews expose the limitations of the Freedson EE and MET prediction equations. Both Crouter et al. (18) and Lyden et al. (63) indicate that when applied to an independent data set, the Freedson model performs well for level locomotion activities, but in most instances underestimates lifestyle activities.

Despite its limitations, and although several studies (40, 54, 72, 89, 110) prior to Freedson et al. (32) addressed the feasibility of using accelerometers to estimate PA in adults and children, Freedson et al. (32) was pioneering research in that it established the count “cut-point method” and described the relationship between accelerometer output and EE. The Freedson approach set the framework for subsequent calibration studies to improve upon, and thus many prediction models have since been developed. Each generation of prediction models however, appears to address one or more flaws inherent to its previous model, only to create or fail to account for additional errors.

**Inclusion of Lifestyle Activities in Calibration**

As evident by the Freedson model's consistent underestimation of EE for non-locomotion activities, researchers began to recognize it may be inappropriate to apply regression models developed on locomotion activities only, to free-living behavior in which a range of activity types (locomotion and non-locomotion) are performed. Swartz et al. (100) employed a protocol consisting of 2 over-ground walking and 26 lifestyle activities (including household and sport activities) to produce a new linear regression model and corresponding count cut-points. The variance in METs explained by accelerometer counts was 31.7%. This is considerably less than the variance explained when Freedson ($R^2$= 0.77) and Hendelman ($R^2$ = 0.59) applied linear regressions to locomotion activities (32, 47). When applied to independent data sets, the Swartz model did improve the underestimation of moderate to vigorous activities (18, 63, 87). However, the improvement observed for moderate-to-vigorous activities was at the expense of overestimating light intensity activities. The y-intercept of this linear model is 2.606 indicating that at 0 counts (no acceleration/movement) an individual's EE is at 2.606 METs, about 1.5 METs higher than what is traditionally used to describe sitting quietly in a chair (1 MET). Thus, activities performed between 1-2.6 METs will always be overestimated. This lack of sensitivity to changes in sedentary and light activity is of considerable importance given the recent evidence that most Americans spend more than half of their waking hours engaged in sedentary behavior (< 1.5 METs) (71) and the subsequent public health focus on reducing sedentary behavior as a means to reduce chronic disease risk factors. These data illustrate the difficulty of accurately assessing a range of activity types and intensities using a single linear shaped regression, and suggest lifestyle activities and/or free-living activity may require a different shaped regression to model the count-EE relationship.

An additional aim of the Swartz study was to determine if a second accelerometer worn on the wrist could improve EE estimates when included with the traditional hip mounted accelerometer (100). Although it seems reasonable that an accelerometer worn on the wrist may help account for the upper body movement characteristic of many lifestyle activities (e.g. ironing, washing dishes), the bivariate regression improved EE estimates by only 2.6% ($R^2 = 0.34$). Several other studies also addressed the feasibility of adding additional monitors to better estimate EE (46, 62, 72). For the most part, these studies conclude that additional monitors placed on either the ankle or wrist were not effective alternatives to the standard hip location. Furthermore, the minor improvement observed when these data are incorporated with the traditional hip data, are offset by the additional cost and time associated with more monitors and the data processing required.

The use of a wide range of activity types in the calibration and the addition of a wrist-mounted accelerometer did not solve the problem of accurately assessing a range of lifestyle activities. Furthermore, the current literature suggests that by better estimating moderate-to-vigorous intensity activities, the linear regression model sacrifices accuracy in the sedentary-to-light intensity range. Taken as a whole, the evidence suggests a single linear regression model will *never* be accurate at estimating EE across a range of activity types and intensities.

**Multiple Regression Models**

The realization that a single linear regression will always have difficulty assessing a range of activity types and intensities led to the development of several multiple regression approaches. Klippel & Heil (56) and Heil et al. (46) developed two-regression (2R) models that use activity "intensity" to direct accelerometer counts to one of two linear regressions of different slopes to predict EE. This technique seems reasonable given that most prediction models are fairly accurate at predicting EE for activities within a narrow intensity range. Theoretically, if counts are directed to a regression model that is better suited to predict EE for their specific intensity range, an improvement in EE estimation should be observed. However, there is an inherent problem with both the Klippel & Heil (56) and the Heil et al. (46) 2R models – both models use count cut-points to distinguish activity intensity. Lyden et al (63) report the average count·min$^{-1}$ for raking is 202.8, while the average count·min$^{-1}$ for descending the stairs is 3245, however these two activities have very similar average energy expenditure values, 5.2 and 5.0 kcal·min$^{-1}$, respectively. These data clearly demonstrate two activities of similar intensity can have drastically different count values due to the nature of the activities. Thus, if count cut-points are used to direct an activity to an intensity-specific regression, inaccurate estimates of EE will be produced.

Crouter et al. (17, 19) used more detail from the acceleration signal to distinguish between lifestyle and locomotion activities. The coefficient of variation (CV) (mean/standard deviation) is used to assess the variability in a minute's worth of counts, which are then directed to either a lifestyle specific regression or a locomotion specific regression to predict EE. These models are based on the premise that locomotion activities are much more rhythmic (and thus less variable) than intermittent lifestyle activities. Additionally, Crouter et al. (17, 19) used more complex exponential and cubic curves to estimate EE for locomotion and lifestyle activities, respectively. A recent paper indicates this method improves EE estimates for unconstrained lifestyle activities, specifically improving estimates across a wider range of activity types and intensities (63). This improvement is likely due to the non-linear cubic function used to estimate EE for lifestyle activities. Non-linear regressions use more free parameters to model the relationship between counts and EE; they do not assume a single, "straight line" relationship across a range of intensities. The same improvement, however, was not observed for locomotion activities. The traditional linear regression models (32, 100) performed better than the exponential regression used in the Crouter model. These data illustrate the difficulty in using more complex regressions to estimate EE. On one hand, they have the *potential* to fit data much more accurately, but also can be "over-fit" to the data from which they were created. In other words, the shape of the regression may be too specific to the data set used in its development and thus, may not transport to independent data sets or extrapolate to activities outside the range of counts from which they were developed as well as simpler regressions. Nonetheless, Crouter et al.'s (17, 19) two-regression model demonstrated that more complex features of the acceleration signal could be used to help characterize activity.

### Handling zero counts

In addition to introducing the multiple regression method, Klippel and Heil (56) were also the first to introduce the idea of an inactivity threshold. In this method, if counts per minute are below a certain threshold they are not directed to a prediction equation, but assigned a predetermined EE value. This method was developed in response to the severe overestimation of sedentary and light intensity activities when regressions designed to improve the assessment of moderate-to-vigorous intensity activities were applied. Since its introduction, the inactivity threshold has been employed by several other regression models (17, 19, 46, 70) and it appears to improve EE estimates. However, controversy remains over the correct count threshold to use and the corresponding EE value to assign (59). This is especially important given that physical activity researchers are increasingly interested in time spent in sedentary and light intensity activity and its relation to health.

### Moving Beyond Traditional Regression Approaches

Since 1998 and Freedson et al (1998) initial calibration study, accelerometer prediction models have continuously evolved in an attempt to improve EE estimates. Each generation of prediction models appears to address one or more flaws inherent to its previous model, only to create or fail to account for additional errors. Despite their increasing complexity, no regression model accurately estimates EE across of range of activity types and intensities.

There are two fundamental reasons for these failures. First, they assume a simple, rigid relationship between counts per minute and EE. Researchers traditionally attempt to fit a regression whose shape is predetermined to complex data sets. The problem with this method is the data are generally much more complex than the regression and thus a rigidly defined shape will never accurately fit a range of data. Second, they all use counts per minute as the sole input into the prediction equation. By integrating and averaging a single acceleration signal over time, the rich features of the signal are destroyed and patterns in the movement are ignored. Using this technique, two very different activities such as walking briskly on a treadmill and vacuuming may have very similar inputs used to predict EE. Rhythmic locomotion activities exhibit repeated patterns of counts that tightly oscillate around the mean (17, 19). Intermittent lifestyle activities (e.g. vacuuming) exhibit counts that are more variable and often have much larger standard deviations than locomotion activities (17, 19). However, when second-by-second counts are averaged over one minute, these differences are eliminated and two very different activities, with very different energy costs, appear very similar. Thus, no matter the slope of the regression, the shape of the regression or how many different regressions are used, if prediction techniques only consider counts per minute, they will not accurately estimate EE across a range of activities. Figure 2.1 illustrates the limitations of the most common regression models as they progressed from 1998 to the present.

In response to these limitations, researchers have begun to apply more sophisticated data processing techniques to estimate EE from accelerometer counts. Many groups have successfully applied various machine learning techniques such as hidden Markov models (HMM), decision trees, cross-sectional time series, multivariate adaptive regression splines and artificial neural networks (nnet) (66, 85). Pober et al. (84) successfully applied HMM to predict activity mode and estimate EE. However, the HMM model is relatively complex and relies on custom software that may be a barrier for many applied researchers. Similarly, Rothney et al. (86) developed an nnet that improves EE estimates compared to traditional regression techniques. This approach holds promise, but at the present, it requires expensive analytical software (Matlab, Mathworks, Natick, MA) and a very complex multiple accelerometer system (Intelligent Device for Energy Expenditure and Activity (IDEEA), MiniSun LLC, Fresno, CA), thus its application to free-living environments and large-scale epidemiologic studies is extremely difficult.

Staudenmayer et al. (97) recognized these more complex methods hold promise, but also recognized the importance of making such methods usable by applied researchers. Using the ActiGraph activity monitor and the open source computing language and statistics package R (101), Staudenmayer et al. (97) developed two simple nnets to identify activity type and estimate EE (lab-nnets). The lab-nnets were developed using a two-step process. First, a training data set of known inputs (accelerometer counts) and known outputs (EE and activity type) was used to "teach" the lab-nnets the structure of the data. In this phase, several combinations of demographic information (e.g. weight, gender) and statistical features of the second-by-second acceleration signal (e.g. standard deviation, skew, coefficient of variation etc.) were tested to determine the inputs that best predicted EE and activity type. For both lab-nnets, two features of the vertical acceleration signal were chosen as inputs: 1) summaries of the distribution of counts and 2) summaries of the temporal dynamics of counts. Both statistical features of the accelerometer signal use a minute's worth of second-by-second counts to summarize the data. After the training phase was complete, the lab-nnets were tested using a leave-one out cross validation technique and the lab-nnet improved EE estimates compared to traditional regression models (rMSE (METs); lab-nnet = 1.26, Freedson = 2.09, Swartz = 1.77, Crouter = 1.61), and correctly identified activity type as sedentary, locomotion, lifestyle, or vigorous sport 88.8% (95% CI: 86.4-91.2%).

Although the lab-nnet calibration process is similar to that of traditional regression approaches (model is trained on a data set of known inputs and known outputs), there are two key reasons why the lab-nnet method improves EE estimates. First, it does not assume a simple parametric relationship between counts and EE. This means the lab-nnet is free to model its shape according to the data rather than trying to fit a simple, predetermined regression with a limited number of parameters, to very complex data. Second, the inputs used by the lab-nnet include more information about a minute's worth of second-by-second accelerometer counts. Staudenmayer et al. (97) used the $10^{th}$, $25^{th}$, $50^{th}$, $75^{th}$ and $90^{th}$ percentiles of a minute's second-by-second counts. Within these distribution summaries common statistics are implicitly included. For example, the $75^{th}$ minus the $25^{th}$ percentile is approximately proportional to the standard deviation and the mean is approximately the weighted average of all five summaries. From this information, we also know something about the coefficient of variation, which is the ratio of the standard deviation to the mean. The flexibility of the lab-nnet allows it to use all of this information as well as the five summaries in its modeling of the relationship between accelerometer counts and EE. The second input, lag-one autocorrelation, tests the relationship between adjacent counts within a minute's worth of second-by-second counts. This provides the lab-nnet information on the temporal dynamics or repeated patterns of observations within the data. In short, the success of the lab-nnet method is due to its inherent flexibility and its use of more information from accelerometer output than traditional regression approaches.

Together the inputs provide the lab-nnet with enough information to improve EE estimates across a wide range of activity intensities and types and to classify the activity into one of four general categories (sedentary, locomotion, lifestyle or vigorous sport). These improvements suggest the lab-nnet method may be more successful than traditional measurement techniques in a free-living environment. Individuals often perform a wide range of activities from sedentary and light intensity lifestyle activities to vigorous sporting activities. It is critical to accurately measure activities across the full spectrum of behavior so that researchers can better understand not only the relationship between specific activities and health, but also the effects of the interactions of various activities (e.g. moderate activity mixed with sedentary time) on health.

The lab-nnet method is more complex than simple regressions and does require a level of statistical knowledge to develop such a method. However, Staudenmayer et al. (97) used the free and open source computing language R (101) to develop the lab-nnets and thus the application of the method is relatively simple. In order to process data researchers must do some level of data cleaning, but limited computational and statistical knowledge is required. This is an improvement from other pattern recognition approaches that are relatively difficult and expensive to apply (66, 68, 84-86).

Rapid improvements in device miniaturization, computational power and extended memory continue to allow for the use of more sophisticated machine learning algorithms to process information from wearable monitors. Using accelerometers to monitor ambulatory activity has many biomedical applications (e.g. tremor analysis, fall identification and prevention, EE estimation, activity classification) and as a result experts from many fields are aggressively pursuing more accurate methods to process these data (65, 67, 85). The challenge remains in developing a method that is easily used by applied researchers. The ideal algorithm will work "off the shelf". It will not require individual calibration, multiple cumbersome monitors, expensive analytical software, and it will be easily translatable to common free-living environments (53).

**Summary and Future Directions**

Traditional accelerometer EE prediction techniques rely on average counts per minute and use simple regressions with limited parameters to model the relationship between accelerometer output and EE. This approach has continuously produced sub par results and thus researchers have begun to explore more sophisticated data processing techniques. Staudenmayer et al. (97) demonstrated the validity of two simple nnets to predict EE and identify activity type. The lab-nnets are more flexible than traditional regressions and use more information from the acceleration signal, resulting in improved performance across a range of activity intensities and types.

The lab-nnet method however, was developed and validated in a laboratory setting, and preliminary observations suggest its performance significantly declines when applied to free-living data. We have refined our lab-nnet to be more appropriate for free-living applications. Our new method is called the sojourn method, and it is a hybrid machine learning technique that combines artificial neural networks with a decision tree. The sojourn method operates in three main steps: using simple parameters from the acceleration signal the sojourn method 1) identifies bouts of activity and inactivity, 2) assigns non-physical activity MET values to inactivity bouts and 3) applies the original lab-nnet to estimate METs for activity bouts (see appendix A for a detailed description of soj-1x and soj-3x). **Study 1 examined the validity of the lab-nnet and two versions of the sojourn method (soj-1x and soj-3x) to assess free-living physical activity and sedentary behavior. Study 2 evaluated the sensitivity of soj-1x and soj-3x to detect change in habitual activity.**

## Sedentary Behavior and Health

Sedentary behavior's (SB) Influence on health is not clear. For years, research has *suggested* SB is negatively associated with health outcomes, but minimal experimental evidence exists, and studies that have manipulated sedentary time generally use models of SB that cannot be generalized to typical free-living environments. The limited state of sedentary behavior research is directly related to the lack of a valid SB measurement tool. The following review will outline the epidemiologic and experimental evidence linking SB to poor health and will highlight how the lack of a suitable measurement technique has severely limited SB research.

### Epidemiologic Evidence

Epidemiologic data has linked SB to poor health for decades. In the 1950's, Morris et al. (77) used vocational studies to compare individuals whose duties caused them to accumulate large amounts of sedentary behavior versus individuals who accumulated light intensity activity throughout the workday. In the famous "double-decker bus study," Morris et al. reported an increased incidence of heart attacks, independent of waist size, in bus drivers compared to conductors (77). The bus drivers spent most of their working day seated, while the conductors spent most of their working day accumulating small amounts of light intensity activity via ambulation. Despite

Morris's groundbreaking research implicating SB as a risk factor for developing coronary heart disease (CHD), researchers did not immediately focus their efforts on understanding the role sedentary behavior plays in determining health. This propensity to avoid SB research can be partly attributed to the difficulty in prescribing, measuring and performing relevant behavior that can be generalized to free-living sedentary conditions.

Within the last ten years an increasingly sedentary population has caused researchers to refocus their efforts and has brought sedentary behavior research to the foreground. A number of prospective and cross-sectional studies report a positive association between SB and incidence of many chronic diseases, chronic disease risk factors, and all-cause and cause specific mortality.

## Prospective Studies

Several very large-scale prospective studies have investigated the effects of sedentary behavior on health (24, 48-50, 55, 111). These studies used large, diverse samples and years of follow-up ranged from 5 to 12.9 years. Using self-reported TV viewing time as a surrogate measure for sedentary behavior, Hu et al. (51) reported a positive relationship between a sedentary lifestyle and incidence of type 2 diabetes in men. The relationship was independent of physical activity and remained significant (though attenuated) after adjusting for body mass index (BMI). Hu et al. (50) reported similar results using self-reported TV viewing time in women. Each 2-hour increment of TV time was associated with a 23% increase in obesity and a 14% increase in risk for diabetes. Although not as strong a relationship, occupational sitting time was also positively associated with obesity (5% increase per 2 hour increment) and risk of diabetes (7% increase per 2 hour increment).

To help establish causality, Wijndaele et al. (111) investigated the effects of baseline TV viewing and change in TV viewing time on changes in biomarkers of cardio-metabolic risk. After five years of follow-up, baseline TV viewing time was not significantly associated with change in any cardiometabolic biomarker, while increases in TV viewing time were significantly associated with increased waist circumference (men and women), increased diastolic blood pressure (women) and increased clustered metabolic risk score (women). The findings were independent of baseline and change in physical activity. This research indicates that increases in TV viewing negatively impacts markers of cardiometabolic health, and further supports the association between sedentary behavior and incidence of chronic disease.

In addition to its association with incidence of chronic disease and chronic disease risk factors, several studies report a positive association between sedentary behavior and mortality from all causes and cardiovascular disease (CVD). Katzmarzyk et al. (55) assessed sedentary behavior by asking a large cohort of Canadians to self-report their sitting time as either 1) almost none of the time, 2) approximately one forth of the time, 3) approximately one half of the time, 4) approximately three forth of the time and 5) almost all of the time. From these data, researchers reported a dose-response relationship between sitting and mortality from all causes and CVD. Using TV time as a measure of sitting, Dunstan et al. (24) reported a similar dose-response relationship. Each 1-hour increment of television viewing associated with an 11% and 18% increase risk of all-cause and CVD mortality, respectively. Like other prospective studies (50, 51, 111) these relationships were independent of physical activity and other potential confounders (e.g. age, BMI, smoking status etc.).

## Cross-sectional Studies

Like the prospective cohorts, several cross-sectional studies use self-reported TV viewing as a measure for sedentary behavior (26, 43, 94, 105). In general, these data support the findings of prospective studies; an independent effect of SB on metabolic health regardless of time spent in physical activity and adiposity status. Using self-reported TV viewing time as a proxy measure, SB has been linked to an increased risk for cardiovascular disease (94), metabolic syndrome (26, 94), obesity (50, 51) and type 2 diabetes (50, 51). Among individuals performing at least 2.5 hours of moderate intensity activity, Healy et al. (43) observed a detrimental dose-response relationship between TV viewing time and metabolic disease risk factors – waist circumference, systolic blood pressure, fasting plasma glucose, 2-h plasma glucose, triglycerides and high density lipoprotein (HDL).

Accelerometers have also been used to objectively estimate SB, physical activity and their effects on metabolic health. Using a <100 $count \cdot min^{-1}$ to identify sedentary activity, these data similarly indicated an independent effect of SB on 2-h plasma glucose, waist circumference and a clustered metabolic risk score (41). Using accelerometers to estimate SB and PA, Healy et al. (42) reported that breaks in SB, independent of total time spent in SB and moderate-to-vigorous PA, are beneficially associated with waist circumference, BMI, triglycerides, and 2-h plasma glucose. One potential mechanism for this beneficial response is the "short-circuiting" of harmful metabolic processes elicited by SB (38). These data indicate that prolonged SB should be especially avoided and that short breaks to stand or walk may significantly improve metabolic health.

**Limitations of Epidemiologic Evidence**

Although TV viewing is the most frequently reported sedentary activity by US adults (Nielson Media Research 2007), it is a self-reported, surrogate measure of sitting. For instance, an individual may report no TV viewing time, but spend ten hours per day seated at a computer; or one may report 3-hours of TV viewing, most of which is done while ambulatory (e.g. getting ready for work, preparing dinner). In addition, TV viewing is repeatedly linked to increased energy intake (11, 39, 104) and unhealthy food choices (39, 51, 52), both of which are linked to obesity, CVD, type 2 diabetes and metabolic syndrome (108). Several prospective and cross-sectional studies did measure other common forms of sitting (e.g. computer use, occupational SB) (33, 49, 55, 94, 105), however, they are all very crude, self-reports of SB and data indicate participants are generally bad at recalling SB (108).

Objective measurement of SB is certainly an improvement over self-reported TV viewing and other sedentary activities. Accelerometers can theoretically capture all sedentary pursuits and breaks in sitting, and they do not rely on participant recall to measure SB. Several count cut-points have been proposed to identify sedentary activity, including < 50 $counts \cdot min^{-1}$ (19), <100 $counts \cdot min^{-1}$ (70) and <150 $counts \cdot min^{-1}$ (59). However, accelerometers and the count cut-point method used to estimate activity from their output were not designed to measure SB.

In addition to the lack of a valid measurement technique, observational studies are further limited in that they do not prove causation. Katzmarzyk et al. (55) concluded there is dose-response relationship between SB and mortality by prospectively examining a large, diverse sample of Canadians. Researchers, however, failed to account for health status at baseline and, thus, it cannot be concluded that SB caused mortality, as it is completely plausible that poor health (e.g. CVD, diabetes, cancer etc.) caused SB.

## Experimental Evidence

Researchers are aware of the need for interventional studies or experimental manipulations of SB to further understand the effects of, and the physiological mechanisms stimulated by SB. The challenge of accurately measuring SB, however, has limited such attempts to highly artificial laboratory-based settings.

Traditionally, researchers have relied on bed-rest in humans and hind-limb immobilization in rodents to understand the physiologic response to SB. These studies indicate that insulin action (74, 83, 92, 95, 98, 108) and lipid metabolism (6, 7, 112) negatively respond to forced inactivity. The metabolic response induced appears to occur within just 1-day of sustained inactivity (7, 92, 98). Several studies speculated changes to insulin signaling, glucose transport, and lipoprotein lipase (LPL) activity may govern these early consequences (7, 83, 98, 109, 112). These data offer insight into the specific physiologic responses elicited by sustained inactivity, but the generalizability to typical free-living settings is questionable.

Bed-rest studies force participants to remain supine for days and/or weeks at a time. This state of inactivity is not equivalent to normal free-living sedentary behavior. Research has confirmed the substantial volume of sedentary time accumulated by otherwise healthy individuals in a free-living environment (71), but the majority of this SB is spent sitting, not lying down. Additionally, it is very likely that while seated (especially during occupational SB), individuals are expending some level of energy via upper body movements (e.g. typing, folding laundry etc.). While the physiologic responses elicited by lying down versus sitting, versus sitting with upper body movement have never been specifically compared, it is completely plausible these states of inactivity result in different physiologic outcomes. In a recent study Stephens et al. examined the effects of more real-life sedentary pursuits (98). On average, participants were confined to a wheel chair for more than 98% of their waking day and while energy balance was maintained insulin action decreased 18%. They were allowed to fidget and use their arms ad libitum during this time but were not allowed to take breaks from sitting. Although this protocol employs prolonged sitting as a stimulus, it still does not reflect true free-living sedentary behavior. For instance, even sedentary individuals break from sitting to walk to the restroom, perform self-care and hygiene activities, and make short walks for various reasons. In a recent laboratory study Dunstan et al (25) reported reductions in post-prandial glucose and insulin responses in individuals who took two-minute breaks from sedentary time every twenty-minutes compared to individuals who did not break-up sedentary time. These data and several observational studies (42, 44) suggests if two individuals accumulate the same total time of SB, but individual one breaks up their sedentary time periodically throughout the day, and individual two accumulates prolonged bouts of sedentary time, the individual who “breaks” will alleviate the detrimental metabolic response (42). The mechanism(s) responsible for this relationship are unknown, but potential explanations could include an exponential relationship between consecutive time spent in SB and the detrimental metabolic response elicited, or a cascade of harmful metabolic responses. If one harmful response is stimulated for a prolonged period of time without being “switched off” (via ambulation), it may eventually elicit an additional harmful response, and so forth. If this is indeed the case, and the goal is to understand the physiologic response induced by SB so that it can ultimately be applied to public health recommendations, it is imperative to understand the physiology of free-living sedentary behavior, not simply exaggerated bouts of extreme inactivity.

Several studies have investigated the effects of increases in free-living inactivity (61, 75). Krogh-Madsen et al. (61) objectively measured two-weeks of reduced, free-living, ambulation. Participants decreased their daily steps from 10,501 to 1,344 on average, resulting in a 7% reduction in $VO_2$max, a significant reduction in insulin action and a significant reduction in leg lean mass. Similarly, Mikus et al (75) reported reduced glycemic control when participants decreased $steps \cdot day^{-1}$ from 12,956 (±769) to 4,319 (±256) for seven days. These data suggest increased free-living SB detrimentally affects health, but both studies were not appropriately designed to address SB. A pedometer does not have the ability to assess body position (e.g. sitting vs. standing), EE or breaks from sedentary time. One might assume decreased steps means increased SB, but this could not be assessed with the tools and methods used to measure the exposure.

### Summary and Future Directions

Taken together, epidemiologic and experimental data strongly suggest sedentary behavior influences cardiovascular and metabolic health. From a public health standpoint, it is essential to comprehensively understand free-living sedentary behavior. **Study 3 evaluated the metabolic response in moderately active individuals to 7 days of increased free-living sedentary behavior.** The improved machine learning techniques validated in Studies 1 and 2 allowed us to study the effects of SB in a free-living environment and allowed us to estimate and evaluate more detailed components of SB than previously possible.

## Specific Aims

To address the knowledge gaps outlined above and to advance the field of physical activity and health, we proposed the following **specific aims:**

### Study 1

1. **To determine the validity of the lab-nnet and two versions of the sojourn method (soj-1x and soj-3x) in measuring free-living physical activity and sedentary behavior.**

   - We compared the algorithm estimates to a criterion measure of direct observation. We evaluated their validity in determining

     a. Time spent in sedentary, light, moderate and vigorous intensity activity

     b. MET-Hours

     c. Breaks from sedentary time

     d. The rate of breaks per sedentary hour (break-rate)

     e. Minutes that qualify towards meeting the Physical Activity Guidelines (qualifying minutes)

     f. The number of bouts that qualify towards meeting the Physical Activity Guidelines (qualifying bouts)

**Study 2**

1. **To evaluate soj-1x and soj-3x's sensitivity to detect change in free-living habitual activity.**

    - We applied soj-1x and soj-3x to three distinct habitual activity levels: sedentary, moderately active and very active to determine its sensitivity to change within an individual.

**Study 3**

1. **To evaluate the metabolic response in moderately active individuals to seven days of increased sedentary behavior.**

    - We used the machine learning techniques validated in Studies 1 and 2 to measuring free-living behavior.

    - We examined how changes in activity and inactivity variables impacted insulin action, fasting glucose, triglycerides and cholesterol.

## Figures

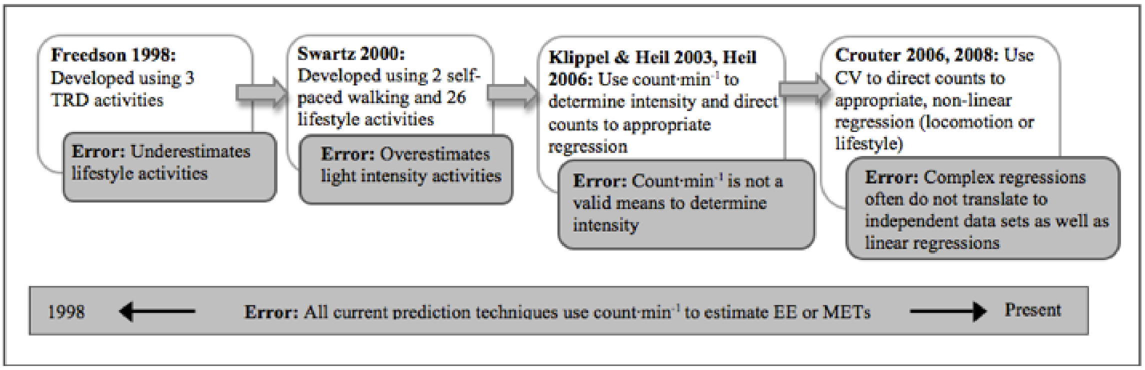


**Figure 2.1: Limitations of common energy expenditure and MET prediction models as they progressed from 1998 to the present**

# CHAPTER III

# VALIDATION OF TWO NOVEL METHODS TO ESTIMATE FREE-LIVING PHYSICAL ACTIVITY AND SEDENTARY BEHAVIOR

## Introduction

Wearable accelerometers are ideal for collecting information about free-living behavior. They can be worn for extended periods of time, impose minimal inconvenience to the participant and researcher, are relatively inexpensive and can produce detailed accounts of physical activity (PA) and sedentary behavior (SB) that are relevant to health (e.g. estimates of energy expenditure, time in MVPA, time spent sedentary) (30). However, methods to process accelerometer output have yet to realize their potential to provide accurate estimates of energy expenditure (EE) in free-living environments. Early work in the field used simple and multiple regressions to estimate METs (14, 20, 32, 76, 100) or kilocalories (32, 46) from accelerometer counts$\cdot$min$^{-1}$. Although these approaches are relatively easy to use and provide reasonable objective estimates of physical activity, their limitations have been well documented (18, 63, 87).

Recent improvements in device miniaturization, computational power and extended memory now allow data to be processed by more sophisticated machine learning algorithms. Several groups have reported success using hidden Markov models, decision trees, cross-sectional time series, multivariate adaptive regression splines and artificial neural networks (66, 85). These methods improve EE estimates and provide more detailed information about active and inactive behaviors than originally possible with traditional regression approaches (12, 21, 84, 86, 97, 114).

In a laboratory calibration study our group recently developed a simple artificial neural network (lab-nnet) to estimate METs from second-by-second ActiGraph (ActiGraph LLC, Pensacola, Florida) accelerometer output (97). The lab-nnet improved MET estimates compared to simple regressions and has been validated on an independent sample (31). By using a single, hip-mounted accelerometer and the open-source computing language and statistics package R (101) our method preserved the simplicity and ease of use afforded by traditional regression approaches. This is particularly important to applied researchers given that most other advanced techniques use expensive analytical software (12, 86) and complex multiple accelerometer systems (4, 28, 29, 86, 113), rendering their application to free-living environments and large-scale epidemiologic studies impractical.

Although the lab-nnet performs well in laboratory settings and uses more detailed information from the acceleration signal than traditional regression approaches, it produces minute-by-minute MET estimates. This approach assumes a minute consists of only a single activity. In a laboratory this is not problematic because participants generally perform activities for a prescribed amount of time, and the start and stop of activities are controlled. Prediction algorithms are then applied to specific bouts of activity. In free-living environments where behavior is unplanned and activity patterns can be random, activities do not start and stop on the minute and several activities can be performed within the same minute (e.g. sit, stand, walk). Figure 3.1 illustrates the challenge of applying an algorithm developed in the laboratory to free-living data. The bottom two panels show 2-minutes and 30-seconds of free-living accelerometer output ($counts \cdot sec^{-1}$). In this example a researcher was observing the participant's behavior and the recorded activities (top panel) were synchronized with the accelerometer output. When the lab-nnet is applied to these data, the five distinct activities are grouped into minute intervals (bottom panel) and METs are predicted for each minute. Preliminary observations indicate this method produces substantial error. It may be necessary to first identify where activities start and stop (middle panel), and then apply the prediction algorithm to identified bouts of activity.

We have refined our lab-nnet to be more appropriate for free-living applications. Our new method is called the sojourn method, and it is a hybrid machine learning technique that combines artificial neural networks with decision tree analysis. The sojourn method uses simple parameters from the acceleration signal and follows a three step progression: 1) identification of bouts of activity and inactivity, 2) assignment of non-physical activity MET values to inactivity bouts and 3) application of the original lab-nnet to estimate METs for activity bouts.

The purpose of this study was to validate two versions of the sojourn method and our original lab-nnet in a free-living environment. The first version of the sojourn method uses sec-by-second counts from the vertical axis only (soj-1x) and the second version uses second-by-second counts from the vertical, anterior-posterior and medial-lateral axes (soj-3x). We compared each method to the criterion direct observation (DO) method.

# Methods

## Recruitment and Eligibility

Seven participants (3 males, 4 females) were recruited from the Amherst, Massachusetts area. Participants were 18-60 years of age and in good physical health (no diagnosed cardiovascular, pulmonary, metabolic, joint, or chronic diseases). All participants completed a health history questionnaire and an informed consent document approved by the University of Massachusetts Institutional Review Board.

## Baseline Visit

Participants reported to the Physical Activity and Health Laboratory following at least a 12-hour overnight fast. Using a standard floor stadiometer and physicians' scale (Detecto; Webb City, MO), height and weight were measured to the nearest 0.25 cm and 0.1 kg, respectively.

At the baseline visit participants also completed a short survey asking about their current physical activity status (PAS). Participants were asked to choose a number which best described their activity in a normal week. Possible responses ranged from 0 to 7 with 0 corresponding to "avoided walking or exertion (e.g. always used the elevator, drove whenever possible instead of walking)", and 7 corresponding to "ran more than 10 miles per week or spent over 3 hours per week in comparable physical activity".

## Experimental Procedures

Participants were directly observed in their free-living environment on three separate occasions. Each observation lasted for approximately ten consecutive hours and during this time participants wore an ActiGraph GT3X accelerometer on their right hip.

**Criterion: Direct Observation**

Participants were met by a trained observer in their natural environment (e.g. home, place of work, school) and observed for approximately ten consecutive hours. A hand-held personal digital assistant (PDA) (Noldus Information Technology; Netherlands) with focal sampling and duration coding was used to record participant behavior (activity type, intensity and duration). Every time behavior changed (e.g. sitting to standing) the observer recorded the new activity type and intensity in the PDA. Each entry was time stamped and the length of each behavior bout was automatically recorded in the PDA. During the ten hour observation time, subjects were allowed to have “private time” when needed. Reasons for “private time” included behaviors such as using the restroom and changing clothes. During these activities, the observer coded “private” on the PDA.

Observers worked in 2-4 hour shifts and a total of three different observers completed all of the observation sessions. Observers completed extensive verbal, written and video training and testing before observing participants in a free-living environment. The training material focused on a specific protocol to avoid disrupting free-living behavior and to accurately record activity type and intensity. When training was complete, each observer was tested using a ~15 minute video of free-living behavior. The video was first coded by a group of experienced observers and study observers’ responses were compared to the experienced observers’ responses using Cohen’s kappa coefficient (κ). In order to be considered “in agreement”, study observers were required to correctly identify both the activity type and intensity. There was a very high level of agreement between the study observers' responses and the experienced observers' (mean $\kappa = 0.92$).

Direct observation is the gold standard method to identify activity type in free-living environments. Additionally, our DO method has been validated to estimate intensity compared to indirect calorimetry. These unpublished data are presented in Appendix B and indicate DO is an accurate and precise method to identify MET-hours, and time spent in categories of intensity.

**ActiGraph GT3X (ActiGraph LLC, Pensacola, Florida)**

Subjects wore the ActiGraph GT3X on their right hip. The GT3X was programmed to collect data from the vertical, anterior-posterior and medial-lateral axes in one-second epochs.

### Data Cleaning and Reduction

For an observation to be included in the analyses valid DO and ActiGraph data were required. Additionally, behavior coded as "private" by the observer along with the corresponding ActiGraph data were eliminated from analyses. All data cleaning and processing were done using the statistics package and computing language *R* (101).

A log of the start and stop of each behavior recorded by the observer was exported to a text file from the PDA using custom software (Noldus: Observer 9.0). These data were used to determine criterion measures of activity and inactivity including, MET-hours, time in categories of intensity, minutes in bouts of activity that qualify towards meeting the physical activity guidelines (qualifying minutes), the number of bouts of activity that qualify towards meeting the physical activity guidelines (qualifying bouts), breaks from sitting and the rate of breaks per sedentary hour (break-rate).

"Qualifying" minutes and bouts are defined as moderate-to-vigorous intensity activity that last at least ten consecutive minutes (16).

ActiGraph data were downloaded and exported to text files using *ActiLife 5.0* (ActiGraph LLC, Pensacola, Florida). These data were then processed in *R* using the lab-nnet, soj-1x and soj-3x algorithms. Descriptions of soj-1x and soj-3x are presented in Appendix A. For a review of the development and performance of the lab-nnet see Staudenmayer et al (97) and Freedson et al (31).

**Statistical Evaluation**

All statistical analyses were performed using the *R* statistics package and computing language. Repeated measures linear mixed models were used to evaluate the performance of the lab-nnet, soj-1x and soj-3x. Algorithm performance was evaluated using three statistical tools: bias, root mean squared error (rMSE) and correlation. The bias, or mean difference between predicted and criterion estimates (Σ[estimate – criterion]/N), is a measure of accuracy and gives information about how the model will perform when applied to a group. In this study a negative bias indicates underestimation by the prediction method; a positive bias indicates overestimation by the prediction method. We also report the 95% confidence interval (CI) of the bias, which provides information about the precision of the estimate. A small CI width indicates a high precision and a large CI width indicates a low precision. If the upper and lower CI's of the bias span 0, then the estimate is *not* significantly different from the criterion at $\alpha$=0.05. The rMSE is the square root of the mean squared error and it provides information about the magnitude of the error: it does not indicate the direction of the error (i.e. over or under-estimation). rMSE offers insight into the size of the error that can be expected when the model is applied to an individual.

## Results

Participant characteristics (mean ± SD) are reported in Table 3.1. During three DO sessions the ActiGraph monitors did not record data and were therefore eliminated from analyses. This resulted in a total of 18 observations (7 participants, 3 observations per participant). After "private time" was eliminated, mean ± SD time per observation was 9.46 ± 0.42 hours.

In general, both soj-1x and soj-3x improved estimates of MET-hours, and moderate and moderate-to-vigorous (MVPA) intensity activity compared to the lab-nnet. Soj-3x also improved estimates of sedentary and light intensity activities, compared to both lab-nnet and soj-1x. Table 3.2 and Figure 3.2 compare the mean (95% CI) DO, lab-nnet, soj-1x and soj-3x estimates of MET-hours and time spent in categories of intensity. According to DO, participants spent on average 346.1 min (304.9-387.3) in sedentary, 161.0 min (123.4-198.6) in light, 45.7 min (33.1-58.3) in moderate and 14.6 min (5.8-23.3) in vigorous intensity activity per observation. In Table 3.2 the bias (average difference between model estimates and direct observation), rMSE (square root of the mean squared error) and correlation for each method compared to DO are reported.

The smaller absolute biases in Table 3.2 and illustrated in Figure 3.3 indicate that soj-1x and soj-3x were more accurate in estimating MET-hours and time in categories of intensity (except for vigorous intensity activity) than our existing lab-nnet. The error bars in Figure 3.3 are the 95% CI of the estimates and represent the precision of the model. We note that because positive (overestimation) and negative (underestimation) errors cancel each other when they are averaged, an unbiased estimate does not always indicate how the model will perform for an individual. The rMSE reported in Table 3.2 offer insight into this.

The lab-nnet and soj-1x produced similarly large rMSE's (95% CI) for sedentary (lab-nnet = 53.1 min (31.1-75.1), soj-1x = 50.2 min (31.8-68.6)) and light (lab-net = 53.3 min (32.8-73.9), soj-1x = 49.7 min (31.5-68.0)) intensity activity. Soj-3x improved these estimates by nearly 50% (26.2 min (12.0-40.4) and 27.6 min (11.4-43.8), respectively). The lab-nnet estimates of moderate and MVPA time also have large rMSE's (moderate = 39.5 min (27.2-51.8), MVPA = 46.4 min (33.3-59.6)). Both soj-1x and soj-3x greatly improved these estimates (moderate: soj-1x = 11.7 min (7.7-15.6), soj-3x = 15.9 min (10.4-21.5) and MVPA: soj-1x = 4.0 min (2.1-5.9), soj-3x = 15.9 min (10.4-21.5)). The lab-nnet performed slightly better for vigorous intensity activity (9.3 min (5.7-12.9)) compared to both soj-1x (10.8 min (6.8-14.8)) and soj-3x (14.4 min (6.3-22.5)).

All model estimates had strong correlations with DO (range: r = 0.49-0.99) and the correlations indicated similar trends in performance as bias and rMSE (Table 3.2 and Figure 3.4). Figure 3.4 plots model estimates against direct observation for each participant. The closer the points fall to the line of identity, the closer the estimate is to DO. Points that fall on the line of identity indicate the estimate is identical to DO.

Since soj-1x and soj-3x identify bouts of activity, they can provide more detailed estimates of behavior, including 1) minutes that qualify towards meeting the physical activity guidelines (qualifying minutes), 2) the number of activity bouts that qualify towards meeting the physical activity guidelines (qualifying bouts), 3) breaks from sedentary time and 4) the rate of breaks per sedentary time (break-rate). Both methods performed well in estimating these metrics. Table 3.2 and Figure 3.4 suggest these estimates are unbiased, have small rMSE's and are strongly correlated with DO. The lab-nnet does not estimate activity bout duration and therefore cannot estimate this level of detail about behavior.

## **Discussion**

In this study we presented and validated two novel methods specifically designed to estimate free-living physical activity and sedentary behavior from a single, hip-mounted accelerometer. By identifying where bouts of activity and inactivity start and stop, and predicting METs for specific bouts, soj-1x and soj-3x greatly improved the performance of the lab-nnet compared to direct observation. Soj-1x and soj-3x also provided accurate estimates of more detailed estimates of behavior, including breaks from sedentary time and minutes that qualify towards meeting the physical activity guidelines (qualifying minutes).

Measuring and classifying human movement from accelerometer (and other) sensors is an active field that has benefited from rapid technological advancements and collaborations from experts in many fields. We are not the first to demonstrate success in using machine learning to process information from on-body sensors (e.g. accelerometers, gyroscopes, heart-rate monitors, ambient sensors, ventilation sensors) (65, 85, 87). Very high levels of performance are generally reported, but performance consistently declines when fewer sensors are used and when methods are applied in free-living conditions (22, 36).

Soj-1x and soj-3x bridge this significant gap in the literature. Both methods are hybrid machine learning models that combine artificial neural networks with decision tree analysis to estimate METs. By combining *a priori* knowledge on human behavior with the flexible non-parametric properties of the lab-nnet these models are better suited to estimate METs from free-living accelerometer output. There are three "key ingredients" to the improved MET estimates observed with soj-1x and soj-3x. These steps, their impact on model performance and their relation to previous methodologies are discussed below. For detailed step-by-step descriptions of soj-1x and soj-3x see Appendix A.

**Identifying Bouts of Activity and Inactivity**

The first step in processing sensor signals with any machine learning technique typically involves dividing the signal into small time segments called windows (85). The central difference between soj-1x, soj-3x and previous approaches is in how the signal is segmented. Laboratory methods most often use a sliding window method where the signal is divided into windows of fixed length. The lab-nnet and simple regression approaches divide the vertical acceleration signal into minute intervals and METs are estimated on a minute-by-minute basis (Figure 3.1). Other laboratory studies using raw acceleration have defined windows from 0.4 to 12.8 seconds (12). When sliding window methods are applied to free-living data where activities are unplanned and performed in bouts of many different durations, model performance declines considerably. This is evident in the current study where the lab-nnet performance significantly declined compared to two previous laboratory validations (31, 97). Studies using raw acceleration and much smaller windows have reported similar observations (4, 22, 28, 29, 36, 68). Using accelerometers positioned on the sternum, wrist, thigh and lower leg, Foerester et al. (29) reported an overall 95.8% classification accuracy in the laboratory. Performance was reduced to 66.7% when the same analytic methods were applied to free-living data. Similarly, Ermes et al. (28) used second-by-second windows and reported a 17% reduction in accuracy when a classification algorithm was applied to free-living data.

Alternatives to the sliding window approach include non-fixed, event-defined or activity-defined windows. Activity-defined windows depend on identifying where (in the signal) activities change. This approach is used in the current study and intuitively seems to be the most appropriate for estimating METs or identifying activity type in free-living environments. In short, soj-1x and soj-3x use the relationship between adjacent counts from the vertical axis to identify where changes in activity may occur (Appendix A). Once the signal is segmented, the hybrid model (artificial neural network- decision tree) is applied to each window (bout). Several methods have been proposed to identify changes in walking and gait patterns (e.g. transitioning from walking to ascending stairs, identifying heel-strike) (79, 93), but we are not aware of this approach being used to identify where bouts of activity and inactivity start and stop, or in the context of physical activity measurement.

**Estimating METs for Bouts of Activity**

Soj-1x and soj-3x models estimate METs for bouts of activity and bouts of inactivity differently. In both models, the percent of non-zero counts from the vertical acceleration signal is used to distinguish activity from inactivity (Appendix A). The lab-nnet is then applied to bouts of activity to estimate METs. Since “inactivities” were not included in the initial calibration of the lab-nnet and given the well-documented challenges of estimating METs for these behaviors (18, 63, 87), we estimate METs for inactivities differently (described below).

In the current study, the approach to dealing with active bouts significantly improved estimates of time in MVPA ($\geq$ 3 METs) (Table 3.2). Both soj-1x and soj-3x produced accurate and precise estimates, while the lab-nnet significantly overestimated time spent in MVPA (Figure 3.3). Soj-1x and soj-3x also had much smaller rMSE's (95% CI) (4.0 min (2.1-5.9) and 7.8 min (4.1-11.8), respectively) compared to the lab-nnet (45.5 min (32.2-58.8)). Small rMSE's suggest the model will work well for an individual – this is supported in Figure 3.4 where we plot individual estimates of MVPA against direct observation. Soj-1x (open triangles) and soj-3x (filled circles) estimates consistently fall much closer to the line of identity than the lab-nnet (open squares).

**Estimating METs for Bouts of Inactivity**

To estimate METs for bouts of inactivity we assign values from Kozey et al (57) and Ainsworth et al (2) to four different types of inactivity: inactivity type 1 (sitting or lying fairly still) = 1 MET, inactivity type 2 (sitting with minor movement) = 1.2 METs, inactivity type 3 (standing fairly still) = 1.5 METs and inactivity type 4 (standing with minor movement) = 1.7 METs. To determine inactivity type soj-1x uses the percent of non-zero counts from the vertical axis and soj-3x uses a simple neural network algorithm trained on free-living data.

Soj-1x did not improve estimates of time in sedentary (< 1.5 METs) and light (1.5-2.99 METs) intensity compared to the lab-nnet (Table 3.2, Figures 3.3 and 3.4). Given that soj-1x uses parameters from only the vertical acceleration signal to distinguish the four types of inactivity (Appendix A), these results were not surprising. It is well established that the acceleration signal from the vertical axis looks very similar for sitting and standing (with minimal movement) activities (19, 58, 63). This is true for both integrated (e.g. counts$\cdot$sec$^{-1}$) and raw acceleration signals and in both laboratory and free-living settings (21, 28, 68, 73).

Recent studies often group sedentary and light intensity behaviors into a single "low" intensity category, or estimate intensity for dynamic behaviors only (e.g. walking, running) (12, 21, 36, 113, 114). Similarly, studies aimed at identifying posture often group sitting and standing into a general "upright" category (28, 68). When this approach is not taken, the largest classification error is reported for these behaviors (12, 21). For example, during "controlled free-living" sitting and standing activities, De Vries et al. (21) reported nearly identical counts$\cdot$sec$^{-1}$ from the vertical axes of a hip-mounted accelerometer, resulting in standing activities being classified as sitting 78.9% of the time.

We developed soj-3x to potentially address the large errors produced by the lab-nnet and soj-1x in distinguishing sedentary and light intensity activity. Soj-3x uses information from three axes (vertical, anterior-posterior and medial-lateral) and the vector magnitude of these axes to first classify inactivity as either sitting or standing. This is done with a simple neural network algorithm (1 hidden layer, 25 hidden units) that was developed and trained on free-living data similar to that used in this study (Appendix A). Inactivity classified as sitting is identified as inactivity type 1 (sitting or lying fairly still) or inactivity type 2 (sitting with minor movement) and is assigned a MET value as is done in soj-1x. Similarly, inactivity classified as standing is identified as inactivity type 3 (standing fairly still) or inactivity type 4 (standing with minor movement) and is assigned a MET value as is done in soj-1x (Appendix A). This approach produced an estimate of sedentary time with a bias and rMSE nearly 50% smaller than both other models (Table 3.2, Figures 3.3 and 3.4).

Midorikawa et al (73) reported that acceleration data from three axes (vertical, anterior-posterior, medial-lateral) improved the classification of low-intensity activities compared to vertical accelerations alone. The overall sensitivity and specificity for distinguishing sitting from standing remained relatively low (75.3% and 64.6%, respectively), but these findings and findings from other laboratory studies (12, 68) suggest information from more axes may be necessary for accurate assessment of low-intensity activities. Results from the current study suggest that in free-living people, this information is also useful. Figure 3.5 shows approximately 20-minutes of free-living data collected from one participant in the current study. According to direct observation, the participant is sedentary for the first third of the example, and standing in light intensity for the remaining time. Using information from the vertical signal only, soj-1x confuses light intensity with sedentary approximately half of the time. Soj-3x uses the additional information from the anterior-posterior and medial-lateral axes to correctly distinguish sedentary from light intensity. We note that if there is "not enough", or "too much" movement in the anterior-posterior or medial-lateral planes soj-3x will continue to confuse sedentary and light intensity activities. However, the smaller bias and rMSE for soj-3x estimates (Table 3.2, Figures 3.3 and 3.4) indicate these errors are much smaller compared to when only the vertical acceleration signal is used (soj-1x).

**Strengths and Limitations**

This study has several important strengths. First, methods were validated under free-living conditions. It is well accepted that performance in the laboratory does not translate to free-living people and best practice recommendations consistently highlight the need for free-living validations (5, 30, 36, 53). Several studies have tested methods in "simulated free-living" environments where participants perform a small subset of basic ambulatory movements and postures (29, 68), but to our knowledge this is the first study to follow participants in their own natural environment and to allow participants to perform an unlimited range of activity types and intensities.

Second, participant behavior was observed and recorded by trained researchers for approximately ten consecutive hours. Other studies have used protocols that require participants to annotate their own behaviors (4, 66). It is unknown how accurate and reliable participant annotated data are, but intuitively this approach seems to have inherent limitations: relying on untrained participants to collect data, high degree of participant burden, inability to capture transitions between activities and inability to capture short bouts of activities, to name a few. Additionally, it is unrealistic for participants to annotate their own behavior for long periods of time, thus the amount and range of data collected are limited. In this study we observed each participant, on three separate occasions, for approximately ten consecutive hours (mean hours ± SD per observation = 9.46 ± 0.42 hours). To our knowledge only one other free-living validation (36) and very few laboratory validations have compared more data to a criterion.

The third, and perhaps most important strength of this study is that the proposed methods use a single, hip mounted accelerometer (ActiGraph GT3X) and an open source computing package (101). The application of previous methods has been limited by complex multi-accelerometer systems and expensive analytical software (66, 67, 85). The proposed methods were successful using a relatively low sampling rate (1 Hz), information from the vertical acceleration signal only (soj-1x) and information from the vertical, anterior-posterior and medial-lateral acceleration signals (soj-3x). We anticipate that future work using much higher sampling rates (e.g. 30-100 Hz) will improve these models, but until recently monitors were not capable of collecting and storing this type of data for prolonged periods of time. Similarly, although performance improved when more information was used, the success of soj-1x is important given that earlier models of the ActiGraph (e.g. 7164, GT1M) record motion in the vertical plane only and thus data collected with these monitors require corresponding processing techniques.

The main limitation of this study was our homogenous sample. Participants were relatively young (age = 25.0 yrs. ± 4.9 (mean ± SD)), lean (BMI = 24.0 ± 2.4) and active (PAS = 6.4 ± 0.5). Although this study had seven participants, we do not consider sample size a limitation. Each participant was observed on three separate occasions, for approximately ten consecutive hours (mean hours ± SD per observation = 9.46 ± 0.42 hours). This resulted in approximately 12,600 minutes of direct observation synchronized with monitor output, much more data than almost all other validation studies. Nonetheless, the proposed methods would benefit from future validations on larger, more diverse samples.

## Summary and Conclusion

In this study we proposed two novel machine-learning methods specifically designed to estimate physical activity and sedentary behavior in free-living people. Both methods use a single hip-mounted accelerometer to identify the start and stop of bouts of activity and inactivity, and both methods improved performance compared to a method previously calibrated in the laboratory. This study also demonstrated the effectiveness of using information from the anterior-posterior and medial-lateral axes to more accurately distinguish sedentary and light intensity activity. Future validations will evaluate the sensitivity of soj-1x and soj-3x to detect change in habitual activity and future refinement will adapt these methods to also identify activity type.

Soj-1x and soj-3x significantly advance the field of physical activity measurement. Using a single commercially available accelerometer, novel machine-learning approaches, and supervised training data collected under free-living conditions, soj-1x and soj-3x provide easy to use, accurate approaches to ESTIMATING PHYSICAL ACTIVITY and sedentary behavior in free-living individuals.

## **Tables**

**Table 3.1: Participant Characteristics (mean ± SD)**

| *N = 7* | |
|---|---|
| Age *(yrs.)* | 25.0 ± 4.9 |
| Body Mass *(kg)* | 71.0 ± 14.5 |
| Waist Circumference *(cm)* | 76.3 ± 7.9 |
| Height *(cm)* | 171.3 ± 9.2 |
| BMI *($kg \cdot m^{-2}$)* | 24.0 ± 2.4 |
| PAS | 6.4 ± 0.5 |

BMI=Body Mass Index, PAS=Physical Activity Status

**Table 3.2: Lab-nnet, Soj-1x and Soj-3x compared to direct observation (DO) (mean (95% CI)) Continued onto next page.**

| *N=18* | DO | Lab-Nnet | Soj-1X | Soj-3X |
|---|---|---|---|---|
| MET-Hours | 16.0 (14.8-17.3) | 21.4 (20.1-22.7) | 16.4 (15.1-17.7) | 16.5 (14.9-18.1) |
| *Bias* | - | 5.4 (4.6-6.2) | 0.3 (-0.2-0.9)+ | 0.5 (-0.1-1.1)+ |
| *rMSE* | - | 5.4 (4.6-6.2) | 1.0 (0.6-1.3) | 1.1 (0.7-1.5) |
| *Correlation* | - | 0.79 (0.53-0.92)* | 0.91 (0.76-0.97)* | 0.93 (0.82-0.97)* |
| Sedentary Minutes | 346.1 (304.9-387.3) | 317.6 (283.2-351.9) | 376.4 (341.7-411.1) | 361.4 (328.9-393.9) |
| *Bias* | - | -28.5 (-59.6- 2.6)+ | 30.3 (3.9-56.7) | 15.3 (-2.1-32.8)+ |
| *rMSE* | - | 53.7 (31.4-76.0) | 50.1 (31.7-68.5) | 26.2 (12.0-40.4) |
| *Correlation* | - | 0.68 (0.30-0.87)* | 0.77 (0.47-0.91)* | 0.91 (0.78-0.97)* |
| Light Minutes | 161.0 (123.4-198.6) | 147.8 (118.2-177.4) | 131.3 (95.2-167.4) | 144.0 (108.6-179.3) |
| *Bias* | - | -13.2 (-46.0-19.6)+ | -29.7 (-56.0--3.4) | -17.0 (-36.3-2.2)+ |
| *rMSE* | - | 55.0 (34.2-75.8) | 49.7 (31.5-68.0) | 27.6 (11.4-43.8) |
| *Correlation* | - | 0.55 (0.12-0.81)* | 0.75 (0.43-0.90)* | 0.86 (0.66-0.95)* |
| Moderate Minutes | 45.7 (33.1-58.3) | 85.2 (71.2-99.2) | 36.8 (26.0-47.6) | 37.3 (24.9-49.7) |
| *Bias* | - | 39.4 (27.1-51.7) | -8.9 (-14.3--3.6) | -8.5 (-16.9-0.0)+ |
| *rMSE* | - | 39.5 (27.2-51.8) | 11.7 (7.7-15.6) | 15.9 (10.4-21.5) |
| *Correlation* | - | 0.58 (0.15-0.82)* | 0.91 (0.77-0.97)* | 0.77 (0.47-0.91)* |
| Vigorous Minutes | 14.6 (5.8-23.3) | 20.7 (13.2-28.1) | 23.0 (15.7-30.2) | 24.8 (15.0-34.6) |
| *Bias* | - | 6.0 (0.7-11.4) | 8.4 (3.1-13.6) | 10.2 (0.7-19.6) |
| *rMSE* | - | 10.2 (6.5-13.8) | 10.8 (6.8-14.8) | 14.4 (6.3-22.5) |
| *Correlation* | - | 0.80 (0.53-0.92)* | 0.80 (0.54-0.92)* | 0.49 (0.04-0.78)* |
| MVPA Minutes | 60.4 (46.8-73.9) | 105.8 (89.3-122.4) | 59.8 (46.4-73.1) | 62.1 (45.9-78.2) |
| *Bias* | - | 45.5 (32.2-58.8) | -0.6 (-3.3-2.2)+ | 1.7 (-3.6-7.0)+ |
| *rMSE* | - | 45.5 (32.2-58.8) | 4.0 (2.1-5.9) | 7.8 (4.1-11.8) |
| *Correlation* | - | 0.63 (0.22-0.86)* | 0.98 (0.94-0.99)* | 0.95 (0.87- |

| | | | | |
|---|---|---|---|---|
| | | | | 0.98)* |
| Qualifying Minutes | 30.2 (15.9-44.5) | | 30.3 (15.9-44.7) | 37.1 (19.4-54.8) |
| *Bias* | - | - | 0.1 (¯1.5-1.7)+ | 6.9 (1.3-12.6) |
| *rMSE* | - | - | 1.4 (¯0.1-2.9) | 7.3 (1.7-12.8) |
| *Correlation* | - | - | 0.99 (0.98-1.00)* | 0.96 (0.89-0.99)* |
| Qualifying Bouts | 1.4 (0.8-2.0) | - | 1.3 (0.7-1.9) | 1.6 (1.0-2.2) |
| *Bias* | - | - | ¯0.1 (¯0.2-0.1)+ | 0.2 (0.0-0.5)+ |
| *rMSE* | - | - | 0.2 (0.0-0.3) | 0.3 (0.1-0.6) |
| *Correlation* | - | - | 0.95 (0.88-0.98)* | 0.92 (0.80-0.97)* |
| Breaks | 29.8 (23.0-36.5) | - | 39.3 (35.3-43.3) | 27.9 (21.8-34.0) |
| *Bias* | - | - | 9.5 (4.9-14.1) | -1.9 (¯5.6-1.8)+ |
| *rMSE* | - | - | 12.1 (9.1-15.0) | 6.1 (3.7-8.6) |
| *Correlation* | - | - | 0.75 (0.44-0.91)* | 0.84 (0.61-0.94)* |
| Break-Rate | 5.7 (4.0-7.4) | - | 6.6 (5.5-7.7) | 5.1 (3.6-6.6) |
| *Bias* | - | - | 0.9 (0.2-1.6) | ¯0.6 (¯1.3-0.1)+ |
| *rMSE* | - | - | 1.6 (1.1-2.0) | 1.2 (0.8-1.7) |
| *Correlation* | - | - | 0.96 (0.89-0.98)* | 0.92 (0.80-0.97)* |

*N=number of observations. +Not significantly different from DO. *Significant correlations*

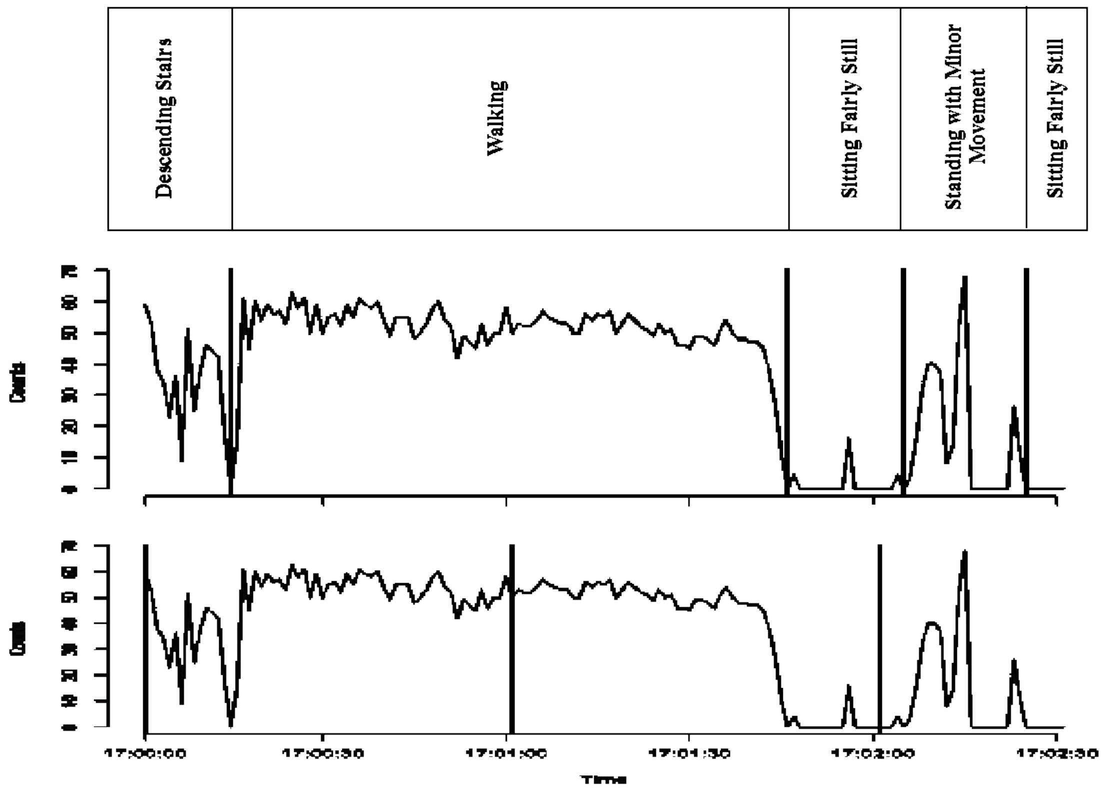


**Figure 3.1: Challenge of measuring free-living physical activity and sedentary behavior**

Bottom and middle panels show 2-min 30-sec of second-by-second counts from the vertical acceleration signal. Top panel shows observer-identified activities. Using the lab-nnet and simple regression approaches the five distinct activities are grouped into minute intervals (bottom panel), resulting in inaccurate MET estimates. In free-living environments it may be more appropriate to identify where bouts of activity start and stop (middle panel) and estimate METs for specific activity bouts.

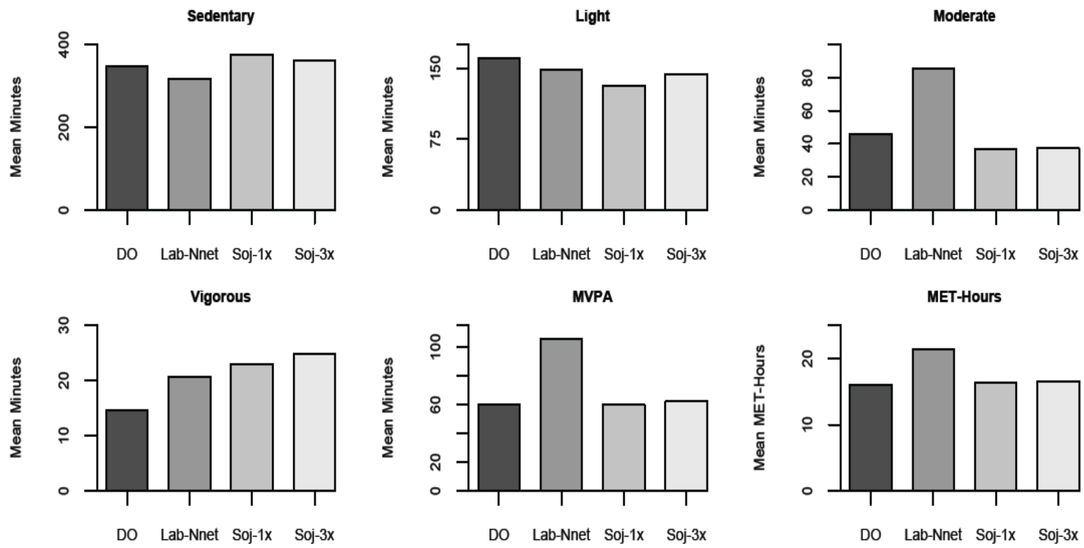


**Figure 3.2: Direct observation, Lab-Nnet, Soj-1x and Soj-3x estimates of time spent in categories of intensity**

Mean estimates of time spent in categories of intensity from direct observation (DO), lab neural network (Lab-nnet), sojourn 1-axis (Soj-1x), sojourn 3-axes (Soj-3x).

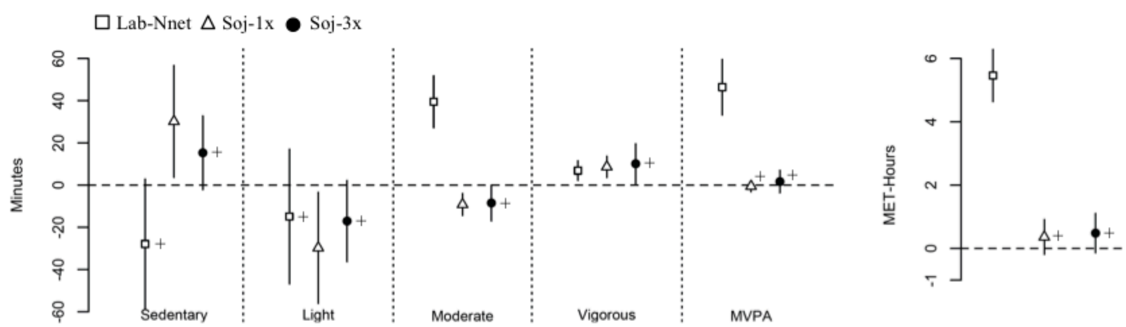


**Figure 3.3: Bias of Lab-Nnet, Soj-1x and Soj-3x estimates of time spent in categories of intensities and MET-hours**

Bias of the Lab-Nnet, Soj-1x and Soj-3x estimates of minutes spent in categories of intensity and MET-Hours. Error bars = 95% CI of the bias and represent the precision of the estimate. + Not significantly different than direct observation.

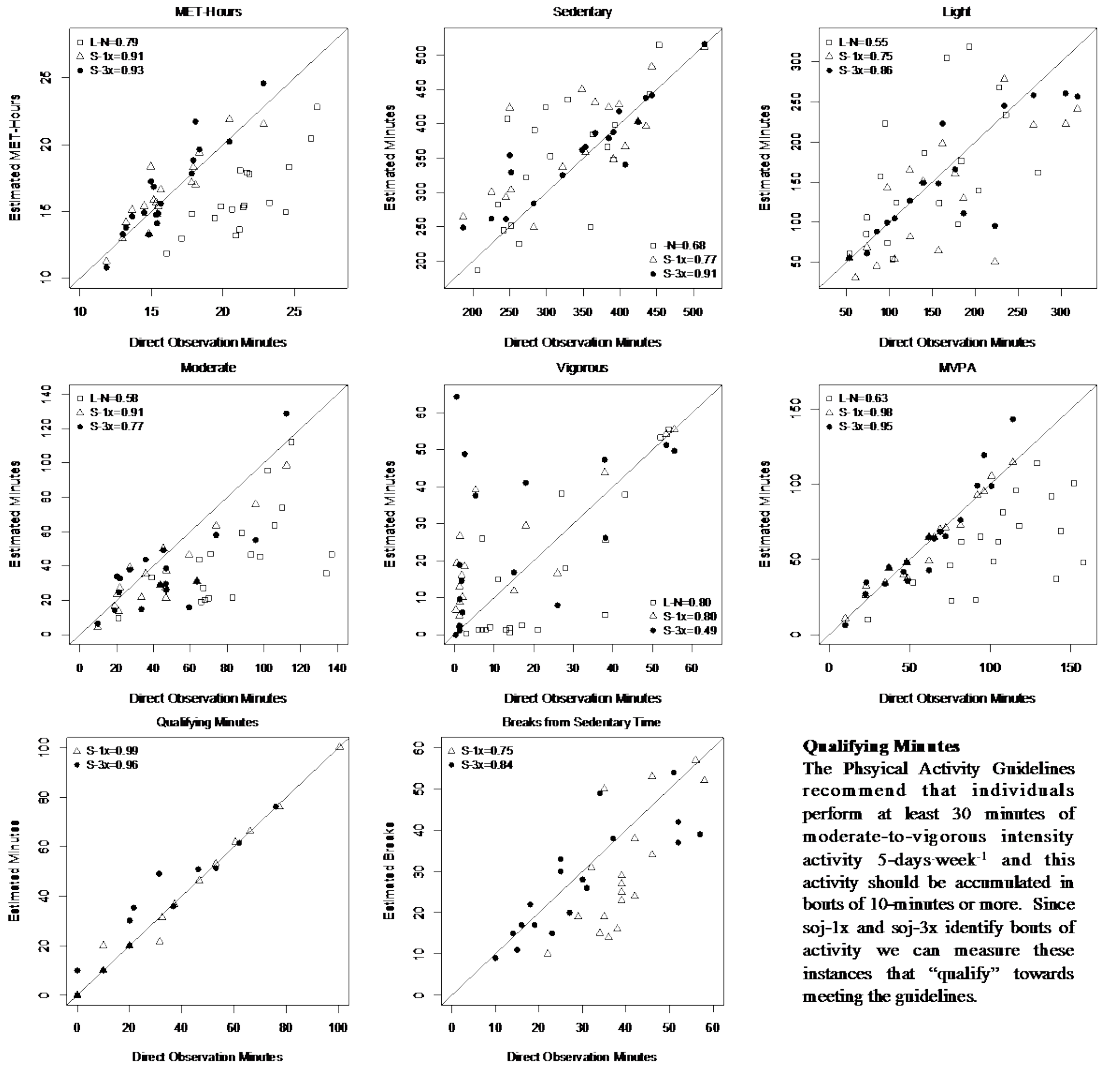


**Figure 3.4: Lab-Nnet, Soj-1x and Soj-3x estimates for each participant**

Model estimates for each participant compared to direct observation. The closer the point falls to the line of identity, the closer the estimate is to direct observation. The correlations between model estimates and direct observation are presented.

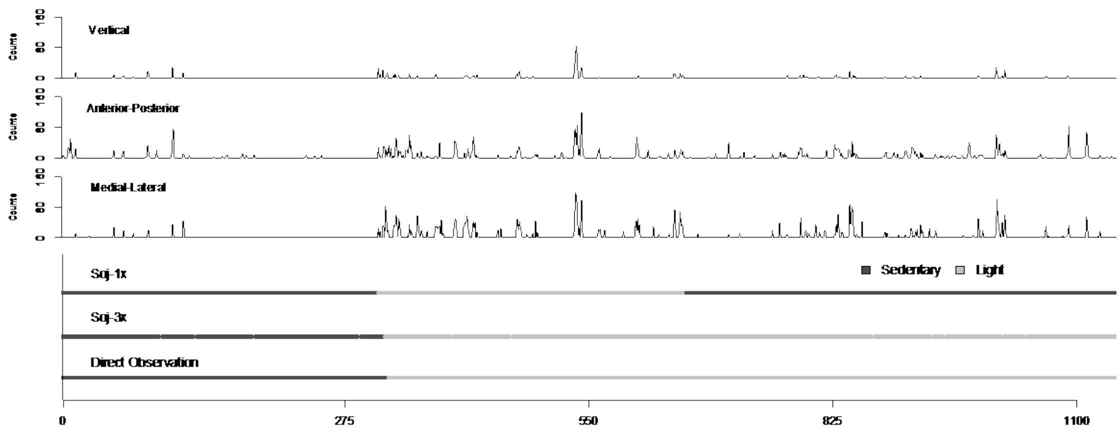


**Figure 3.5: Second-by-second counts from vertical, anterior-posterior and medial-later axes (top). Corresponding Soj-1x and Soj-3x estimates compared to direct observation (bottom)**

Top: Second-by-second acceleration signal from the vertical, anterior-posterior and medial-lateral axes for ~20 minutes of observation time from one participant. Bottom: Corresponding soj-1x and soj-3x estimates of sedentary and light intensity time compared to direct observation. These data illustrate an example of when the additional information from the anterior-posterior and medial-lateral axes help soj-3x correctly identify light intensity activity where soj-1x inaccurately estimates this activity as sedentary using information from the vertical axes alone.

# CHAPTER IV

# SENSITIVITY OF THE SOJOURN METHOD TO DETECT CHANGE IN FREE-LIVING HABITUAL ACTIVITY

## Introduction

The sojourn method is a data processing technique used to estimate free-living physical activity (PA) and sedentary behavior (SB) from a single ActiGraph accelerometer. It is a hybrid machine-learning approach that combines artificial neural networks with decision tree analyses to estimate METs. By combining *a priori* knowledge on human behavior with the flexible non-parametric properties of a neural network, the sojourn method is well suited to estimate METs from free-living accelerometer output. We have developed two versions of the sojourn method: sojourn 1-axis and sojourn 3-axes. As their names imply, sojourn 1-axis (soj-1x) uses information from one axis (vertical), while sojourn 3-axis (soj-3x) uses information from three axes (vertical, anterior-posterior and medial-lateral). Both methods use simple parameters from the acceleration signal and follow a three step progression: 1) identification of bouts of activity and inactivity, 2) assignment of non-physical activity MET values to inactivity bouts and 3) application of the original lab-nnet to estimate METs for activity bouts (Appendix A).

Since 1998 and the original "Freedson cut-points" (32) accelerometers have been popular tools to estimate physical activity in free-living environments. Advances in miniaturized sensing technology allow for the collection and storage of much more data than originally possible. Consequently, researchers are actively exploring the use of sophisticated machine-learning techniques to improve activity estimation (66, 85).

Several groups have demonstrated success in using hidden Markov models (HMM) (66, 84), support vector machines (36, 114), decision trees (4, 12, 36, 68, 114), instance-based learning (ILB) (4), naïve Bayes (4, 114), and artificial neural networks (21, 28, 36, 86, 114). Existing methods however, have yet to realize their potential in measuring activity under free-living conditions and suffer from practical limitations including, multi-sensor systems that are expensive and not feasible to be worn for extended periods of time under free-living conditions.

Soj-1x and soj-3x address some of these limitations by using a single commercially available accelerometer and supervised training data collected under natural free-living conditions. This approach produces more accurate estimates of important free-living activity and inactivity variables (Chapter III). We note that we use the terms "free-living" and "natural" to mean activities were not prescribed and participants were free to perform any activity within their own environment (e.g. home, work, school etc.). Two recent studies indicate soj-1x and soj-3x produce valid estimates of MET-hours per day, time spent in categories of intensity, qualifying minutes and break-rate ((96), Chapter III). Compared to a criterion of direct observation (DO), these estimates were more accurate than two traditional regression approaches (20, 32) and a neural network developed in the laboratory (97) (Chapter III, (96)).

The next step in developing soj-1x and soj-3x was to determine their sensitivity to detect change in habitual activity. Practically, these data are important for assessing change in an individual consequent to an intervention. A valid tool will detect true change when it has occurred and will remain stable when it has not. Therefore the purpose of this study was to evaluate the sensitivity of soj-1x and soj-3x to detect change in habitual activity within an individual. Specifically, we evaluated the sensitivity of soj-1x and soj-3x to detect change in MET-hours per day, time in categories of intensity, qualifying minutes, qualifying bouts, number of breaks and break-rate, when applied to three, seven day free-living conditions: Sedentary, Moderately Active and Very Active.

## Methods

### Recruitment and Eligibility

Thirteen participants were recruited from the Amherst, Massachusetts area. Participants were between the ages of 18-60 years, in good physical health (no diagnosed cardiovascular, pulmonary, metabolic, joint, or chronic diseases), currently participating in at least 150 minutes of moderate activity per week and were *not* employed in an occupation that required sustained moderate intensity activity (e.g. mail carrier, retail, construction). These criteria were set in order to ensure participants could safely complete the conditions described below. All participants completed an informed consent document approved by the University of Massachusetts Institutional Review Board and a health history questionnaire.

### Baseline Visit

Participants reported to the Physical Activity and Health Laboratory following at least a 12-hour overnight fast. Using a standard floor stadiometer and physicians' scale (Detecto; Webb City, MO), height and weight were measured to the nearest 0.25 cm and 0.1 kg, respectively.

To help determine eligibility participants also completed a short survey asking about their current physical activity status (PAS). Participants were asked to choose a number which best described their activity in a normal week. Possible responses range from 0 to 7 with 0 corresponding to “avoided walking or exertion (e.g. always used the elevator, drove whenever possible instead of walking)”, and 7 corresponding to “ran more than 10 miles per week or spent over 3 hours per week in comparable physical activity”. Eligible participants reported a PAS of at least 5 (ran 1-5 miles per week or spent 30-60 minutes in comparable physical activity).

### Experimental Procedures

Each participant completed three, seven day conditions: sedentary, moderately active and very active. Conditions were based on the current Physical Activity Guidelines recommendation of 150 minutes per week of at least moderate intensity activity and were designed to represent three distinct behavior patterns important in surveillance research (16).

#### Sedentary Condition

The sedentary condition represented people who are nearly entirely sedentary and perform minimal activity beyond baseline activities of daily living (16). Participants were prohibited from participating in structured, occupational or leisure time exercise, and were instructed to limit their time standing/walking.

#### Moderately Active

The moderately active condition represented people sufficiently meeting the physical activity guidelines, such as activity levels subsequent to an exercise intervention study. During this condition participants were prescribed 150-200 minutes of structured/purposeful moderate intensity activity or 75-100 minutes of vigorous intensity activity (16). Participants were instructed not to alter their lifestyle activity outside of the prescribed exercise.

**<u>Very Active</u>**

The very active condition represented people who perform at least twice as much activity as prescribed by the physical activity guidelines. During this condition participants were prescribed at least 300 minutes of structured/purposeful moderate intensity activity or 150 minutes of vigorous intensity activity (16). Participants were required to accumulate the prescribed activity by performing at least 60 minutes of structured/purposeful exercise on at least 5 of the 7 days of the condition. Participants were also asked to limit their time sitting and to increase their lifestyle activity. In general, participants were encouraged to be as active as possible during this condition and there was no upper limit to the amount of activity participants could perform.

## Measurements

**<u>Primary Outcome Measure</u>**

During each condition participants wore an ActiGraph GT3X (ActiGraph LLC, Pensacola, Florida) on their right hip for at least ten hours per day. The device was set to collect acceleration in the vertical, anterior-posterior and medial-lateral planes and in one-second epochs. Output from the ActiGraph was processed using soj-1x and soj-3x and estimates of MET-hours, time in categories of intensity, qualifying minutes, qualifying bouts, number of breaks and break-rate were produced (described below).

**Ancillary Measures**

Several ancillary measures were used to verify compliance to the condition requirements (e.g. participants actually were sedentary during the sedentary condition) and to help facilitate participants own self-monitoring of their compliance.

1. *Direct Observation: The Observer XT* (Noldus Information Technology, Netherlands). Once during each condition participants were directly observed in their free-living environment for approximately ten consecutive hours. Using a hand-held personal digital assistant (PDA) (Noldus Information Technology; Netherlands) with focal sampling and duration coding a trained observer recorded the participant's behavior (103). Every time body position changed (e.g. went from sitting to standing) the observer recorded the activity type and intensity (METs) in the PDA. Each entry was time stamped and the length of each activity bout was automatically recorded by the PDA. During the ten hour observation time, subjects were allowed to have "private time" when needed. Reasons for "private time" included behaviors such as using the restroom and changing clothes. During these activities, the observer coded "private" on the PDA. Behavior coded as "private" by the observer along with the corresponding ActiGraph data were eliminated from analyses.

   Observers worked in 2-4 hour shifts and a total of three different observers completed all of the observation sessions. Observers completed extensive verbal, written and video training and testing before observing participants in a free-living environment. The training material focused on a specific protocol to avoid disrupting free-living behavior and to accurately record activity type and intensity. When training was complete, each observer was tested using a ~15 minute video of free-living behavior. The video was first coded by a group of experienced observers and study observer responses were compared to the experienced observers' responses using a Cohen's kappa coefficient ($\kappa$). In order to be considered "in agreement", study observers were required to correctly identify both the activity type and intensity. There was a very high level of agreement between the study observers' responses and the experienced observers' (mean $\kappa = 0.92$).

Direct observation is the gold standard method to identify activity type in free-living environments (5). Additionally, our DO method has been validated to estimate intensity compared to indirect calorimetry. These unpublished data are presented in Appendix B and indicate DO is an accurate and precise method to identify MET-hours, and time spent in categories of intensity.

2. *The activPAL* (PAL Technologies, Glasgow, Scotland). During each condition participants wore an activPAL activity monitor on the midline of the thigh, one-third of the way between the hip and knee. Using information about the position of the thigh, the activPAL estimates time spent lying, sitting and standing. When the wearer is in the standing position, the activPAL also records number and frequency of steps. During unconstrained conditions, the activPAL is reportedly accurate 93.6% of the time (35).
3. *Omron Pedometer* (Omron Healthcare Group, Kyoto, Japan) – During each condition participants wore an Omron pedometer to help facilitate compliance with the condition requirements. This device is valid for measuring steps per day

(91) and has been used to provide referent goals for individuals to meet activity guidelines (107). The Omron provides information on steps per day in real time, thus it is useful in providing an easy to interpret, tangible goal for participants to self-monitor their activity. Participants were given daily step goals for each condition: sedentary < 5,000 steps per day, moderately active 8,000-10,000 steps per day and very active >12,000. These goals were based on cut-points empirically established to relate steps per day to activity levels (107).

**Data Cleaning and Reduction**

ActiGraph data were downloaded and exported to text files using *ActiLife 5.0* (ActiGraph LLC, Pensacola, Florida) and all data cleaning and processing was done using the statistics package and computing language *R* (101). Wear time was determined from detailed monitor logs that participants completed daily. Participants recorded the time they put the monitors on in the morning and the time they removed them at night. Participants also recorded anytime they removed the monitors during the day and the reason why they removed them (e.g. shower). At least ten hours of ActiGraph data were required for a day to be considered valid and at least four valid days (including one weekend day) were required for a week to be considered valid (71, 106). Valid data were processed using soj-1x and soj-3x to produce estimates of MET-hours per day, time in categories of intensity (sedentary < 1.5 METs, light 1.5-2.99 METs, moderate 3-5.99 METs, vigorous ≥ 6 METs and moderate-to-vigorous (MVPA) ≥ 3 METs), minutes in bouts of activity that qualify towards meeting the physical activity guidelines (qualifying minutes), the number of these bouts (qualifying bouts), the absolute number of breaks from sedentary time and the rate of breaks per sedentary hour (break-rate). "Qualifying" minutes are defined as moderate-to-vigorous intensity activity that last at least ten consecutive minutes.

### Statistical Evaluation

To evaluate the sensitivity of soj-1x and soj-3x to detect change in habitual activity variables a repeated measures linear mixed model with likelihood ratio testing was used. We made these comparisons between the three conditions: sedentary-moderately active, sedentary-very active and moderately active-very active. The likelihood ratio test examined if the addition of condition as an independent variable resulted in a significantly better fit ($p<0.05$). If it did not, the variability in the estimate was too large to detect the change within subjects. Although we expected variability both across days for a participant and between participants within a given condition, this approach assumes participants were overall compliant with condition requirements and that there was a meaningful change between conditions. To support these assumptions we present descriptive data for each individual that 1) compare the estimated change between conditions from soj-1x and soj-3x to the estimated change from the activPAL and 2) compare soj-1x and soj-3x estimates to ten hours of direct observation per condition. For these comparisons we use select activity and inactivity variables important to physical activity surveillance and intervention studies.

## Results

Thirteen participants completed three, seven day conditions (39 observations). Participant characteristics (mean ± SD) are reported in Table 4.1. Due to researcher error during device initialization (e.g. device was set to collect data in 1-axis instead of 3-axes) and general device malfunction (e.g. data would not download), data from four observations were eliminated (one from the sedentary condition, two from the moderately active condition and one from the very active condition). This resulted in ten sedentary-moderately active comparisons, eleven sedentary-very active comparisons, and ten moderately active-very active comparisons. Mean (95% confidence interval [CI]) monitor wear time was similar for each condition: sedentary = 13.1 hours (12.7-13.6), moderately active = 13.4 (13.0-13.8), very active = 13.8 (13.4-14.2) (Table 4.2).

Table 4.2 and Figure 4.1 compare activity and inactivity variables (mean (95% CI) for each condition. Soj-1x and soj-3x detected a significant change between conditions in MET-hours per day, qualifying minutes and percent of time spent in categories of intensity, except for light intensity activity, where soj-1x detected no change between sedentary-moderately active and soj-3x detected no change between any conditions. Both methods detected no change in number of breaks between any conditions, and a change in break-rate between sedentary-very active and moderately active-very active, but no change between sedentary-moderately active.

Figure 4.2 compares estimated change in MVPA (top panel) and percent time sedentary (bottom panel) from soj-1x, soj-3x and the activPAL for each participant. In general, soj-1x and soj-3x estimates of change were very similar to the activPAL. According to the activPAL mean (95% CI) increase in MVPA between sedentary-moderately active was 39.1 min (34.2-44.1), compared to 45.0 (37.2-52.8) and 44.4 min (37.1-51.7) for soj-1x and soj-3x, respectively. According to the activPAL mean (95% CI) increase in MVPA between moderately active-very active was 45.4 (28.8-61.9), compared to 43.9 (19.1-68.6) and 43.9 (19.1-68.6) for soj-1x and soj-3x, respectively. According to the activPAL mean (95% CI) decrease in percent time sedentary between sedentary-moderately active was -7.3% (-10.2--4.5), compared to -3.5% (-8.7-1.8) and -4.7% (-9.7-0.3) for soj-1x and soj-3x, respectively. According to the activPAL mean (95% CI) decrease in percent time sedentary between moderately active-very active was -11.9% (-19.1--4.8), compared to -7.5% (-12.6--2.3) and -6.9% (-11.7--2.0) for soj-1x and soj-3x, respectively. Figure 4.3 compares estimated MET-hours (points) to direct observation (bars). During the ten hour observations, ten of thirteen participants increased MET-hours from sedentary to moderately active to very active as intended by the study design. Both soj-1x and soj-3x correctly identified 90% (9 of 10) of these instances. Three participants (1, 4 and 10) did not increase MET-hours as expected. Soj-1x identified 66.7% (2 of 3) of these instances, while soj-3x identified 100% of these instances.

## Discussion

This study demonstrated that two novel machine-learning methods specifically designed for use in free-living people are sensitive to changes in habitual activity. Using a single hip mounted accelerometer, soj-1x and soj-3x precisely measured important activity and inactivity variables during three distinct free-living conditions (sedentary, moderately active and very active) and successfully detected intra-individual changes between conditions. This study provides important evidence that soj-1x and soj-3x can be applied in free-living environments to identify distinct habitual activity levels important in surveillance research and to identify intra-individual changes consequent to an intervention.

The current Physical Activity Guidelines recommend at least 150 minutes per week of moderate or 75 minutes of vigorous intensity activity for health (16). It is also recommended that this activity be achieved in bouts lasting at least ten consecutive minutes (16). In this study the prescribed conditions were designed to represent individuals not meeting the guidelines (sedentary), individuals sufficiently meeting the guidelines (moderately active), and individuals performing at least twice the recommended activity (≥ 300 minutes of moderate intensity activity per week) (very active). Physical activity researchers most often classify an individual into one of these categories using estimates of MET-hours or time spent in moderate-to-vigorous intensity activity (MVPA) (16, 45, 106). In this study both methods detected increases in MET-hours per day and time spent in MVPA between sedentary-moderately active, sedentary-very active and moderately active-very active (Table 4.2, Figure 4.1).

Unique features of the soj-1x and soj-3x algorithms are the identification of where bouts of activity and inactivity start and stop and the estimate of the duration of these bouts (Appendix A). This information can be used to provide more detailed measures of behavior such as qualifying minutes, qualifying bouts, breaks from sedentary time and break-rate. Qualifying minutes are minutes in bouts of activity that qualify towards meeting the physical activity guidelines (MVPA that lasts at least ten consecutive minutes). This type of activity has been linked to health benefits (16) and thus may be a more appropriate metric to evaluate an individual's habitual activity level. Importantly, soj-1x and soj-3x detected increases in qualifying minutes between sedentary-moderately active, sedentary-very active and moderately active-very active (Table 4.2, Figure 4.1). Break-rate (breaks$\cdot$sed-hour$^{-1}$) did not change according to both soj-1x and soj-3x between sedentary-moderately active, but did change between sedentary-very active and moderately active-very active. Thus, although percent sedentary time significantly decreased between both sedentary-moderately active and moderately active-very active (Table 4.2, Figure 4.1), these data indicate bouts of sedentary time were accumulated similarly during the sedentary and moderately active conditions. This was not surprising given that during the sedentary and moderately active conditions individuals were given no instructions regarding breaking-up sedentary time, while during the very active condition participants were instructed to not only reduce, but to break-up sedentary time as much as possible.

A valid tool will detect meaningful change when it has occurred and will remain stable when no change has occurred. This study was designed to evaluate sensitivity to meaningful change and we expected true change in habitual activity variables between conditions. However, we also expected variability both across days for a participant and between participants within a given condition. Direct observation and activPAL data from each condition support these expectations. Figure 4.2 shows that soj-1x and soj-3x estimates of change in MVPA and percent time sedentary were very similar to the activPAL, which has been shown to accurately estimate MVPA and sedentary time in free-living individuals (59, 80). These descriptive data suggest two things: 1) participants were compliant with condition requirements and 2) soj-1x and soj-3x were sensitive to changes on an individual level. Similarly, although we expected MET-hours to increase from sedentary to moderately active to very active, Figure 4.3 shows within and between participant variability in MET-hours identified by direct observation (bars). These data illustrate soj-1x (top panel) and soj-3x's (bottom panel) success in detecting the expected increase in MET-hours (soj-1-x and soj-3x: nine out of ten participants (90% agreement with DO) and their success in recognizing instances that did not follow this trend (soj-1x:

two out of three participants (66.7% agreement with DO), soj-3x: three out of three participants (100% agreement with DO). We note that in some instances estimates between conditions were very similar (e.g. participant 10) and defining relevant change will ultimately depend on the application.

We also note the precision of soj-1x and soj-3x. Figures 4.2 and 4.3 suggest both methods are not only accurate, but also precise. Precision is the inverse of variance and provides information about the size of the random error of the prediction. By definition random error is unpredictable and has implications for how well a tool can detect change between conditions. The small errors observed when soj-1x and soj-3x were compared to the activPAL and DO are generally similar across participants (Figures 4.2 and 4.3). Practically this means when used in an intervention, both methods will be sensitive to detecting a true increase or decrease in activity. It is likely that the precision of most accelerometer-based measurement tools will decrease as participants increase the range of activity types performed. This is supported by many laboratory-based calibrations where measurement errors are influenced by activity type (18, 19, 63, 87) and illustrated in the current study by participant five. During the very active condition, participant five performed large amounts (~3 hrs.) of road cycling on several days of the condition. Wearable acceleration sensors typically do not perform well for cycling (18, 21, 97) and no other participant performed a similar activity; thus the large disparate error for participant five during the very active condition (Figures 4.2 and 4.3). This means if a participant performs new activities consequent to an intervention (e.g. cycling), the precision of the estimate could be affected, leading to challenges in detecting true change.

## Strengths and Limitations

This study has several important strengths. First, soj-1x and soj-3x were evaluated under free-living conditions. It is well accepted that performance in the laboratory does not translate to free-living people and best practice recommendations consistently highlight the need for free-living evaluations (5, 30, 36, 53). Second, we evaluated performance of soj-1x and soj-3x to detect three distinct habitual activity levels important in physical activity surveillance and intervention research. This was done during seven day conditions, the typical time frame for objective physical activity assessment. And lastly, we used direct observation and the activPAL to provide insight into algorithm performance and to confirm compliance to condition requirements. Direct observation is a gold standard criterion used in free-living validations (5) and the activPAL has been validated numerous times under both laboratory and free-living conditions (34, 35, 58, 64, 88).

The main limitation of this study was our homogenous sample. Participants were relatively young and lean: mean (± SD) age = 24.8 (5.2) years and BMI = 23.8 (1.9) $kg \cdot m^{-2}$. Future evaluations would benefit from a more diverse sample (e.g. older individuals) that performs a wider range of activity types. Although this study had thirteen participants, we do not consider sample size a major limitation. Three distinct conditions were performed for seven days and mean wear-time for each condition was approximately 13-hours. This resulted in > 1000 hours of free-living monitor data. A second limitation of this study is that within the study design we were not able to robustly assess soj-1x and soj-3x's specificity to change: their stability when no change has occurred. To address this, future studies would benefit from having a group that changes behavior and a group that does not.

## Summary and Conclusions

It has previously been shown that soj-1x and soj-3x produce more accurate estimates of physical activity and sedentary behavior than methods developed in the laboratory (Chapter III). This study provides further evidence that soj-1x and soj-3x can be applied in free-living environments to accurately assess PA and SB and to detect change in these behaviors. Several groups have demonstrated success in using machine-learning approaches to process output from body worn accelerometers (66, 67, 85), however to our knowledge this is the first study to evaluate sensitivity to change. It is noteworthy that using just one-hip mounted sensor, soj-1x and soj-3x algorithms were not only sensitive to change in MET-hours and MVPA (measures typically used to distinguish habitual activity), but were also sensitive to change in sedentary time and the rate of breaks per sedentary hour. These results are very timely given the recent emphasis on understanding how sedentary behavior and breaks from sedentary time influence health (24, 25, 42, 44, 55, 105). As sedentary behavior research expands and investigations aim to understand how sedentary to vigorous intensity activity interact to influence health, it is very advantageous to have an accurate and precise data processing method that is valid in free-living conditions and requires information from only a *single* sensor.

## Tables

**Table 4.1: Participant Characteristics (mean ± SD)**

| *N = 13* | |
|---|---|
| Age *(yrs.)* | 24.8 ± 5.2 |
| Body Mass *(kg)* | 68.2 ± 13.1 |
| Height *(cm)* | 168.5 ± 10.6 |
| BMI *($kg \cdot m^{-2}$)* | 23.8 ± 1.9 |
| PAS | 6.4 ± 0.7 |

BMI=Body Mass Index, PAS=Physical Activity Status

**Table 4.2: Soj-1x and Soj-3x estimates of activity and inactivity variables by condition**

| | Soj-1X | | | Soj-3X | | |
|---|---|---|---|---|---|---|
| | Sedentary | Moderately Active | Very Active | Sedentary | Moderately Active | Very Active |
| Wear Time *(Hours)* | 13.1 (12.7-13.6) | 13.4 (13.0-13.8) | 13.8 (13.4-14.2) | 13.1 (12.7-13.6) | 13.4 (13.0-13.8) | 13.8 (13.4-14.2) |
| MET-Hours | 19.8 (19.0-20.7)+# | 22.7 (22.0-23.4)*# | 27.0 (25.8-28.2)*+ | 18.2 (17.7-18.8) | 22.3 (21.6-23.1) | 27.6 (26.4-28.7) |
| % Sedentary | 70.0 (67.8-72.3)+# | 64.9 (62.5-67.2)*# | 58.3 (56.2-60.4)*# | 70.4 (68.0-72.6)+# | 64.8 (62.6-67.0)*# | 58.8 (56.6-61.1)*+ |
| % Light | 23.4 (21.5-25.2)# | 24.8 (22.6-27.0)# | 27.3 (25.5-29.1)+* | 24.5 (22.4-26.6) | 25.2 (23.1-27.3) | 26.4 (24.5-28.2) |
| % Moderate | 4.4 (3.8-4.9)+# | 6.5 (5.9-7.0)*# | 8.1 (7.2-9.0)*+ | 4.0 (3.5-4.5)+# | 6.4 (5.7-7.0)*# | 9.1 (8.0-10.2)*+ |
| % Vigorous | 2.2 (1.8-2.6)+# | 3.9 (3.3-4.4)*# | 6.3 (5.4-7.2)*+ | 1.0 (0.8-1.2)+# | 3.6 (3.0-4.3)*# | 5.7 (4.9-6.6)*+ |
| MVPA *(Minutes)* | 52.0 (45.1-58.9)+# | 76.0 (86.4-54.8)*# | 106.4 (127.9-55.9)*+ | 39.1 (34.7-43.5)+# | 78.8 (73.0-84.5)*# | 121.8 (111.3-132.2)*+ |
| Qualifying Minutes | 10.8 (5.1-16.5)+# | 37.9 (32.7-43.1)*# | 70.8 (59.6-82.0)*+ | 6.1 (3.8-8.4)+# | 42.5 (36.9-48.1)*# | 82.8 (71.7-93.9)*+ |
| Qualifying Bouts | 0.6 (0.4-0.8)+# | 1.9 (1.6-2.2)* | 2.4 (2.0-2.8)* | 0.5 (0.3-0.7)+# | 2.2 (1.8-2.5)*# | 2.8 (2.4-3.2)+# |
| Breaks | 55.6 (52.9-58.3) | 54.8 (51.5-58.1) | 55.9 (53.3-58.6) | 38.5 (36.2-40.9) | 40.1 (37.2-42.9) | 41.0 (38.7-43.3) |
| Break-Rate *(Brks·Sed-Hr$^{-1}$)* | 6.2 (5.8-6.6)# | 6.6 (6.1-7.1)# | 7.3 (6.8-7.7)*+ | 4.5 (4.0-4.9)# | 4.9 (4.4-5.3)# | 5.4 (4.9-5.8)*+ |

*Ten sedentary-moderately active comparisons, eleven sedentary-very active comparisons, and ten moderately active-very active comparisons . * significantly different than sedentary, + significantly different than moderately active, # significantly different than very active*

# Figures

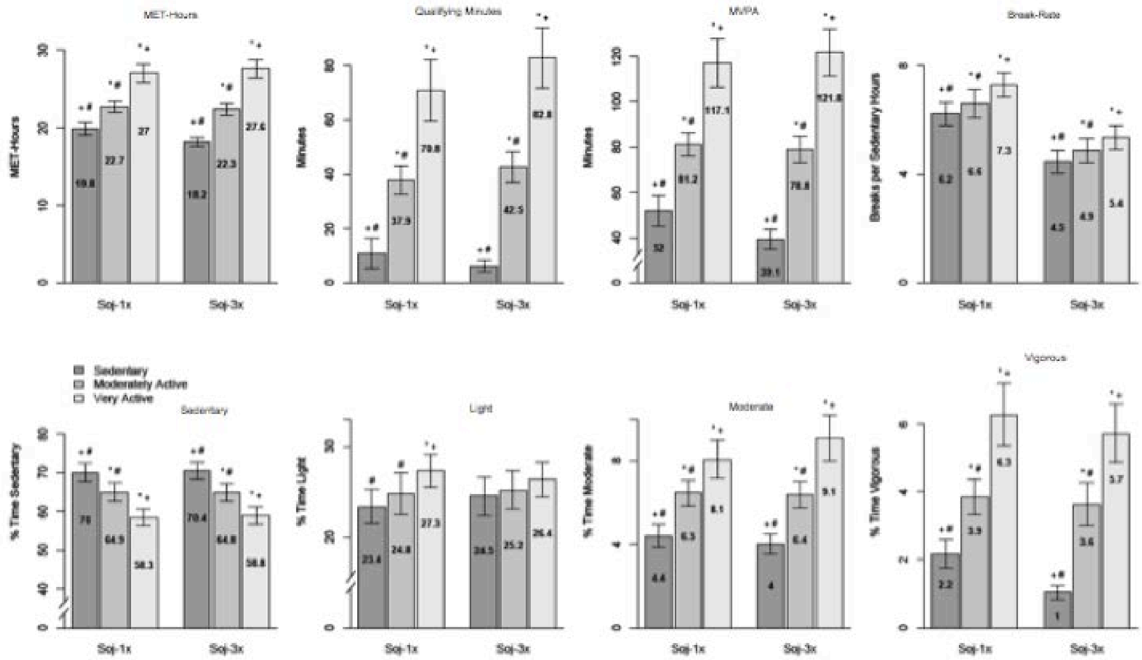


**Figure 4.1: Mean estimates from Soj-1x and Soj-3x for each condition**

Mean estimates from Soj-1x and Soj-3x for each condition. The errors bars are the 95% CI's of the estimate. * significantly different than sedentary, + significantly different than moderately active, # significantly different than very active: p<0.05.

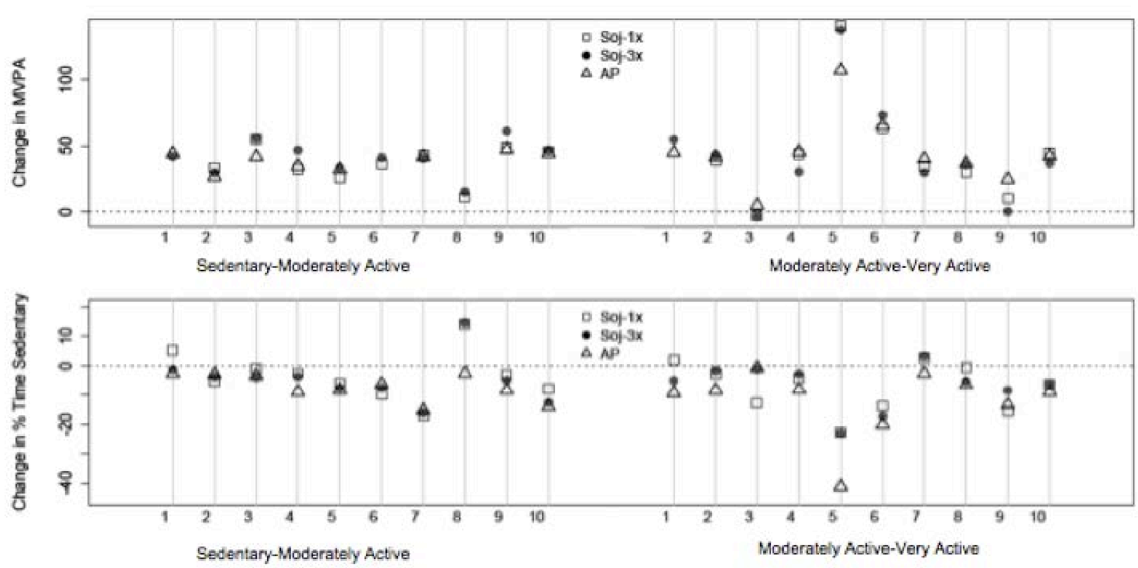


**Figure 4.2: Soj-1x and Soj-3x estimates of change compared to the activPAL**

Soj-1x and Soj-3x estimates of change compared to the activPAL for each participant. Participants with missing ActiGraph data were not included for clarity.

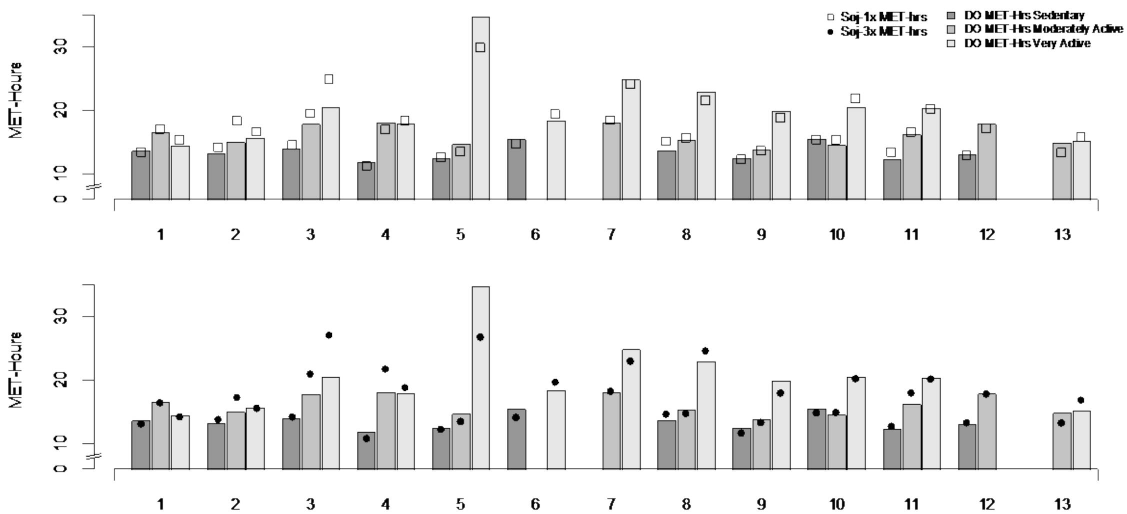


**Figure 4.3: Soj-1x and Soj-3x estimates of MET-hours compared to direct observation**

Soj-1x (top) and Soj-3x (bottom) estimates of MET-hours compared to direct observation (bars). Note participants 6,7,12 and 13 are each missing one observation.

# CHAPTER V

# METABOLIC RESPONSE TO SEVEN DAYS OF INCREASED SEDENTARY BEHAVIOR

## Introduction

Sedentary behaviors are defined as seated or reclining behaviors that require low levels of energy expenditure (e.g. < 1.5 METS) (81), and comprise 55 to 70% of waking hours (70). Habitual sedentary behavior (which will be referred to as inactivity) primarily consists of sitting/lying activities, with short intermittent bouts of light and intensity activity. Epidemiologic evidence indicates inactivity is associated with a host of poor health outcomes, including increased risk of obesity (49, 50), metabolic syndrome (26, 94), type 2 diabetes (50, 52), cardiovascular disease (27, 94), and premature mortality (24, 55, 105). Although these relationships have been predominantly established using self-reported surrogate measures of sedentary behaviors (e.g. TV viewing), investigations using objective measurements from accelerometers support these findings (41, 44, 45). In large nationally representative samples, Healy et al (41, 44, 45) report positive associations of inactivity with biomarkers of cardiovascular and metabolic risk and these relationships persist after controlling for important confounders including physical activity.

It has been suggested that sedentary behaviors stimulate and/or inhibit physiologic mechanisms responsible for regulating disease risk factors (e.g. high blood pressure, elevated triglycerides and cholesterol) (37, 38). However understanding the physiologic response to habitual inactivity has been challenging. In free-living environments sedentary behaviors are ubiquitous and spontaneous (71), making them very difficult to study in the laboratory. Traditionally, researchers have relied on bed-rest in humans and hind-limb immobilization in rodents. These studies indicate that insulin action (7, 74, 83, 92, 95, 98, 109, 112) and lipid metabolism (7, 112) negatively respond to sustained sedentary behaviors and speculate changes to insulin signaling, glucose transport, and lipoprotein lipase (LPL) activity may govern these consequences (7, 83, 98, 109, 112). Although these data offer insight into the specific physiologic responses elicited by extreme sedentary behaviors, their generalizability to more typical free-living settings is questionable. For example, breaks from sedentary behaviors may attenuate their negative effects. Additionally, surveillance and laboratory studies report reduced risk associations when sedentary behaviors are frequently interrupted and prolonged sedentary bouts are avoided (25, 42, 44).

Recent sedentary behavior research has expanded by exposing participants to short term experimental conditions more relevant to free-living sedentary pursuits (25, 98). In a controlled laboratory study, Dunstan et al (25) reported that short (2-min) light and moderate intensity interruptions in sedentary behaviors improve postprandial glucose and insulin levels compared to prolonged sedentary time. The sedentary conditions imposed in this study were comparable to work-place SB (e.g. sitting doing paperwork) and leisure time SB (e.g. sitting watching television) with scheduled light and moderate intensity interruptions (breaks), and thus are more directly applicable to public health. These data are limited however in that they examine the acute effects of a 1-day exposure to behaviors performed for a fixed frequency and length. The logical next step would be to obtain detailed estimates of active and sedentary behaviors during a longer intervention in free-living individuals. By precisely measuring changes in active and sedentary behavior dose these data would allow for the investigation into potentially important confounding relationships and interactions, and may expose new features of SB relevant to health.

Therefore, the purpose of this study was to investigate the metabolic response to seven days of increased free-living sedentary behavior in moderately active individuals. To do this we applied the newly developed soj-3x algorithm to obtain detailed estimates of active and sedentary behaviors from a single hip-mounted accelerometer and investigated the effects of increased SB on markers of cardiometabolic health.

## Methods

### Recruitment and Eligibility

Eleven participants (4 males, 7 females) were recruited from the Amherst, Massachusetts area. Participants were between 18-60 years of age and in good physical health (no diagnosed cardiovascular, pulmonary, metabolic, joint, or chronic diseases) and currently participating in at least 150 minutes of moderate intensity activity per week. All participants completed a health history questionnaire and an informed consent document approved by the University of Massachusetts Institutional Review Board.

### Baseline Visit

Participants reported to the Physical Activity and Health Laboratory following at least a 12-hour overnight fast. Using a standard floor stadiometer and physicians' scale (Detecto; Webb City, MO), height and weight were measured to the nearest 0.25 cm and 0.1 kg, respectively. Participants also completed a short survey asking about their current physical activity status (PAS). Participants were asked to choose a number which best described their activity in a normal week. Possible responses ranged from 0 to 7 with 0 corresponding to "avoided walking or exertion (e.g. always used the elevator, drove whenever possible instead of walking)", and 7 corresponding to "ran more than 10 miles per week or spent over 3 hours per week in comparable physical activity". To be eligible to continue, participants must have reported a 5 or greater on the PAS.

### Experimental Procedures

Participants completed two, seven day conditions. The first condition was an active condition in which participants were instructed to maintain their normal daily activity, including exercise. Within 24-hours of completing the active condition, participants began the seven day inactive condition. During this time participants were instructed to increase their sedentary time as much as possible, to limit their time standing and walking and to refrain from structured, leisure time or occupational physical activity. Participants were instructed to accumulate no more that 5000 $steps \cdot day^{-1}$ during the inactive condition and all participants wore an Omron pedometer to facilitate compliance. This device is valid for measuring steps per day (91) and has been used to provide referent goals for individuals to meet activity guidelines (107).

### Detailed Estimation of Active and Sedentary Behaviors

During each condition participants wore an ActiGraph GT3X (ActiGraph LLC, Pensacola, Florida) on their right hip for at least ten hours per day. The device was set to collect accelerations in the vertical, anterior-posterior and medial-lateral planes in one-second epochs. Output from the ActiGraph was processed using the soj-3x algorithm to estimate MET-hours, time in categories of intensity (sedentary < 1.5 METs, light 1.5-2.99 METs, moderate 3-5.99 METs, vigorous ≥ 6 METs and moderate-to-vigorous (MVPA) ≥ 3 METs), qualifying minutes, qualifying bouts, number of breaks and break-rate. Qualifying minutes are minutes in bouts of activity that qualify for meeting the physical activity guidelines and are defined as moderate-to-vigorous intensity activity that last at least ten consecutive minutes. Qualifying bouts are the number of these bouts. Number of breaks is the absolute number of breaks from sedentary time and break-rate is the rate of breaks per sedentary hour.

The soj-3x algorithm is a machine-learning approach that was specifically developed for use in free-living people. By identifying when bouts of activity and inactivity start and stop, soj-3x has been shown to produce accurate and precise measures of free-living behavior (Chapters III and IV). For a detailed description of the soj-3x algorithm and its validation see Appendix A and Chapter III and IV, respectively.

### Markers of Cardiometabolic Health

#### Oral Glucose Tolerance Test

On the morning following the seventh day of each condition participants reported to the laboratory following a 12-hour overnight fast. A catheter was inserted into a forearm vein, fasting blood samples were taken followed by a standard 2-hour oral glucose tolerance test (OGTT). Subjects ingested 75g of glucose (Sun Dex, Fisher Healthcare, Houston, TX) within 5 minutes, and blood samples were collected every 30 minutes for the next 2 hours. Samples were centrifuged immediately at (3,000 x g) for 15 minutes and plasma was aliquotted into polystyrene tubes and stored at -80°C until analysis.

a. *Insulin Action.* Glucose and insulin concentrations were measured at five time points (0, 30, 60, 90 and 120 minutes). Plasma insulin concentrations were determined using a radioimmunoassay kit (Millipore Corporation; Chicago, IL) specific for human insulin. Plasma glucose concentrations were determined using the glucose oxidase method (GL5 Analox Analyzer [Analox Instruments, Lunenberg, MA]). Insulin sensitivity was calculated using the whole body insulin sensitivity index (10,000/square root of [fasting glucose x fasting insulin] x [mean glucose x mean insulin during OGTT]) established by Matsuda and DeFronza (composite-insulin sensitivity index (C-ISI)) (69). C-ISI represents a composite of hepatic and peripheral tissues and considers insulin sensitivity in the basal state and after a carbohydrate load. C-ISI is strongly correlated (r=0.73) with the direct measure of peripheral insulin sensitivity derived from the hyperinsulinemic-euglycemic clamp (69). Areas under the glucose and insulin curves were also calculated using the trapezoidal method.

b. *Fasting Lipids.* Fasting plasma was collected in sterile syringes and transferred to vacutainers for triglyceride (TG) and cholesterol (total, HDL, LDL) concentration analysis. Plasma triglyceride concentration was determined using an enzymatic colorimetric assay kit (Sigma Chemical, St. Louis, MO), and total cholesterol and HDL concentrations were determined using the cholesterol oxidase method (Analox Instruments, Lunenberg, MA). LDL was calculated from measured TG, total cholesterol and HDL levels (LDL = total cholesterol - (TG / 5 + HDL)).

**Data Cleaning and Reduction**

ActiGraph data were downloaded and exported to text files using *ActiLife 5.0* (ActiGraph LLC, Pensacola, Florida) and all data cleaning and processing was performed using the statistics package and computing language *R* (101). Wear time was determined from detailed monitor logs that participants completed daily. Participants recorded the time the monitor was put on in the morning and the time at the monitor was removed at night. Participants also recorded anytime monitors were removed during the day and the reason why the monitor was removed (e.g. shower). At least ten hours of ActiGraph data were required for a day to be considered valid and at least four valid days (including one weekend day) were required for the condition to be considered valid (71, 106). Valid data were processed using soj-3x (Appendix A) to produce estimates of MET-hours per day, time in different activity intensity categories, qualifying minutes, qualifying bouts, number of breaks and break-rate.

### Statistical Evaluation

All statistical analysis were performed using R-software programs (101). Significance levels were set at $p<0.05$. To evaluate the change in activity variables and markers of cardiometabolic health from the active to inactive condition a repeated measures linear mixed model with likelihood ratio testing was used. As a secondary analyses we fit linear regression models to evaluate the relationship between the observed cardiometabolic changes and changes in activity and inactivity variables.

## Results

Eleven participants completed the study (Table 5.1). Due to errors in initialization one participant had monitor data from the vertical axis only. Because soj-3x requires acceleration from three axes (vertical, anterior-posterior, medial-lateral), soj-1x (vertical axis only) was used to process this participant's monitor output for both conditions. Soj-1x (Appendix A) has previously been shown to be accurate, precise and sensitive to change in free-living environments (Chapters III and IV).

### Activity and Inactivity Variables

Table 5.2 shows estimated (mean (95% CI)) activity and inactivity variables during the active and inactive conditions. Participants significantly reduced MET-hours (25.2 (23.7-26.8) to 18.5 (17.9-19.2)), minutes spent in MVPA (87.6 (75.6-99.7) to 35.3 (30.5-40.2)) and qualifying minutes (45.8 (34.2-57.4) to 4.5 (1.7-7.2)) during the inactive condition. Time spent sedentary significantly increased 11.5% (9.0%-13.9%) in the inactive condition, while the number of breaks and rate of breaks (break-rate) from sedentary time were significantly reduced. Figure 5.1 illustrates how time spent in sedentary, light, moderate and vigorous intensity activity changed from the active to inactive condition.

## Markers of Cardiometabolic Health

### Body mass, BMI and waist circumference

Body mass, BMI and waist circumference did not change from the active to inactive condition (Table 5.2).

### Insulin action

After seven days of inactivity, fasting glucose and insulin concentrations were similar to pre-inactivity concentrations. In response to a glucose load, area under the glucose curve also did not change post the inactive condition (Figure 5.2). Conversely area under the insulin curve was significantly elevated in response to the glucose load after the inactive condition (Figure 5.2), suggesting more insulin was needed to dispose of the same amount of glucose. There was a significant 17.9% (95% CI: 5.4-30.2) decrease in the composite insulin sensitivity index (C-ISI) after the inactive condition.

**<u>Fasting lipids</u>**

There were no significant differences in any fasting lipid (TG, total cholesterol, HDL, LDL) concentrations after the inactive condition.

### Secondary Analyses

As secondary analyses we used linear regression to evaluate the relationship between change in activity and inactivity variables and change in C-ISI. Despite our small sample, these data revealed a significant negative relationship between change in the number of breaks from sedentary time and change in C-ISI ($p=0.001$, $r=0.83$, $R^2=0.69$) (Figure 5.3). These results indicate that participants who continued to take breaks from sedentary time despite significantly increasing total sedentary time, had a smaller decrease in C-ISI (i.e. breaks from sedentary time attenuated the negative response to increased total sedentary time). This relationship was stronger ($p<0.001$) when changes in sedentary and moderate time were controlled. Independently, changes in sedentary time, moderate intensity activity and $steps \cdot day^{-1}$ were not significantly related to change in C-ISI ($r=0.0$, $r=0.1$, $r={}^{-}0.2$, respectively) (Figure 5.3). However, when number of breaks was controlled there was a significant negative relationship between change and in C-ISI and change in sedentary time ($p<0.05$) (multiple-$R^2=0.81$) and a significant positive relationship between change and in C-ISI and change with moderate intensity activity ($p<0.05$) (multiple $R^2=0.81$).

## Discussion

This free-living intervention, seven days of increased inactivity resulted in a significant reduction in insulin action of 17.9% (95% CI: 5.4-30.2) in healthy volunteers. Similar to previous studies, no changes in fasting lipids were observed (23, 61). The significant contribution of this study is that it was performed in free-living people who decreased activity and accumulated time in sedentary behaviors in ways similar to real-world applications. Using a newly developed algorithm specifically developed for use in free-living people, we obtained detailed estimates of active and sedentary behaviors and were able to consider the effects of multiple features of activity and inactivity independently and simultaneously. From this design we were able to provide further evidence that breaks from sedentary behaviors may attenuate the negative impact of sedentary behaviors on insulin action.

### Free-Living Model of Sedentary Behavior

It is well accepted that stopping exercise and extreme inactivity (e.g. bed rest) cause significant reductions in insulin action in both animal and human models (7, 74, 83, 92, 95, 98, 109, 112). There is also a growing body of epidemiologic evidence indicating that too much time in sedentary behaviors, independent of physical activity, is associated with mortality, chronic disease and markers of cardiometabolic health (105). The current study used an ecological design to study the impact of inactivity on markers of cardiometabolic health. In a natural setting, participants were prohibited from exercise and encouraged to sit as much as possible for seven days, but took breaks from sedentary behaviors and accumulated small amounts of light, moderate and vigorous intensity activity as dictated by their natural environment. This model is directly relevant to real-world applications where moderately active individuals increase sedentary behaviors for short periods of time (e.g. illness, injury, vacation). Longer periods of increased or chronic inactivity likely result in more severe and/or additional (e.g. increased fasting lipids) responses, but these results suggest decreased insulin action may be an initial response to inactivity. Results from a recent study indicate that overweight sedentary (not meeting the physical activity guidelines) individuals who were at risk for cardiovascular disease (had at least two recognized risks factors) spent 68.8% (SD: ±7.5) of their day in sedentary time, accumulated 46.6 min (SD: ±17.7) in moderate-to-vigorous intensity activity and took 43.3 breaks (SD: ±12.1) from sedentary time. These data are similar to the 73.2% sedentary time (95% CI: 70.6-75.8), 35.3 min of moderate-to-vigorous intensity activity (95% CI: 30.5-40.2) and 39.7 breaks from sedentary time (95% CI: 30.9-40.2) observed during the inactive condition in the current study, and suggest such behavior may contribute to factors associated with cardiovascular and metabolic disease.

**Detailed Estimation of Active and Inactive Behaviors**

Two recent studies examined the effects of reduced steps$\cdot$day$^{-1}$ on markers of cardiometabolic health in free-living people. After just 14 days and three days, both studies reported significant reductions in insulin action when healthy active volunteers reduced steps$\cdot$day$^{-1}$ from 10,501 (SD: ± 808) to 1,344 (SD: ± 33) and 12,956 (SD: ± 769) to 4,319 (SD: ± 256), respectively (61, 75). The current study employs more detailed estimates of active and sedentary behaviors in relation to changes in insulin action. Regression analyses revealed a significant positive association between breaks from sedentary behaviors and C-ISI. Independent of total time in sedentary behaviors and time in MVPA, the number of breaks explained 69% of the variance in C-ISI from the active to inactive condition (Figure 5.3). It's worth noting one participant increased breaks$\cdot$day$^{-1}$ by ~15 during the inactive condition and experienced an increase in C-ISI (Figure 5.3). When this participant was removed from analyses the relationship between C-ISI and breaks$\cdot$day$^{-1}$, although attenuated, remained significant ($p<0.03$, $R^2=0.61$). When the number of breaks was controlled, significant relationships were revealed for total time in sedentary behaviors and time in MVPA ($p<0.05$). These free-living data complement previous observational and laboratory studies (25, 42, 44) in implicating breaks from sedentary behaviors as an important player in mediating the negative physiologic response to increased sedentary behavior. We anticipate that detailed measures will continue to expose characteristics of inactivity important in disease initiation and development, and that advances in objective monitoring tools and analyses applied in free-living settings will have direct public health and clinical implications.

In the current study, participants significantly decreased steps$\cdot$day$^{-1}$ from 10,221 (9,178-11,264) to 4,308 (3,868-4,749). Regression analysis revealed this decrease was not independently associated with the observed decrease in insulin action ($r=-0.2$) (Figure 5.3). A prescription to decrease steps$\cdot$day$^{-1}$ is easy for participants to understand and self-monitor (via pedometer), making it an attractive protocol for imposing free-living sedentary behavior interventions. Intuitively, it seems reasonable that if an individual significantly decreases steps$\cdot$day$^{-1}$ they also increase time spent sedentary. In the current study however, this was not observed. Figure 5.4 compares changes in steps$\cdot$day$^{-1}$ and total time in sedentary behaviors. These data show that larger decreases in steps$\cdot$day$^{-1}$ did not necessarily translate to larger increases in sedentary time ($r=^{-}0.1$). Further work is needed to comprehensively evaluate the relationship between metrics of activity and inactivity, but these data suggest steps$\cdot$day$^{-1}$ cannot be used as a surrogate for time in sedentary behaviors.

**Potential Mechanisms and Energy Balance**

It is well documented that nutrient intake and energy availability impart direct effects on insulin action (60, 82). Evidence also shows that the metabolic benefits afforded by exercise are at least in part due to an induced state of energy deficit (10, 78, 99). Similar mechanisms likely contribute reduced insulin action during sustained inactivity. Stephens et al (98) compared metabolic responses to 1-day of sustained sitting while in energy surplus or balance. Compared to an active condition, insulin action was dramatically reduced by 39% while in energy surplus. This effect was attenuated 18% when caloric intake was restricted and energy balance was maintained. In the current study, participants were given instructions to consume the same meal on the evening prior to their OGTT's, but were otherwise given no dietary instructions. Thus it seems reasonable to surmise that during the inactive condition participants were in a state of energy surplus given their reduced expenditure and this may have played a role in the observed reduction in insulin action. However, our 17.9% (95% CI: 5.4-30.2) reduction in insulin action is very similar to results reported by Stephens et al (98) during energy balance. Additionally, in the current study participant weight remained stable from the active to inactive condition (Table 5.2), suggesting energy balance was maintained. Future work should carefully measure energy intake, but nonetheless, our results support previous work in suggesting the metabolic maladaptations observed with increased SB are not solely induced by excess energy availability.

Other factors proposed to alter insulin action during inactivity include disturbances in sympathetic activity and important counter regulatory hormones (e.g. cortisol, glucagon, epinephrine and norepinephrine) (1, 8, 9, 95), lipoprotein lipase activity (7, 112), insulin signaling (61), glucose transport (83, 109), vascular structure and function (102) and muscle blood flow (102). Distinct from energy status, low levels of local muscle activation are thought to contribute to these disturbances (37, 38).

**Strengths and Limitations**

Important strengths of this study include the within-participant design, the use of a free-living model of inactivity and the detailed estimation of multiple features of active and sedentary behaviors. Controlled laboratory studies have revealed important consequences of sustained inactivity. The current study expands this evidence through a free-living intervention that allowed for the simultaneous evaluation of important activity and inactivity variables. This type of design has only recently been made possible through improvements in the objective measurement of free-living PA and SB.

The major limitation of this study is our small, homogenous sample. Despite our small sample we were able to identify important relationships between distinct activity/inactivity variables and reduced insulin action. However, future work is needed to confirm the current results and to uncover additional associations in larger, more diverse groups. For example, it may initially seem surprising that an independent association of MVPA and insulin action was not observed from the active to inactive condition, but this may be due to the lack of between participant variance in how MVPA changed from the active to inactive condition. Participants were relatively young, healthy and active. Additional work is needed to evaluate the potential influences of age, sex, BMI, activity status and health status. A secondary limitation of our study is that we did not control or measure energy intake. Future mechanistic studies would especially benefit from controlling and measuring energy intake.

### Summary

This study provides further evidence that increased time in sedentary behaviors significantly alters metabolic function and that breaks from sedentary behvaiors may attenuate this response. The significant contribution of this study is that these results were observed using a novel free-living model of inactivity where participants performed intermittent bouts of ambulatory activity characteristic of typical habitual inactivity. These bouts of active and sedentary behaviors were precisely estimated using an objective-monitoring tool. Future investigations of inactivity will benefit from measuring and evaluating even more detailed estimates of active and sedentary behaviors such as the length and frequency of active and sedentary bouts.

It is well documented that extreme inactivity (e.g. bed-rest) initiates a host of physiologic responses that promote rapid cardiometabolic dysfunction. The current study presents experimental evidence that increases in ecological sedentary behavior significantly reduce cardiometabolic function.

## Tables

**Table 5.1: Participant Characteristic (mean ± SD)**

| *N=11: 4 Males, 7 Females* | |
|---|---|
| Age *(yrs.)* | 24.9 ± 5.5 |
| Body Mass *(kg)* | 73.1 ± 19.2 |
| Height *(cm)* | 170.0 ± 11.2 |
| BMI *($kg \cdot m^{-2}$)* | 25.0 ± 4.1 |
| Waist Circumference *(cm)* | 73.1 ± 12.2 |
| PAS | 6.4 ± 0.7 |

BMI=Body Mass Index, PAS=Physical Activity Status

**Table 5.2: Intervention variables during active and inactive conditions (mean·day$^{-1}$ (95% CI)) Continued onto next page.**

| | Active Condition | Inactive Condition |
|---|---|---|
| *Activity and Inactivity Variables Estimated by Soj-3x* | | |
| MET-Hours | 25.2 (23.7-26.8) | 18.5 (17.9-19.2)* |
| Time Sedentary (%) | 60.7 (58.2-65.2) | 73.2 (70.6-75.8)* |
| Time Light (%) | 28.1 (24.6-31.7) | 22.5 (19.9-25.1) |
| Time Moderate (%) | 6.0 (4.9-7.1) | 3.4 (2.9-3.9)* |
| Time Vigorous (%) | 4.2 (3.3-5.0) | 0.9 (0.7-1.3)* |
| MVPA (%) | 10.2 (9.0-11.5) | 4.3 (3.7-5.0)* |
| Time Sedentary (minutes) | 528.1 (495.2-561.0) | 607.0 (571.5-642.4)* |
| MVPA (minutes) | 87.6 (75.6-99.7) | 35.3 (30.5-40.2)* |
| Qualifying Minutes | 45.8 (34.2-57.4) | 4.5 (1.7-7.2)* |
| Qualifying Bouts | 2.0 (1.5-2.4) | 0.4 (0.2-0.6)* |
| Number of Breaks from Sedentary Time | 42.1 (36.4-47.8) | 39.7 (30.9-40.2)* |
| Break-Rate (brks·sed-hr$^{-1}$) | 5.0 (4.1-5.9) | 4.1 (3.2-5.0)* |
| Steps | 10,221 (9,178-11,264) | 4,308 (3,868-4,749)* |
| *Markers of Cardiometabolic Health* | | |
| BMI (kg·m$^{-2}$) | 25.0 (22.5-27.4) | 24.9 (22.1-27.7) |
| Waist Circumference (cm) | 78.4 (71.2-85.7) | 77.4 (69.6-85.2) |
| Fasting Plasma Glucose (mg·dL$^{-1}$) | 93.9 (90.0-97.8) | 94.4 (88.7-100.9) |
| Fasting Plasma Insulin (*u*U·ml$^{-1}$) | 14.6 (10.9-18.3) | 15.9 (11.9-19.9) |
| 120-min Plasma Glucose (mg·dL$^{-1}$) | 94.1 (77.6-110.7) | 108.5 (95.5-121.5) |
| 120-min Plasma Insulin (mg·dL$^{-1}$) | 45.5 (26.7-64.3) | 86.4 (64.0-108.8)* |
| AUC-Glucose | 125.3 (109.9-140.6) | 135.5 (120.8-150.1) |
| AUC-Insulin | 80.2 (67.0-93.3) | 107.4 (84.7-130.2)* |
| Composite Insulin Sensitivity Index | 2.9 (2.3-3.5) | 2.4 (1.8-3.1)* |
| Total Cholesterol (mg·dL$^{-1}$) | 176.7 (167.9-185.4) | 180.6 (171.1-190.1) |
| LDL (mg·dL$^{-1}$) | 169.1 (159.8-178.3) | 171.4 (163.3-179.5) |
| HDL (mg·dL$^{-1}$) | 57.3 (51.0-63.6) | 57.0 (49.7-64.4) |
| Triglycerides (mg·dL$^{-1}$) | 112.0 (80.5-143.6) | 136.2 (100.2-172.2) |

BMI=Body Mass Index, AUC=Area Under Curve, LDL=Low Density Lipoprotein, HDL=High Density Lipoprotein. * Significantly different than Active Condition

## Figures

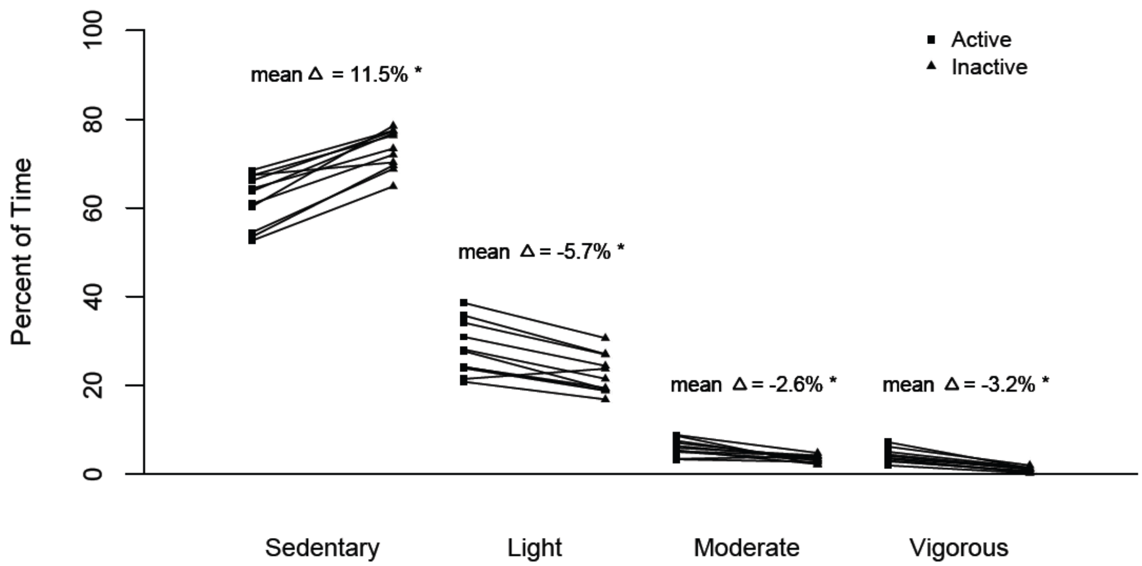


**Figure 5.1: Change in habitual activity from active to inactive condition**

* Significantly different than active condition.

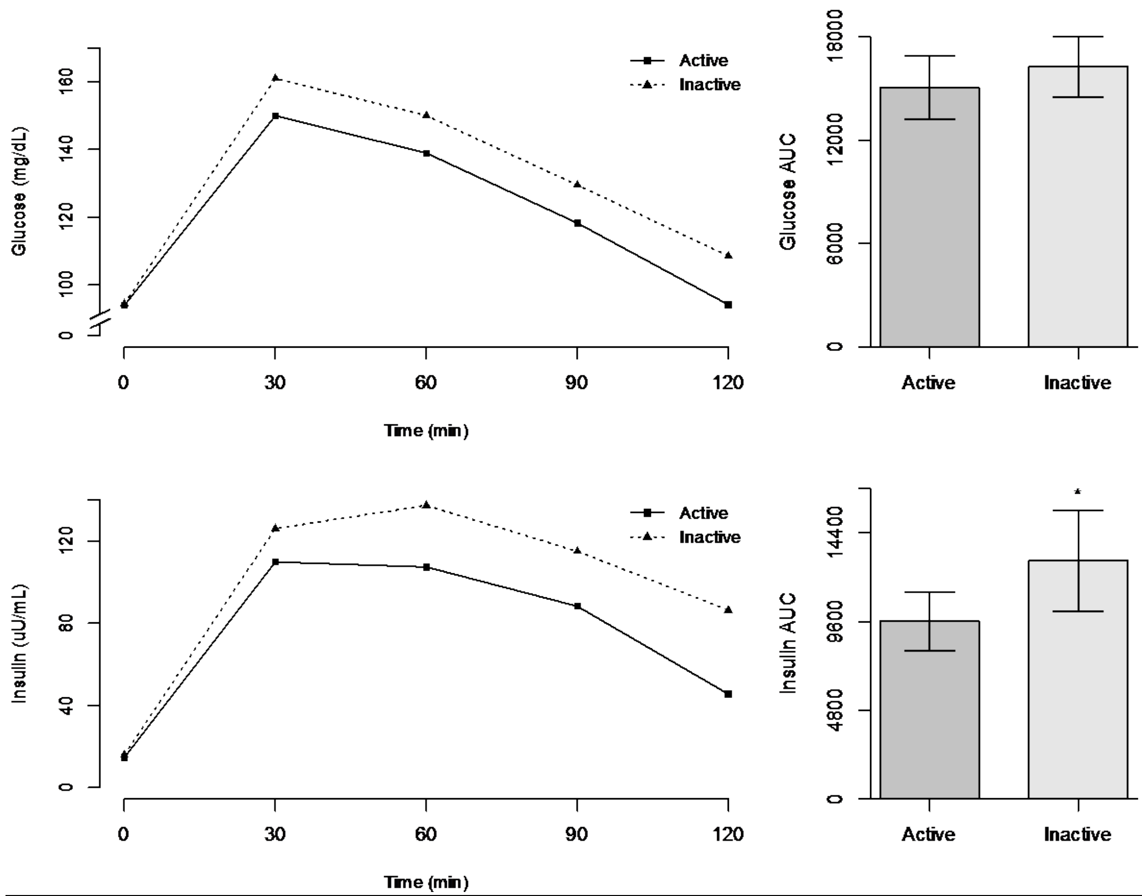


**Figure 5.2: Plasma glucose and insulin during OGTT. Area under glucose and insulin curves**

Plasma glucose (top) and insulin (bottom) levels during 2-hour OGTT.  AUC = area under curve. * Significantly different than active condition.

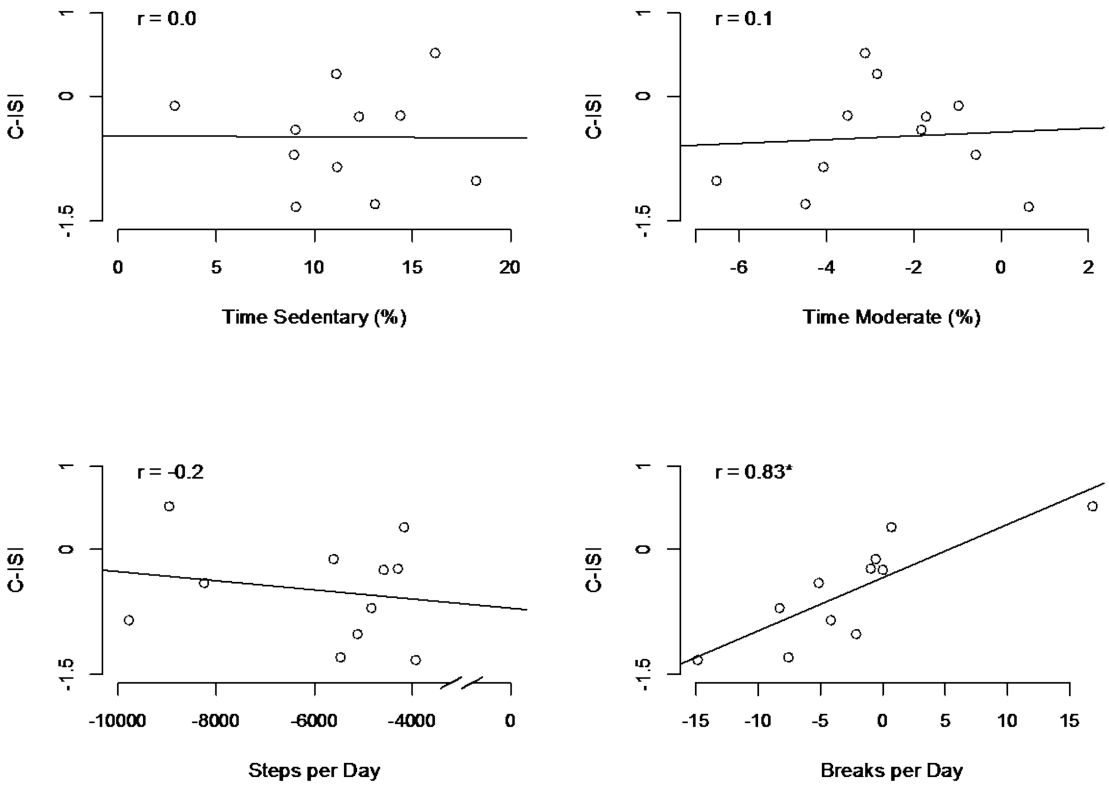


**Figure 5.3: Change in insulin action relative to change in activity and inactivity variables**

Relationship between change in insulin action and activity and inactivity variables. C-ISI = Composite Insulin Sensitivity Index. *Significant correlation.

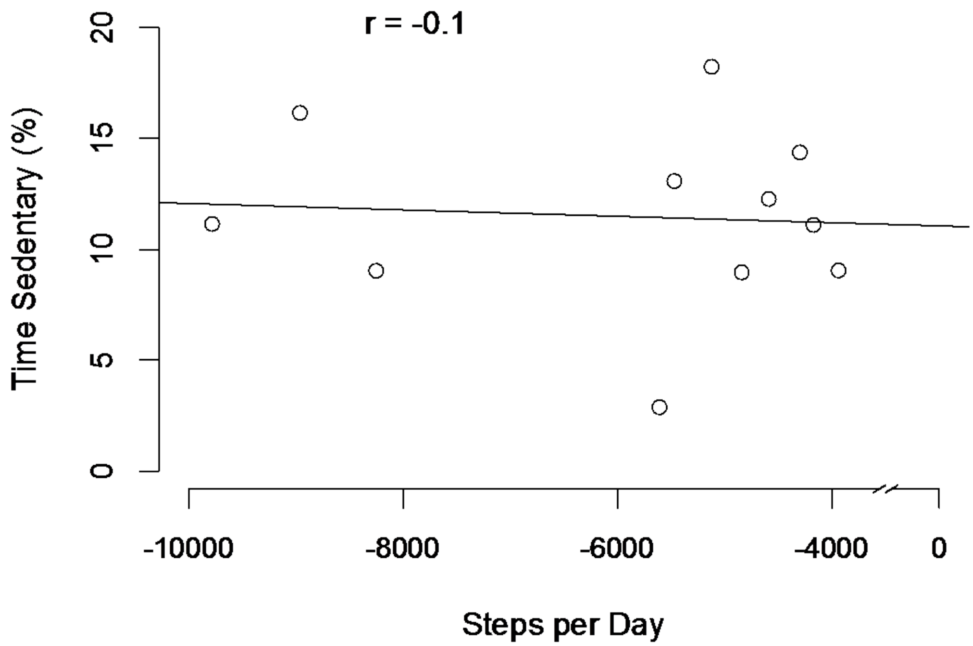


**Figure 5.4: Change in sedentary time relative to change in steps per day**

Relationship between change in steps per day and time sedentary.

# CHAPTER VI

# SUMMARY AND CONCLUSION

In 2008, the US Department of Health and Human Services issued the first-ever federally mandated Physical Activity Guidelines for Americans (16). The Guidelines are based on an extensive review of the scientific literature which notes a clear association between physical activity (PA) and a reduced risk for chronic disease, morbidity and mortality (16). The review also points out the limited knowledge of the dose-response relationship between PA and health and emphasizes the need to expand sedentary behavior (SB) research. The Physical Activity Guidelines Advisory Committee (PAGAC) cites poor measures of PA and SB exposure as a major contributing factor to these knowledge gaps. This dissertation directly addressed these issues by first adapting a machine-learning method for measuring PA and SB for use in free-living people (study 1), verifying that these methods detect change in active and sedentary behavior (study 2) and then applying our refined method to measure and evaluate the effects detailed components of PA and SB exposure on markers of cardiometabolic health during a short inactivity intervention (study 3).

## Study 1 and Study 2

Body worn accelerometers are ideal for measuring PA and SB in free-living people. They are small, unobtrusive, relatively inexpensive and easy to use. However, the data processing techniques used to convert accelerometer output into meaningful metrics have predominantly been developed in laboratory settings where PA and SB behaviors are scripted and performed for a prescribed period of time. As a result, these techniques perform poorly when they are used in free-living settings where behaviors are unplanned and discontinuous. Chapters III and IV (studies 1 and 2) provide the first measurement method specifically designed for use in free-living people and the first validation to use direct observation as a criterion in participant natural free-living environment.

The sojourn method is a hybrid machine-learning model that combines artificial neural networks with decision tree analysis to estimate METs. By combining *a priori* knowledge on human behavior with the flexible non-parametric properties of neural networks the sojourn method considerably improves MET estimates in free-living people compared to methods developed in the laboratory. Furthermore, Chapter III provides two versions of the sojourn method: soj-1x, which uses accelerations (1Hz) from the vertical axis, and soj-3x, which uses accelerations (1Hz) from the vertical, anterior-posterior and medial-lateral axes. There are three “key ingredients” to the improved MET estimates observed with soj-1x and soj-3x. First, they use simple parameters from the acceleration signal to identify where bouts of activity and inactivity start and stop. Second, MET values are assigned to bouts of inactivity according to the Compendium of Physical Activities (2) and Kozey et al (57). And third, MET values for activity bouts are estimated using a neural network (97). In addition to improving MET estimates, soj-1x and soj-3x also provide more detailed features of PA and SB than possible with previous methods, including qualifying minutes, qualifying bouts, breaks from sedentary and the rate of breaks from sedentary time. The main contribution of soj-3x is that it improved estimates of sedentary and light intensity time in comparison to soj-1x. Using additional information from the anterior-posterior and medial-lateral axes, soj-3x is more sensitive to the subtle differences between sedentary and light intensity behaviors. This is very timely given the recent emphasis on understanding sedentary behaviors and that previous methods often resorted to simply grouping sedentary and light behaviors into a single "low" intensity category (65, 67, 85).

A useful measurement tool is not only accurate, but also precise. The precision of a prediction algorithm has implications for its validity in detecting change between conditions. Chapter IV (study 2) provides evidence that soj-1x and soj-3x are sensitive to changes in habitual activity within an individual. Both methods were sensitive to change, and distinguished three activity levels (sedentary, moderately active and very active) that have important implications for health. These data are particularly important for intervention and surveillance research.

In addition to improving MET estimates compared to previous models, soj-1x and soj-3x have several important strengths. First, both methods use a single commercially available accelerometer. Several previous machine-learning approaches have demonstrated some success in free-living people, but require complex multi-sensor devices that cannot be worn for extended periods of time (86, 113). Second, the low sampling rate (1 Hz) used in both methods is of value. We anticipate future work with higher sampling rates (e.g. 30-100 Hz) will improve these methods, but prior to 2009 and the release of the ActiGraph GT3X, most accelerometer-based activity monitors were not capable of collecting and storing a large amount of raw acceleration data (30-100Hz). Consequently, data collected using these devices (e.g. ActiGraph GT1M and 7164) will not benefit from algorithms that use raw signals. Third, soj-1x and soj-3x operate in the R statistical computing environment (101). R is a free and open source software, making soj-1x and soj-3x easily shared with other researchers. Measuring human movement from body worn sensors is an active field and several groups have demonstrated success in using machine-learning to translate accelerometer output into important PA and SB metrics, but the complexity of the devices and/or statistical computing required prevent most methods from being used by applied researchers.

Chapters III and IV not only provide two novel methods that significantly improve PA and SB estimation in free-living people, but provide an important example of a free-living calibration and validation. It is well recognized that laboratory calibration and validation are not directly transferable to free-living environments (5, 36), but the research community has yet to embrace the idea of performing these studies in free-living settings. Because direct observation is highly labor intensive most groups avoid free-living studies or use participant annotated data for comparison. Chapters III and IV illustrate the value of direct observation as a criterion and demonstrate the importance of free-living calibration and validation. It is anticipated that these studies will motivate researchers to conduct similar work in the future.

Although soj-1x and soj-3x greatly improved free-living PA and SB measurement, they have yet to realize their potential. Future work should refine the algorithms to extract estimates of duration. At present, duration estimates are embedded in the algorithms but we have yet to extract this information to produce meaningful summary statistics of metrics such as length and frequency of active and sedentary behaviors. Additionally, soj-1x and soj-3x should be adapted to estimate activity type. Again, both algorithms are currently set up for this, but nonetheless require a bit of refinement to extract this information. And finally, soj-1x and soj-3x should be validated on a more diverse sample. The samples used in the current studies were relatively homogenous: they were young, lean and active. We foresee the sojourn method being relevant for most groups, but it may be that other populations require algorithm parameters be set differently (e.g. the threshold to identify active vs. inactive behaviors will be lower in older adults).

**Study 3**

Sedentary behaviors are ubiquitous and spontaneous, making it very difficult to conduct laboratory-based studies that effectively expose the corollary of SB. The few studies that have experimentally manipulated SB relied on highly artificial laboratory environments (e.g. prolonged bed rest in humans; hind-limb immobilization in rodents), making it difficult to translate results to behavior more reflective of "normal" free-living conditions. Recent studies have employed free-living protocols, but all used steps$\cdot$day$^{-1}$ as their only measure of active and inactive behavior. Results from Chapters III and IV support the use of both soj-1x and soj-3x in free-living PA and SB interventions. Because soj-3x was more sensitive to sedentary and light intensity activities, we chose soj-3x to capture detailed estimates of PA and SB during a seven day inactivity intervention.

The main contributions of study 3 are that we 1) used a free-living model of sedentary behavior that is specifically relevant to public health and clinical settings and 2) used soj-3x to capture detailed estimates of active and sedentary behaviors. By studying SB under free-living conditions we were able to consider the interaction of other behaviors performed by predominantly sedentary individuals. Even the most sedentary people accumulate some level of light and even moderate-to-vigorous intensity activity.

Chapter V (study3) provides evidence that these behaviors interact to influence the cardiometabolic response to increased sedentary behavior. Despite our small sample (N=11), the results support epidemiologic and laboratory data suggesting that breaks from sedentary time play an important role in determining the physiologic response to SB. Study 3 also provides further evidence that reduced insulin action is an early adaptation to increased SB.

Although these data have the potential to impact how future research on SB is conducted, future work using a larger, more diverse sample is needed to confirm these results. Future studies should consider more features of PA and SB including activity type and the number and frequency of active and sedentary behaviors. Future studies would also benefit from more direct measures of cardiometabolic health (e.g. hyperinsulinemic euglycemic clamp). Nonetheless, study 3 provides important experimental evidence supporting the growing body of epidemiologic evidence identifying SB as a cardiometabolic risk factor.

## Conclusion

This dissertation has the potential to significantly influence the field of Physical Activity and Health. Studies 1, 2 and 3 use novel methods to 1) improve PA and SB measurement and 2) improve our understanding of the physiologic response to too much SB. To our knowledge, soj-1x and soj-3x are the first data processing methods specifically designed for use in free-living people and study 1 is the first free-living validation of any data processing method used to translate accelerometer output to metrics of PA and SB. Study 3 provides one of the first free-living SB interventions that measured detailed components of both PA and SB and thus some of the first experimental evidence that increases in SB under typical free-living conditions is deleterious to health.

The novel methods used in studies 1, 2 and 3 can ultimately be used to better define the dose of physical activity and sedentary behavior linked to health, and have the potential to broaden our understanding of how these behaviors interact in real world environments to collectively influence health.

# APPENDICES

# APPENDIX A

# THREE MACHINE LEARNING TECHNIQUES TO ESTIMATE METS FROM A SINGLE HIP-MOUNTED ACCELEROMETER

## Laboratory Neural Network

The laboratory neural network (lab-nnet) was developed (N=48) and trained (N=277) on large, diverse samples and a wide range of activity types and intensities (31, 97). The lab-nnet uses two features from the second-by-second accelerometer signal to estimate METs. The first feature is a summary of the distribution of counts in 1-minute. Specifically, the $10^{th}$, $25^{th}$, $50^{th}$, $75^{th}$ and $90^{th}$ percentiles of a minute's second-by-second counts are used. Neural networks are inherently flexible, allowing them to also use common statistics (mean, standard deviation, coefficient of variation) that are implicitly included in this summary. The second feature is the lag one autocorrelation of the counts in 1-minute. This is a measure of temporal dynamics and it summarizes the relationship between adjacent counts within a given minute.

The lab-nnet is a single hidden layer model without a skip layer connection. It has 25 hidden units and before fitting the model, covariates were centered and scaled so that each had a range of -1 to 1. For a detailed description of the development of the lab-nnet see Stuadenmayer et al (97) and Freedson et al (31).

## The Sojourn Method – Soj-1x and Soj-3x

The sojourn method is a hybrid machine learning approach that combines artificial neural networks with decision trees to estimate METs. By combining *a priori* knowledge on human behavior with the flexible non-parametric properties of the lab-nnet, the sojourn approach is well suited to estimate METs from free-living accelerometer output. We have developed two versions of the sojourn method: sojourn 1-axis and sojourn 3-axes. As their names imply, sojourn 1-axis (soj-1x) uses information from one axis (vertical), while sojourn 3-axis (soj-3x) uses information from three axes (vertical, anterior-posterior and medial-lateral). Both methods were developed and trained on the same data set (N=6). Experimental procedures for the development stage were identical to those described in this study. Both methods operate in three main steps: 1) identify bouts of activity and inactivity, 2) assign non-physical activity MET values to inactivity bouts and 3) apply the lab-nnet to estimate METs for activity bouts.

**Sojourn 1-Axis**

Soj-1x uses counts$\cdot$sec$^{-1}$ from the vertical acceleration signal of a hip mounted ActiGraph activity monitor. It requires five constants, three percentages (5%, 12% and 55%) and two time cutoffs (10 sec and 90 sec). The constants were chosen by grid search with the objective of minimizing the sum of the mean squared errors of its estimates. The step-by-step method is outlined below and illustrated in Figure 9.

1. To estimate bouts of activity and inactivity the soj-x first identifies alternating intervals of various lengths where all counts are zeros (no movement of hips) or all counts are positive (movement of hips). Intervals of long zeros (≥90 sec) are identified as inactivity type 1 (sitting or lying fairly still). Intervals of long positive counts (≥10 sec) are identified as activity. When an interval is short it is identified as "undetermined". Since there can be short intervals of positive counts during inactivity due to fidgeting or small movements, and there can be short intervals of zeros during activity if someone briefly stands still, these instances are temporarily

called “undetermined”. This process and the constants used to identify long and short intervals are illustrated in Figure 9.

2. The next step is to identify “undetermined” intervals as activity, or one of four types of inactivity: 1) sitting or lying still, 2) sitting with minimal movement, 3) standing still or 4) standing with minimal movement. Before doing this, adjacent “undetermined” intervals are combined into longer intervals that have both zero and positive counts. The duration and percentage of non-zero counts are then used to identify “undetermined” intervals. Inactivity types 1-4 are assigned a non-physical activity MET value based on the Compendium of Physical Activities and several calibration studies (2, 57). Figure 9 illustrates this process, the constants used and the MET values assigned to intervals of inactivity.

3. The last step of soj-1x is to estimate MET values for activity bouts. This is done by applying the previously calibrated and validated lab-nnet (97) to activity bouts. If the activity bout last for less than 120-seconds, the lab-nnet is applied to the entire bout (e.g. one MET value is estimated for the activity bout). If the bout is longer than 120-seconds, it is segmented into 40-second intervals and the lab-nnet estimates one MET value for each interval. Intervals less than 40-seconds in length are combined with the previous interval and the lab-nnet is applied to the combined interval. For example, an activity bout lasting 150 seconds will first be broken up into three 40-second intervals (120-seconds). The remaining 30-seconds will then be combined with the last 40-second interval, resulting in two 40-second intervals and one 70-second interval. The lab-nnet is then applied to each interval, resulting in three estimated MET values for the entire activity bout.

## Sojourn 3-Axes

Soj-3x uses counts$\cdot$sec$^{-1}$ from the vertical, anterior-posterior and medial-lateral acceleration signals of a hip mounted ActiGraph activity monitor. Soj-3x is different from soj-1x in two primary ways: 1) we identify the start and stop of activity and inactivity intervals differently, and 2) we apply a neural network that uses acceleration information from three axes to distinguish inactivity intervals as either sedentary or light intensity before we assign specific MET values. It requires five constants, one acceleration threshold (15 counts$\cdot$sec$^{-}$1), one time cutoff (30 sec) and three percentages (5%, 12% and 70%). The constants were chosen by grid search with the objective of minimizing the sum of the mean squared errors of its estimates. The step-by-step method is outlined below and illustrated in Figure 10.

1. To identify the start and stop of activity and inactivity intervals, soj-3x identifies instances of rapid acceleration or deceleration. Rapid accelerations or decelerations are defined as instances where the absolute difference between adjacent counts from the second-by-second vertical acceleration signal is greater than the acceleration cutoff ($\geq$15 counts$\cdot$sec$^{-1}$). In other applications, similar methods have been used to identify falls (which can be thought of as extreme posture transitions) from body worn accelerometers (85). If these intervals are less than the time cutoff (30-sec), they are combined with neighboring intervals until the combined interval is longer than the time cutoff.
2. The next step is to identify intervals as either activity, or 1 of four inactivity types (described in soj-1x). First, activity is distinguished from inactivity using the percentage of non-zero counts from the vertical axis. To determine inactivity types 1-4, a neural network is applied to inactivity intervals to first distinguish

sedentary (inactivity types 1-2) and light intensity (inactivity types 3-4). Specific MET values for sedentary and light intensity activities are assigned based on the percentage of non-zero counts in the interval. Figure 10 illustrates this process, the constants used and the MET values assigned to intervals of inactivity.

   a. The neural network uses information about the duration of the interval and two statistical features from the vertical, anterior-posterior and medial-lateral axes, and the resultant vector magnitude of these axes:

      i. Distribution of second-by-second counts – $10^{th}$, $25^{th}$, $50^{th}$, $75^{th}$ and $90^{th}$ percentiles of an interval's second-by-second counts

      ii. Lag-1 autocorrelation – measure of relationship between adjacent counts within an interval

3. The neural network previously developed and calibrated in the laboratory (lab-nnet) (97) is applied to activity intervals to estimate METs. This process is identical to the activity MET estimation process described in soj-1x above.

**Note:** The purpose of soj-3x is to estimate METs. In step 2 we distinguish sedentary from light intensity before assigning specific MET values to types of inactivity. These general intensity categories are determined from a neural network that was trained to distinguish sitting from standing activities. All sitting intervals are identified as sedentary and standing/non-sitting intervals are identified as light. Similarly, inactivity types 1-4 are assigned non-physical activity MET values based on the Compendium of Physical Activities and several calibration studies (2, 57). These methods use activity type classification to improve MET estimates, an approach that is gaining momentum (13) and recently shown to improve energy expenditure estimates (3, 22).

# Figures

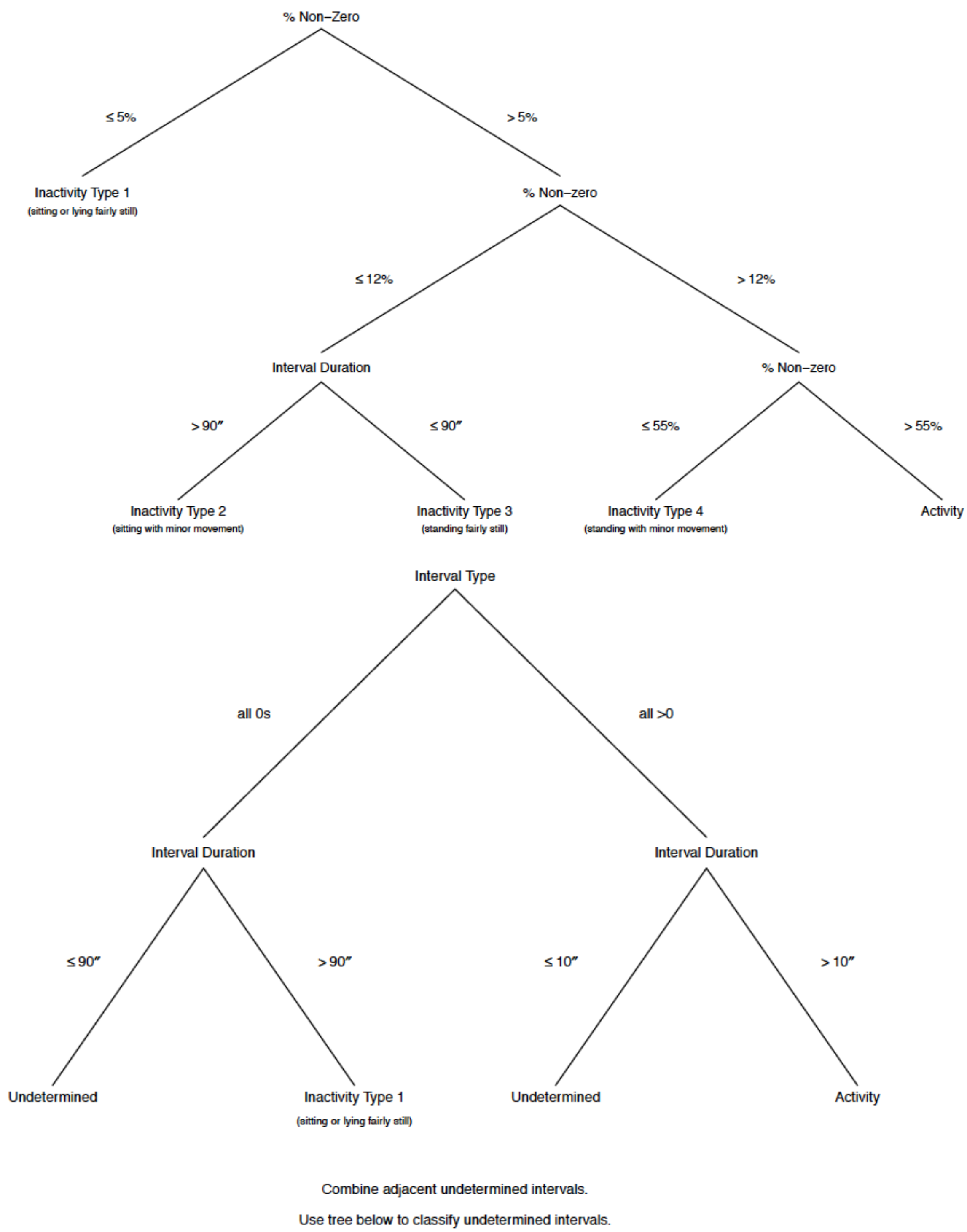


**Figure A.1: Sojourn 1-axis**

Sojourn 1-axis (soj-1x) algorithm for estimating METs from free-living accelerometer data.  Adapted from Staudenmayer et al (Under Review).

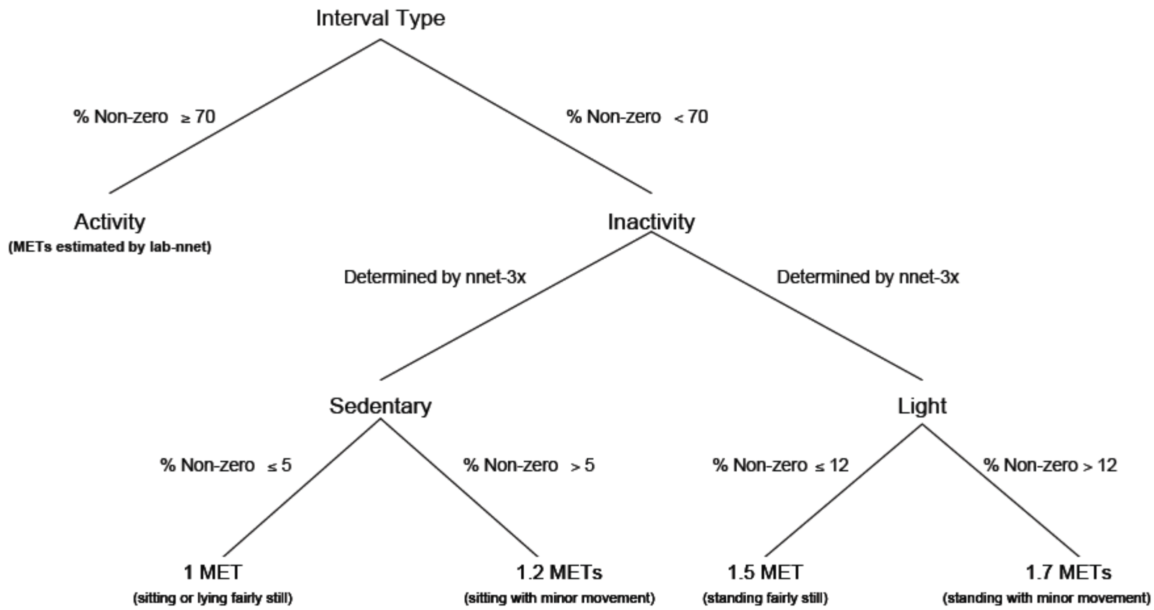


**Figure A.2: Sojourn 3-axes**

Sojourn 3-axis (soj-3x) algorithm for estimating METs from free-living accelerometer data.

## APPENDIX B

## DIRECT OBSERVATION COMPARED TO INDIRECT CALORIMETRY

Fifteen participants were observed on three separate occasions for 2-consecutive hours each time. During this time participants performed free-living activities while wearing the Oxycon Mobile metabolic system (Cardinal Health, Yurba Linda, California). The oxycon mobile is a portable respiratory gas exchange system that measures ventilation and expired concentrations of oxygen and carbon dioxide through a facemask. Trained observers recorded participants' activity type, intensity and duration in the PDA.

On one occasion the Oxycon Mobile did not record valid data, resulting in a total of 44 observations. Table B.1 and Figures B.1 direct observation estimates are compared to indirect calorimetry. In general, these data indicate DO accurately estimates MET-hours and minutes in sedentary (<1.5 METs), light (1.5-2.99 METs), moderate (3.0-5.99 METs), vigorous (≥ 6 METs) and moderate-to-vigorous (≥ 3 METs). The largest bias (Table B.1 and Figure B.2) and rMSE (Table B.1) were produced for time in sedentary and light intensity, with DO tending to underestimate sedentary (bias (95% CI) = -5.4 min (-11.4-0.6)) and overestimate light (bias (95% CI) = 6.6 min (1.1-12.0)) intensity activity. Figure B.2 illustrates the bias and precision (error bars) of DO compared to indirect calorimetry.

In this study, researchers were trained to identify almost all seated activities as sedentary (exceptions included activities such as weight lifting, biking etc.) and all standing/ambulatory activities as at least light intensity. Visual examination of the direct observation records synchronized with indirect calorimetry data revealed that in some instances when an individual was standing/walking, the indirect calorimeter measured <1.5 METs. Although it is possible that a standing (non-seated) activity is <1.5 METs, these instances would be nearly impossible to identify by a direct observer. This is a limitation of using direct observation as a criterion if the goal is to precisely estimate energy expenditure (EE), but it may also be an advantage. Evidence suggests the posture of sitting (i.e. low levels of lower body muscle activation) is detrimental to health regardless of EE (within reason: i.e. 1.4 (sedentary) vs. 1.6 METs (light)) (7, 37, 38), thus if the application of direct observation is to distinguish behaviors that are meaningful to health (i.e. sitting vs. standing instead of 1.4 vs. 1.6 METs), it may be of more value to use posture to distinguish activities than EE. An ideal criterion will accurately identify both EE and posture (activity type), but these data illustrate the advantages/disadvantages of gold-standard criterions for PA and SB assessment, and illustrate the importance of choosing a criterion relevant to the application of interest (e.g. health outcomes).

## Tables

**Table B.1: Direct observation compared to indirect calorimetry**

| | Indirect Calorimetry mean (95% CI) | Direct Observation mean (95% CI) |
|---|---|---|
| MET-Hrs. | 5.4 (4.5-6.4) | 4.8 (4.0-5.5) |
| *Bias* | - | ¯0.7 (¯0.9-¯0.4) |
| *rMSE* | - | 0.8 (0.6-1.1) |
| Sedentary Minutes | 58.3 (49.2-67.4) | 52.9 (43.8-62.1) |
| *Bias* | - | ¯5.4 (¯11.4-0.6) |
| *rMSE* | - | 14.7 (10.4-19.1) |
| Light Minutes | 26.0 (22.1-29.9) | 32.6 (26.5-38.6) |
| *Bias* | - | 6.6 (1.1-12.0) |
| *rMSE* | - | 14.0 (10.0-18.1) |
| Moderate Minutes | 25.2 (17.6-32.9) | 24.8 (16.1-33.5) |
| *Bias* | - | ¯0.4 (¯3.6-2.8) |
| *rMSE* | - | 5.4 (2.7-8.2) |
| Vigorous Minutes | 10.5 (4.6-16.3) | 9.7 (3.4-16.0) |
| *Bias* | - | ¯0.7 (¯3.5-2.0) |
| *rMSE* | - | 4.0 (1.5-6.5) |
| MVPA Minutes | 35.7 (26.1-45.3) | 34.5 (25.0-44.0) |
| *Bias* | - | ¯1.2 (¯2.7-0.3) |
| *rMSE* | - | 2.6 (1.5-4.0) |

*N (number of observations) = 44*

## Figures

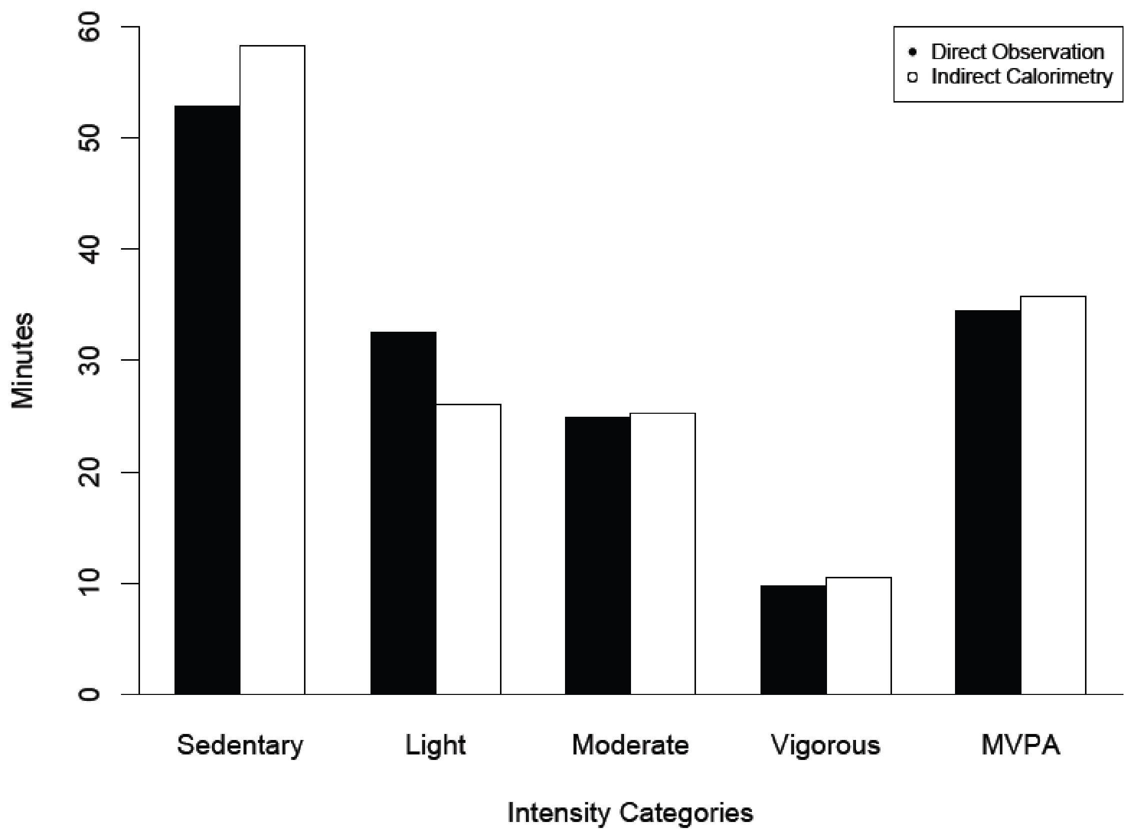


**Figure B.1: Direct observation compared to indirect calorimetry**

Direct observation estimates of minutes in categories of intensity compared to indirect calorimetry. N=44.

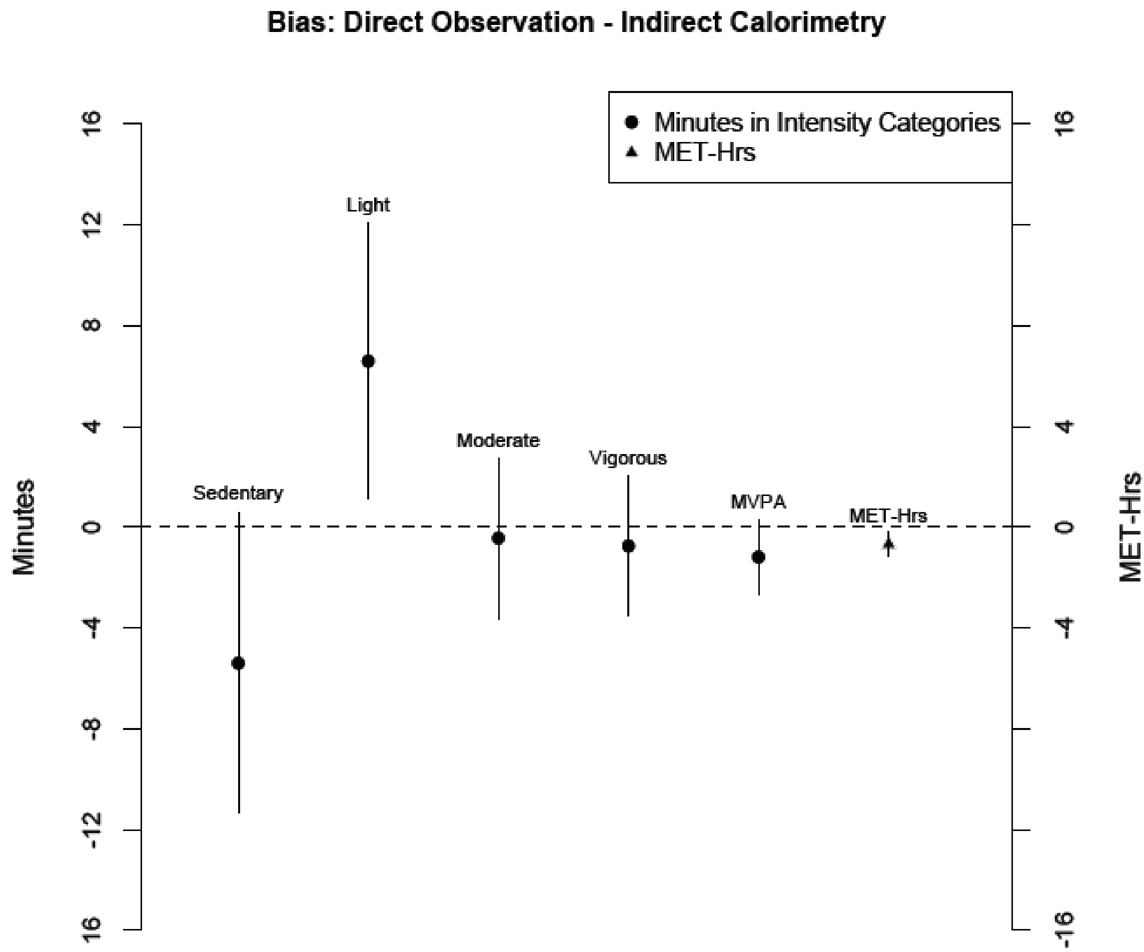


**Figure B.2: Bias of direct observation estimates of time in categories of intensity and MET-hours compared to indirect calorimetry**

Bias and precision (error bars) of direct observation estimates of minutes in categories of intensity and MET-hours.

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