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Neonatal Non Nutritive Suckling Waveform Extraction, Characterization, and Classification

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Neonatal Non Nutritive Suckling Waveform Extraction, Characterization, and Classification

A Dissertation submitted in partial satisfaction of the
requirements for the degree
Doctor of Philosophy

in

Engineering Sciences (Mechanical Engineering)

by

Phuong Truong

Committee in charge:

Professor James Friend, Chair
Professor Yu-Hwa Lo
Professor Truong Nguyen
Professor Michael Tolley

2023

The Dissertation of Phuong Truong is approved, and it is acceptable in quality and form for publication on microfilm and electronically.

University of California San Diego

2023

DEDICATION

In memory of my father, Tho Truong.

EPIGRAPH

Breastfeeding is the mother's gift to herself, her baby, and the earth.

—Pamela K. Wiggins

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author was the primary investigator and author of this paper.

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ABSTRACT OF THE DISSERTATION

Neonatal Non Nutritive Suckling Waveform Extraction, Characterization, and Classification

by

Phuong Truong

Doctor of Philosophy in Engineering Sciences (Mechanical Engineering)

University of California San Diego, 2023

Professor James Friend, Chair

Breastfeeding is a natural biologic function that benefits both mothers and infants by protecting their health and development. Since the 1950s, breastfeeding rates have dropped dramatically, despite nearly 80% of mothers attempting to breastfeed. Breastfeeding cessation is caused by many factors from both mother and infant, with many reporting nipple pain, poor milk transfer, and poor infant weight gain as a few of the many contributors. An infant's ability to suckle in a coordinated manner is a key element to successful breastfeeding. When uncoordinated or irregular, an infant's suckling may cause pain, poor latch, and poor milk transfer ultimately increases a mother's risk of breastfeeding cessation by disrupting her ability to nurse or pump. In the past two decades, many devices and systems have been developed to address the issue of infant oral motor coordination, particularly in pre-term infants that lack of the necessary oral motor developments due to their premature birth. Abnormal suckling behavior in full term infants have been largely overlooked as many have turned to surgical intervention to resolve congenital oral dysfunction, with little evidence of long-term benefits. Despite rising trends in the last decade in surgical interventions to resolve breastfeeding issues, breastfeeding cessation rates continue to climb. A lack of standardized objective measurement tools for general screening of infant suckling to guide data-driven intervention remains a challenge within the clinical community. This dissertation studies non-nutritive suckling behavior in full-term healthy infants. To address the need for standardize objective measurement tools, a non-nutritive suckling measurement system was designed and developed to enable real-time measurement of infant suckling vacuum. Accompanying software was created to enable clinicians to interact and interface with the data in real-time for rapid diagnosis and analysis in regions of interest. The system was used in clinical evaluation of 91 healthy full term infants to establish normative data for non-nutritive suckling. Once normative data was sufficiently collected, data from abnormal suckling behavior caused by a common congenital condition were studied and analyzed. Extensive signal processing was performed to extract characteristic features from non-nutritive suckling signals such as max vacuum, mean vacuum, suckling frequency, burst duration, sucks per burst, and three principal frequency components describing signal shape. Machine learning algorithms were used to assist with anomaly detection to determine of abnormal suckling behavior can be automatically determined based on normative data. Case evaluations are studied in conjunction with clinical notes and assessments to determine congruence or disconsensus between traditional examinations and objective measurements. Confounding evidence of clinical inconsistency using standard evaluation methods are discussed as apart of the larger goal of shedding light on the degree of subjectivity that affects intervention and diagnosis of breastfeeding difficulties caused by infant suckling irregularities. Finally, the work is summarized and future directions are described to lay the foundation for continued

advancement in the field, technology, and clinical practices.

Chapter 1

Introduction

1.1 Breastfeeding

Breastfeeding is a natural biologic function that fosters attachment and safeguards the health of mothers and babies. The growing body of research shows breastfeeding mothers experience lower risks of reproductive organ cancers, type II diabetes, cardiovascular disease and mental health disorders, and breastfeeding infants experience lower risks of infectious diseases, gastrointestinal and respiratory health issues, allergies, type II diabetes, hypertension, and obesity [16–20]. During breastfeeding, mother-infant dyads must have strong compatibility, attachment, and positioning in order to successfully nurse. When infants properly latch to the breast during breastfeeding, their mouths are held wide open, lips curved back [1]. Shown in Figure 1.1 is an illustration of normal infant suckling and attachment to the breast. The teat, formed by the nipple and most of the areola is pulled in towards the soft palate of the oral cavity. When the infant tongue depresses, this forms a local vacuum that draws the nipple and milk contents into the oral cavity. The tongue then compresses to collect and swallow milk [2]. This coordination enables the infant to follow a suck-swallow-breath cycle during breastfeeding as they learn and refine their oral-motor coordination. When breastfeeding is well-established, the mother's milk supply begins regulation based on a

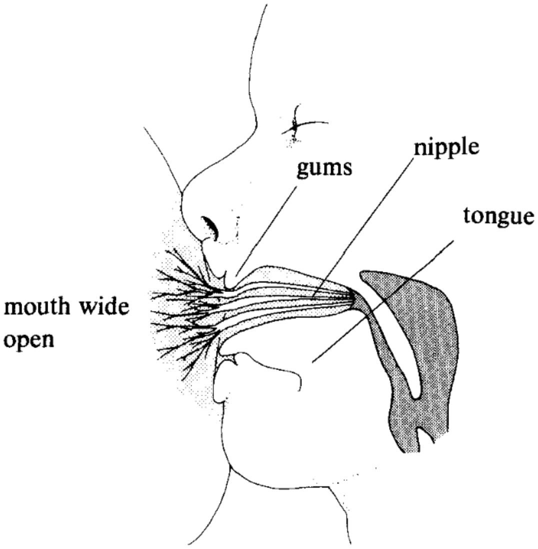


Figure 1.1: Illustration drawn from ultrasounds imagery shows infant breastfeeding in the correct position [1, 2].

supply-demand relationship and continues to produce more milk based on the frequency and degree in which her breasts are emptied [21].

1.1.1 Breastfeeding Cessation

The Center for Disease Control and Prevention (CDC), the World Health Organization (WHO), the American Academy of Pediatrics (AAP), among many other health organizations, recommend infants exclusively breastfeed for at least six months to attain optimal benefits [3]. While, advantages of breast milk far outweigh formula, rate of exclusive breastfeeding at six months post-birth fall to a staggering 25%, according to the CDC's 2022 National Immunization Survey [3]. Figure 1.2 shows the breastfeeding trends in the United States among children born in 2019 [3]. This reflects a 75% breastfeeding cessation statistic despite the fact that 80% of mothers attempt to breastfeed, indicating an initial interest in providing infant nutrition via breast milk. While breastfeeding cessation is due to a number of factors attributed by both mother and infant, many mothers report nipple pain, poor latch, and infant weight gain as major barriers to breastfeeding. Infant abnormal suckling behavior

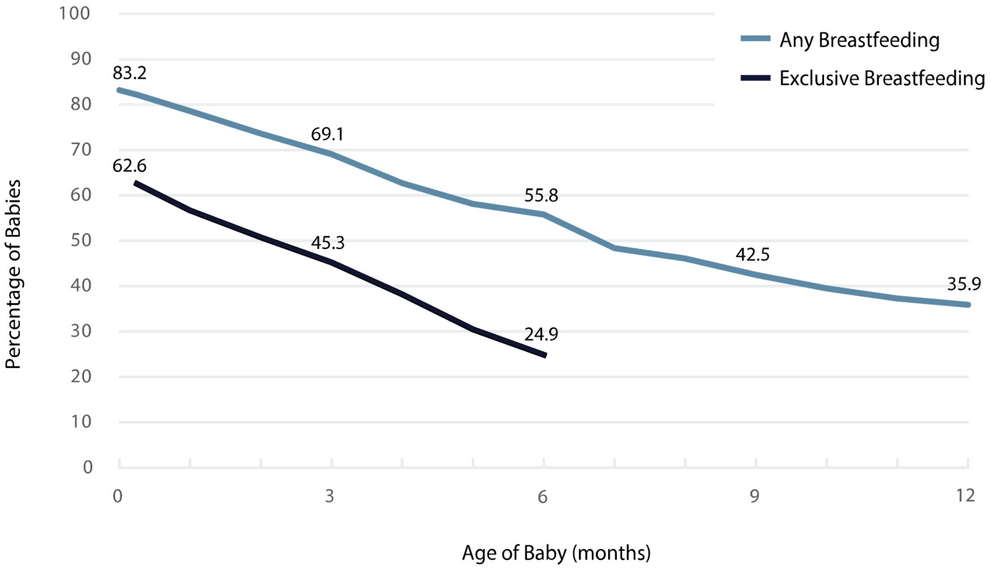


Figure 1.2: Breastfeeding percentages of any and exclusive breastfeeding in the first twelve months of life of children population born in 2019 [3].

such as high suck vacuum can lead to maternal nipple damage and laceration, and low suck vacuum can lead to poor latch and milk transfer resulting in down regulation of supply [22, 23].

1.1.2 Current Standard Care

Breastfeeding rates reached an all-time low in the 1970s when only one in four women even attempted to breastfeed [23]. In the last few decades, healthcare providers have attempted to improve breastfeeding rates through education, awareness, resources, and support [23, 24]. Specialized professionals such as lactation consultants, speech-language pathologists, and pediatricians have been integrated into medical care teams to help support mothers and infants reach breastfeeding goals and assist with breastfeeding difficulties [23]. Despite extensive efforts to increase medical access to breastfeeding support, disparities in exclusive breastfeeding rates at six months remain relatively low. Breastfeeding difficulties are attributed by a number of factors, including mastitis (breast infection), positioning, latch, infant oral dysfunction, infant failure to thrive, pain, insufficient milk, and fatigue. Figure 1.3

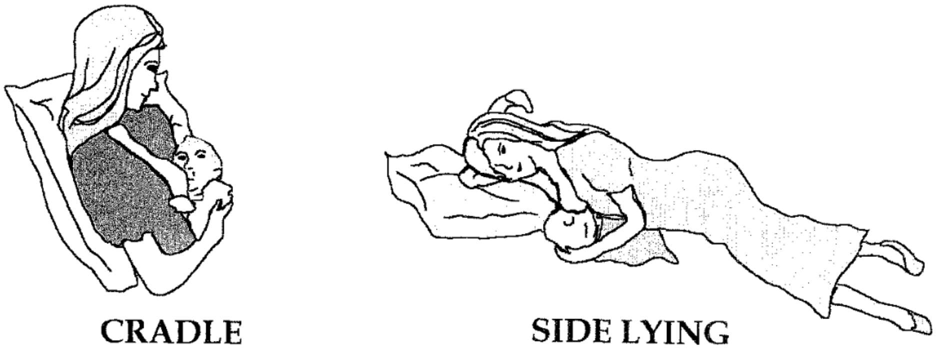


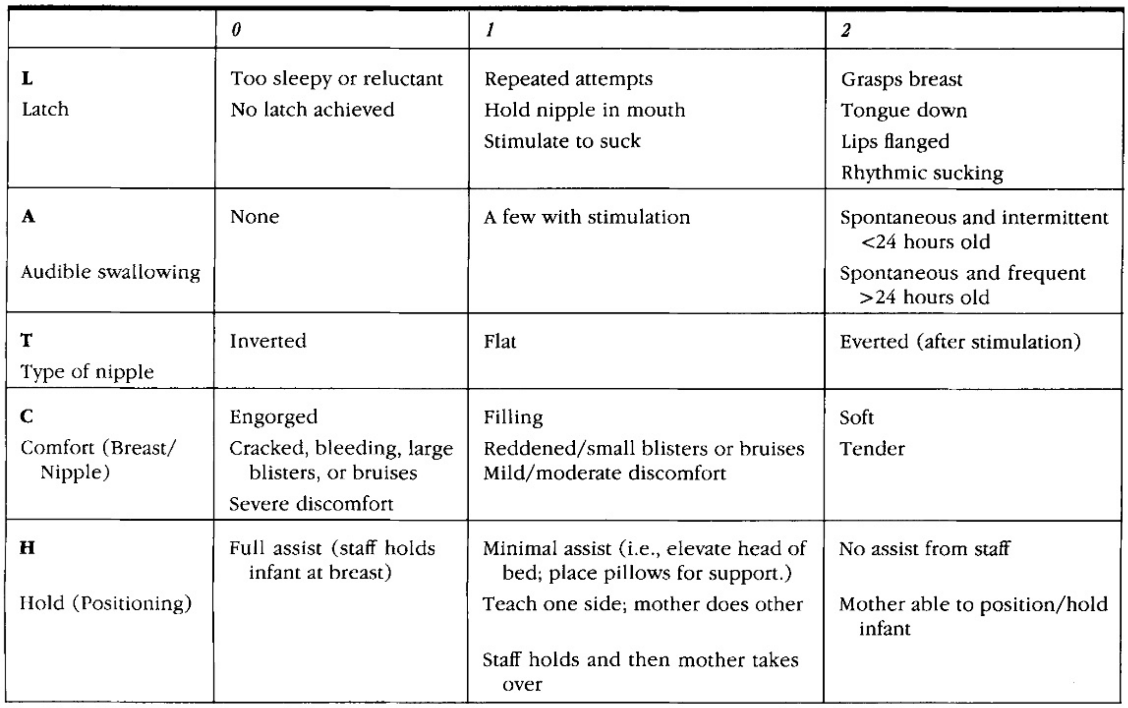
Figure 1.3: Breastfeeding percentages of any and exclusive breastfeeding in the first twelve months of life of children population born in 2019 [3].

Figure 1.4: LATCH Table to determine breastfeeding efficacy. [4].

shows two common types of feeding positions (cross cradle, side lying) among many other types such as football hold, laid back, cradle, and upright) [25]. These factors and symptoms determine if intervention should be maternal focused, infant focused, or maternal-infant dynamic. Approximately 70% of mothers experience breastfeeding difficulties, reporting particularly on pain from cracked or lacerated nipples that lead to inability to nurse, breast infection, and down regulation of milk [26, 27]. Figure 1.4 shows examples of nipple trauma that leads to persistent pain, laceration, bleeding, and inability to feed [4, 25].

1.1.3 Existing Evaluation Methods

To determine causality of pain, health professionals initially rely on observations and their clinical experience to help mothers and infants reposition and use an iterative approach to determine if certain positions can resolve the issue. Clinical assessment tools to qualitatively assess breastfeeding such as LATCH scoring system [5] have been introduced



	0	*1*	*2*
L Latch	Too sleepy or reluctant No latch achieved	Repeated attempts Hold nipple in mouth Stimulate to suck	Grasps breast Tongue down Lips flanged Rhythmic sucking
A Audible swallowing	None	A few with stimulation	Spontaneous and intermittent <24 hours old Spontaneous and frequent >24 hours old
T Type of nipple	Inverted	Flat	Everted (after stimulation)
C Comfort (Breast/ Nipple)	Engorged Cracked, bleeding, large blisters, or bruises Severe discomfort	Filling Reddened/small blisters or bruises Mild/moderate discomfort	Soft Tender
H Hold (Positioning)	Full assist (staff holds infant at breast)	Minimal assist (i.e., elevate head of bed; place pillows for support.) Teach one side; mother does other Staff holds and then mother takes over	No assist from staff Mother able to position/hold infant

Figure 1.5: Breastfeeding pain attributed by nipple laceration, fissures, or cracking. [5].

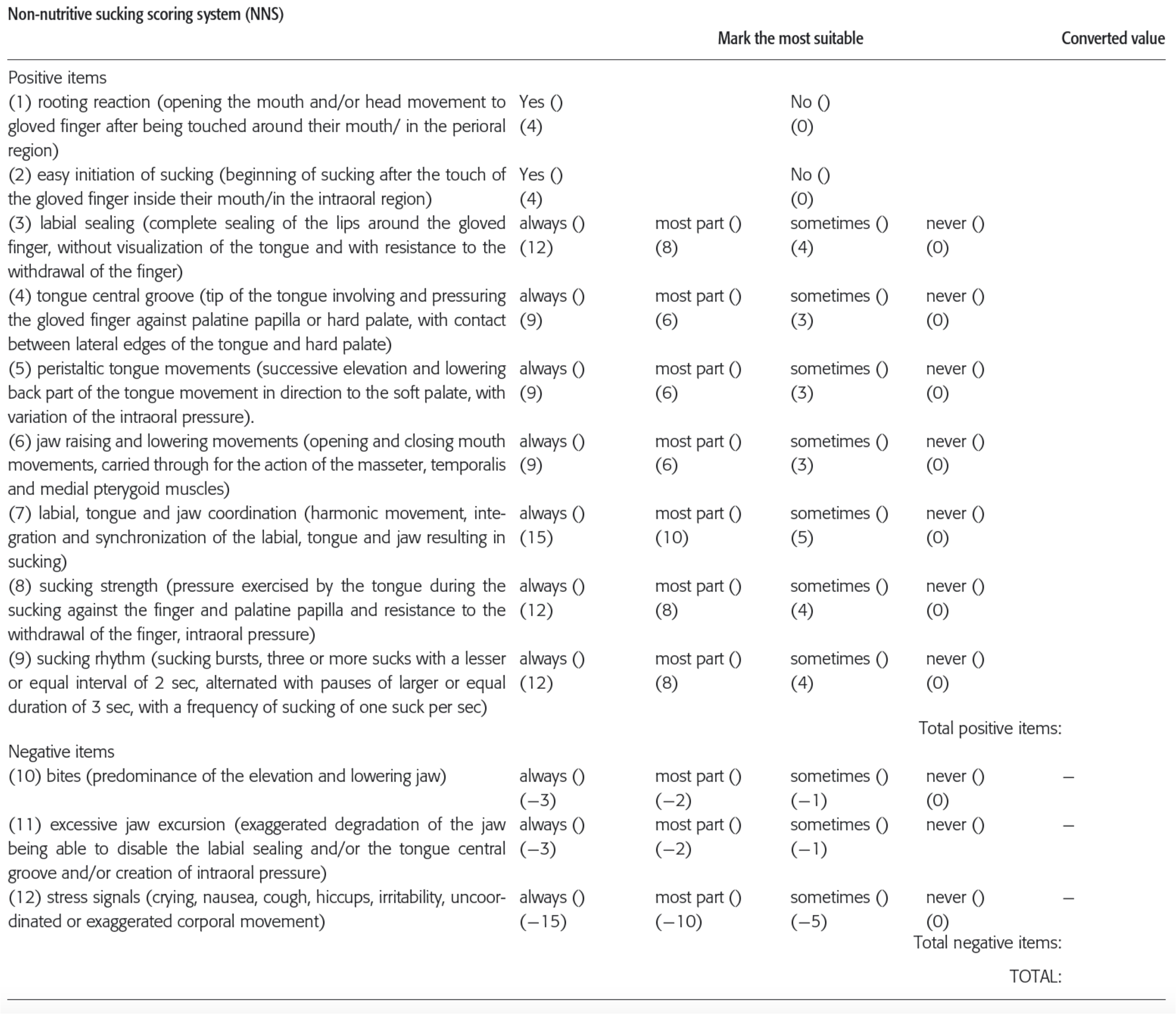
to assist practitioners. The system numerically scores 0, 1, or 2 in the five key areas of breastfeeding. A LATCH score is out of 10 and helps track improvements between breastfeeding sessions. Figure 1.5 shows the LATCH chart. LATCH acronym describes key breastfeeding characteristics:

> "L" is for how well the infant latches onto the breast. "A" is for the amount of audible swallowing noted. "T" is for the mother's nipple type. "C" is for the mother's level of comfort. "H" Is for the amount of help the mother needs to hold her infant to the breast [5].

Like many scoring systems designed to assess breastfeeding [6, 28], LATCH suffers from qualitative and subjective assessment that changes depending on a clinician's experience, consistency, and observations. In the last two decades, infant-focused intervention has risen in popularity to resolve breastfeeding pain with limited standardized objective measurement tools to guide and justify intervention strategies. Assessment tools such as the Non-Nutritive Suck Assessment Tool (using a clinician's gloved finger) [29, 30] by their nature are subjective and affect consistency, accuracy, and repeatability. Oral motor assessment in digital suck assessment method is guided by visual and tactile feedback specific to the clinician. Clinicians attempt to interpret the vacuum strength, frequency, tongue movement, seal, and rhythm as a means to determine the infant's feeding readiness or oral dysfunction. While the assessment tool attempts to qualitatively determine oral function, the approach remains subjective, inconsistent, and varies in interpretation depending on the clinician's experience. Figure 1.6 shows the Non-Nutritive Suck Assessment Tool proposed by Neiva et al. [6]. The challenge remains to provide an objective measurement capability to assist clinicians during infant-focused assessment of breastfeeding difficulties, particularly as they relate to infant suckling and coordination.

1.1.4 Non-Nutritive Suckling and Nutritive Suckling

Neurological development in a fetus at 28 weeks gestation first shows signs of suckling ability continues to evolve post-postpartum. An infant's ability to coordinate suckling, swallowing, and breathing is an essential nutritional requirement and is an indicator of their neurological development as observed in studies with premature infants [31]. Suckling patterns differ in frequency and magnitude in the presence or absence of fluid, producing two types of suckling, nutritive and non-nutritive suckling. Nutritive suckling patterns may be observed through breastfeeding or bottle-feeding using a fluid such as breast milk or formula. In non-nutritive suckling, infants suckle based on basic instinct on a pacifier, empty or uninitiated breast, finger, or object in which no fluid is transferred [32–34]. Non-nutritive suckling establishes a foundation [33, 35]. Figure 1.7 shows a schematic of infant suckling in the context of swallow and breathe coordination for non-nutritive suckling and nutritive suckling. During breastfeeding, neonates begin with non-nutritive suckling to stimulate the milk ejection reflex in mothers and switch to nutritive suckling. As observed in studies with premature infants or those with brain injury during or before birth, non-nutritive suckling is key to successful nutritive suckling due to the increased in complexity of oral motor coordination [31].



Non-nutritive sucking scoring system (NNS)

	Mark the most suitable				Converted value
Positive items					
(1) rooting reaction (opening the mouth and/or head movement to gloved finger after being touched around their mouth/ in the perioral region)	Yes () (4)		No () (0)		
(2) easy initiation of sucking (beginning of sucking after the touch of the gloved finger inside their mouth/in the intraoral region)	Yes () (4)		No () (0)		
(3) labial sealing (complete sealing of the lips around the gloved finger, without visualization of the tongue and with resistance to the withdrawal of the finger)	always () (12)	most part () (8)	sometimes () (4)	never () (0)	
(4) tongue central groove (tip of the tongue involving and pressuring the gloved finger against palatine papilla or hard palate, with contact between lateral edges of the tongue and hard palate)	always () (9)	most part () (6)	sometimes () (3)	never () (0)	
(5) peristaltic tongue movements (successive elevation and lowering back part of the tongue movement in direction to the soft palate, with variation of the intraoral pressure).	always () (9)	most part () (6)	sometimes () (3)	never () (0)	
(6) jaw raising and lowering movements (opening and closing mouth movements, carried through for the action of the masseter, temporalis and medial pterygoid muscles)	always () (9)	most part () (6)	sometimes () (3)	never () (0)	
(7) labial, tongue and jaw coordination (harmonic movement, integration and synchronization of the labial, tongue and jaw resulting in sucking)	always () (15)	most part () (10)	sometimes () (5)	never () (0)	
(8) sucking strength (pressure exercised by the tongue during the sucking against the finger and palatine papilla and resistance to the withdrawal of the finger, intraoral pressure)	always () (12)	most part () (8)	sometimes () (4)	never () (0)	
(9) sucking rhythm (sucking bursts, three or more sucks with a lesser or equal interval of 2 sec, alternated with pauses of larger or equal duration of 3 sec, with a frequency of sucking of one suck per sec)	always () (12)	most part () (8)	sometimes () (4)	never () (0)	
				Total positive items:	
Negative items					
(10) bites (predominance of the elevation and lowering jaw)	always () (−3)	most part () (−2)	sometimes () (−1)	never () (0)	−
(11) excessive jaw excursion (exaggerated degradation of the jaw being able to disable the labial sealing and/or the tongue central groove and/or creation of intraoral pressure)	always () (−3)	most part () (−2)	sometimes () (−1)	never ()	−
(12) stress signals (crying, nausea, cough, hiccups, irritability, uncoordinated or exaggerated corporal movement)	always () (−15)	most part () (−10)	sometimes () (−5)	never () (0)	−
				Total negative items:	
				TOTAL:	

Figure 1.6: Assessment tool using a clinician's gloved figure to assess infant non-nutritive suckling [6].

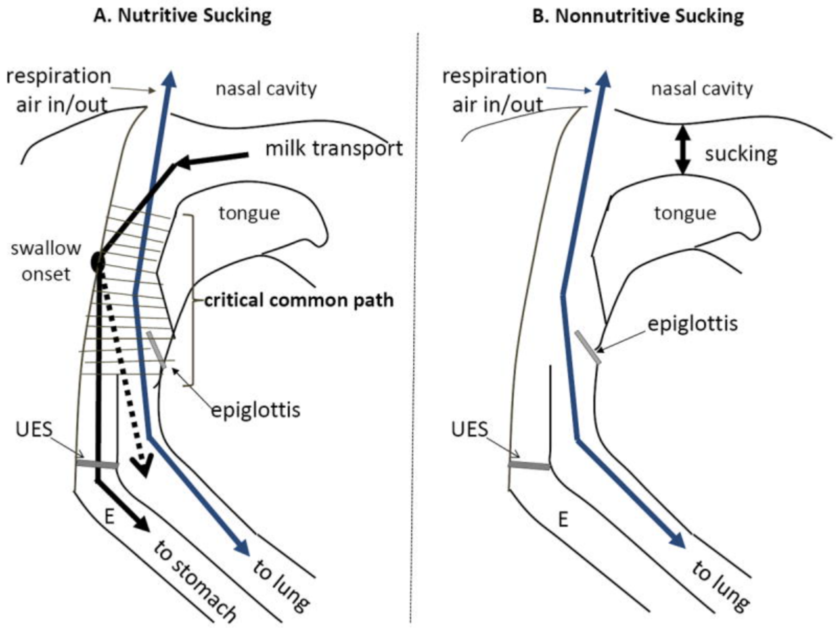


Figure 1.7: Schematic of infant suckling in non-nutritive and nutritive conditions [7].

Since the 1940s and 1950s, infant suckling was studied to better understand the underlying factors to milk transfer [31]. Infant suckling was comprised of two components: suction and compression/expression. These two components described the vacuum generated and tongue force exerted by the infant during suckling. Compression/expression pressure is caused by the movement of the tongue in contact with the hard palate. This skill was reported to develop first in a study with preterm infants with immature oral feeding behavior [7, 32, 36]. Figure 1.8 shows the oral motor development in non-nutritive suckling in preterm infants [7, 36]. In suction, infants seal their lips around the breast or pacifier and lower their jaw to increase volume in the oral cavity to generate a local vacuum. The rhythmic pattern between suction and expression characterizes the complete non-nutritive profile [32].

In 1958, Colley et al. [8] used water-filled tubes attached to manometers shown in Figure 1.9 to measure suckling and swallowing pressure changes in fourteen infants between five weeks to seven months old. The study show negative pressure magnitudes depended on the ease of milk flow in bottle-fed infants, such that suck vacuums increases as milk becomes difficult to obtain. This study reaffirmed that sucking rather than the squeezing of the teat

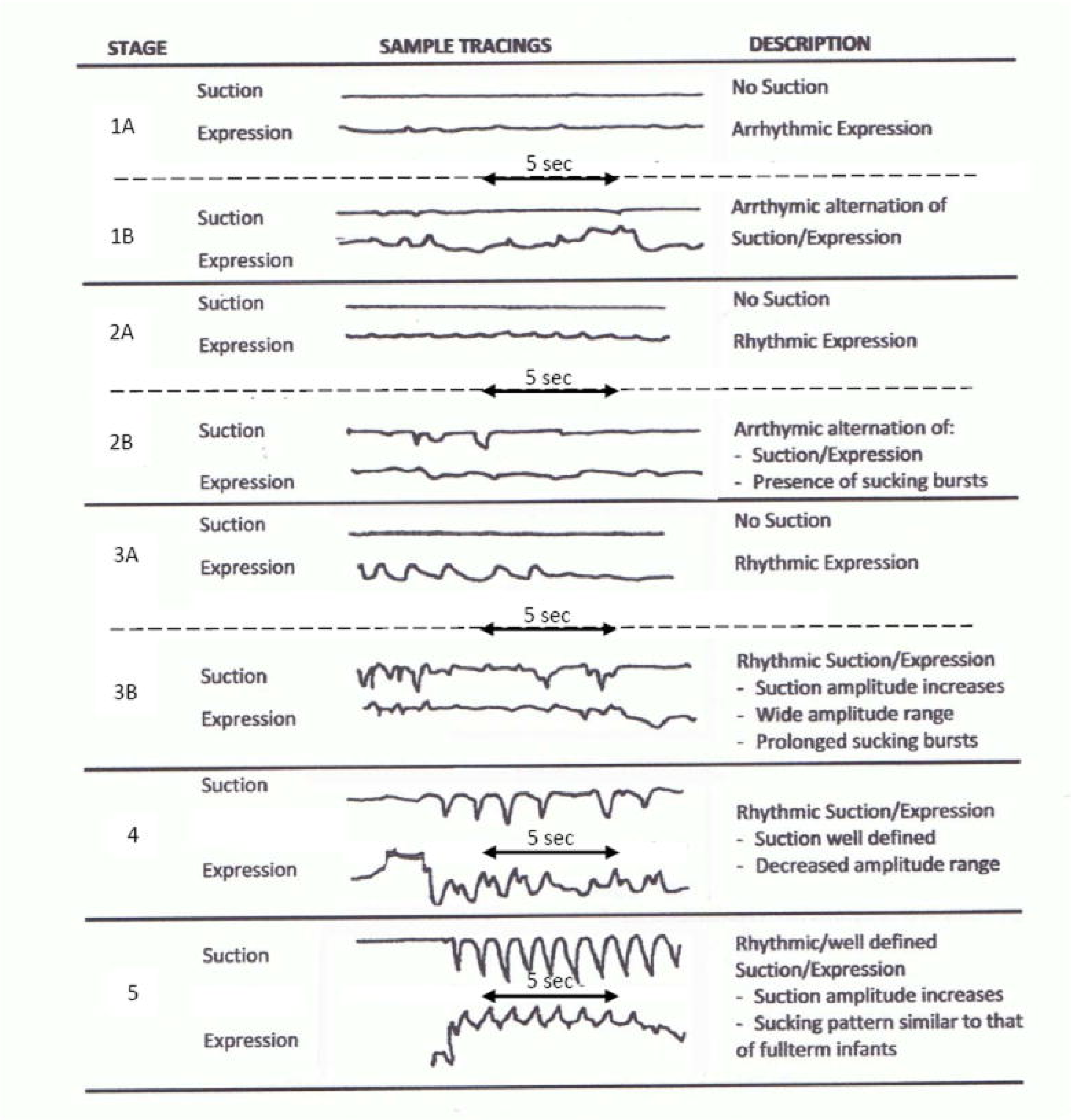


Figure 1.8: Infant suckling skills is comprised of two components: suction and expression. Studies with preterm infants show expression (force from the tongue) is developed before suction [7].

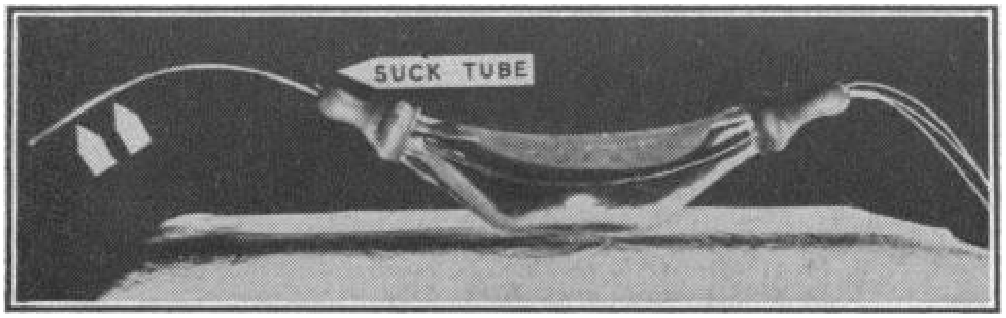


Figure 1.9: Colley et al. experimental set up for measuring infant non nutritive suck [8].

plays a significant role in obtaining milk. Subsequently, studies that followed evolved to track infant suckling as an indicator of neurological development and expand suckling parameters extracted from the non-nutritive sucking signal (suck duration, number of bursts, mean burst, etc.) [37–41]

Other studies in the last two decades through the use of ultrasound have demonstrated suckling vacuum to be an important component to milk transfer. Geddes et al. [10, 42, 43] spearheaded extensive ultrasound studies to better understand the connection between the oral movements and corresponding vacuum. Ultrasound of the infant's oral cavity breastfeeding observed fluid flow was correlated with infant tongue depression and the production of maximum vacuum. The experimental setup involved a fluid-filled feeding tube connected to a pressure transducer to record pressure changes, and ultrasound equipment placed under the infant's chin. Figure 1.11 shows the experimental set up. The study concluded that vacuum played a significant role in the removal of milk during breastfeeding. Figure 1.10 shows infant ultrasound images at various time points during suckling. Infant normal suckling exhibits a smooth and regular sinusoidal signal as indicated by ultrasound studies in conjunction with intraoral pressure measurements. While ultrasound provides a clear and objective window into infant intraoral mechanics, the methodology requires skilled technicians to read ultrasound images and ultrasound equipment to implement. As a result, ultrasound has not been adopted in the clinic widely as an objective tool for infant-focused diagnosis of breastfeeding difficulties.

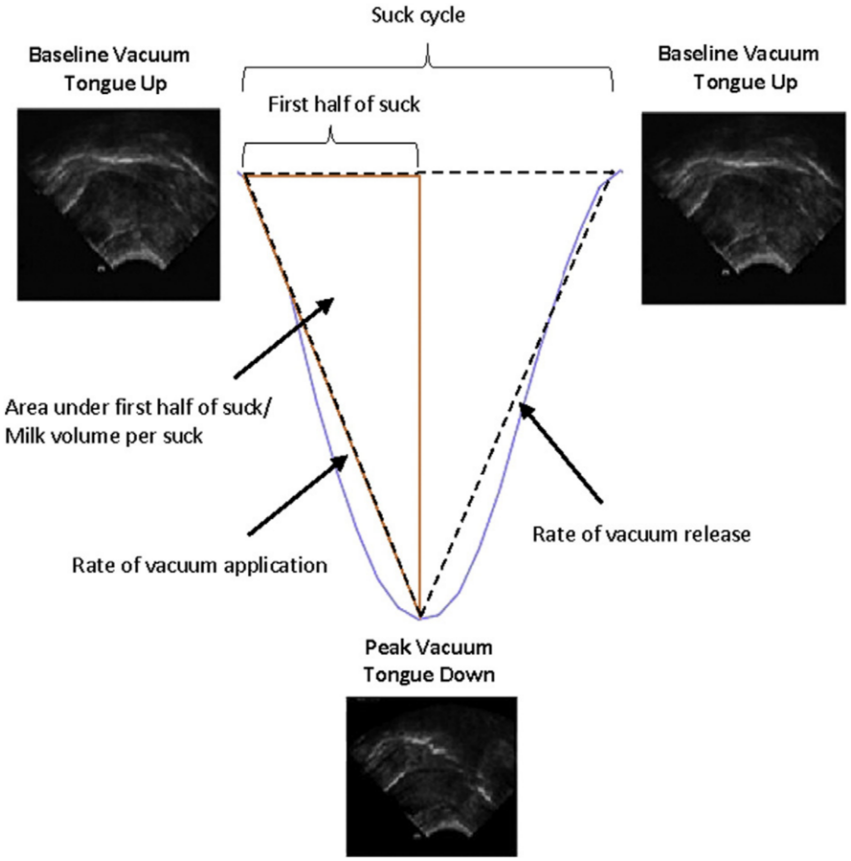


Figure 1.10: Ultrasound evaluation of infant during breastfeeding [9, 10].

Figure 1.11: Experimental configuration of intraoral measurements and ultrasound during breastfeeding [9, 10].

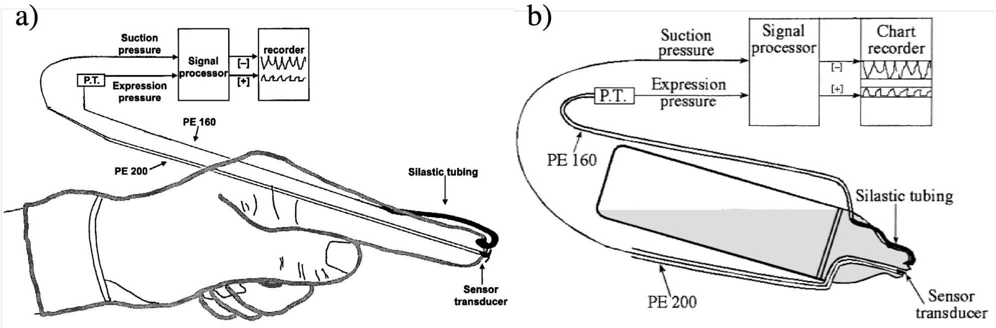


Figure 1.12: Dual sensitized catheter system proposed by Lau et al. to measure suction and expression via a) digital approach b) bottle approach. [11].

1.2 State of the Art in Non-Nutritive Suckling Measurements

To overcome the need for objective measurement instruments to measure non-nutritive suckling, many research groups have developed unique devices and systems [7, 11, 13–15, 44–56]. While devices and systems that study healthy term infants do exist, most developed instrumentation target non-nutritive suckling in preterm infants due to their inability to suckle as a result of premature neurological development.

For instance, Medoff-Cooper [37, 40] studied non-nutritive suckling to highlight the importance of abnormal neurological development indicated by premature suckling behavior and why non-nutritive sucking is an important foundation for understanding infant oral motor skills and feeding readiness.

Lau et al. [11, 36, 50] devised a dual catheter-based system connected to an index finger or bottle for sensitized digital suck assessment of both suction and expression pressures. Challenges with this approach have been described in the literature as invasive, low accuracy, and non-repeatable [57]. Figure 1.12 shows the proposed design from Lau et al [11].

The commercially available NTrainer system [58] in Figure 1.13 measures expression pressure using cantilever displacement caused by tongue force and provides pulsating stimulation to simulate NNS signal. This device focuses particularly on training and tracking

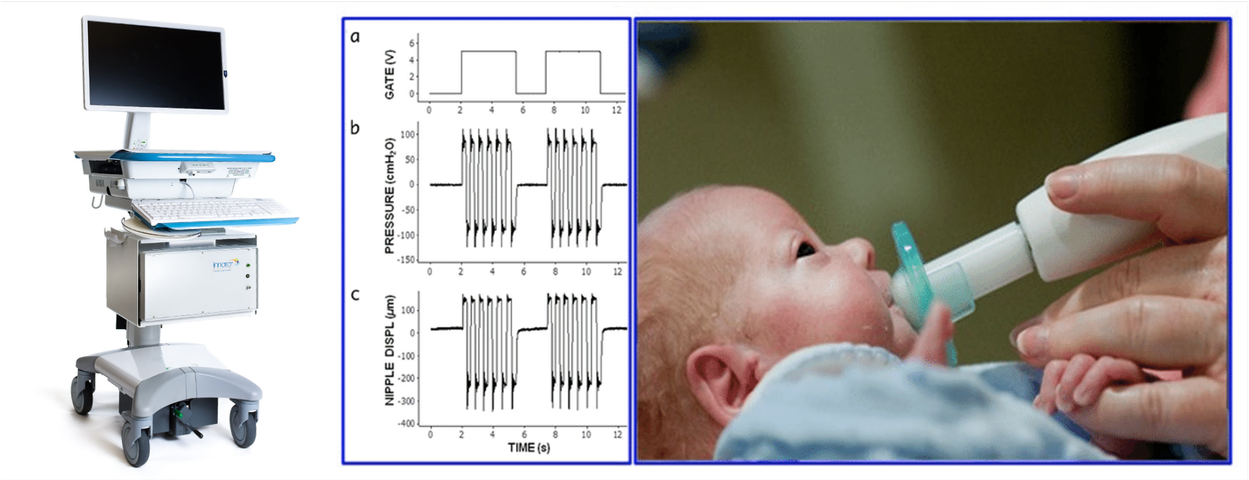


Figure 1.13: NTrainer system in use to train premature infants how to coordinate suckling [12].


[redacted]

Figure 1.14: Sensorized pacifier system proposed by Grassi et al. [13].

NNS expression pressure in preterm infants to help them attain coordinated feeding behavior and development. Challenges with this approach include the limited measurement of only expression pressure from displacement measurements, costly and bulky equipment, and the design specifically for premature infants.

In 2015, Grassi et al. [13] proposed a sensitized pacifier with dual pneumatic sensing to capture suction and expression pressures. The system is comprised of a modified pacifier with accompanying measurement software to observe the basic traces and signals of expression and suction. While the system was capable of measuring both expression and suction, no real time analysis was available for the clinician to interpret non-nutritive suckling characteristics. Figure 1.14 shows the system proposed by Grassi and Figure 1.15 shows the resulting suckling signal recorded in the study.

More compact forms of the technology emerged in recent years. Akbarzadeh et

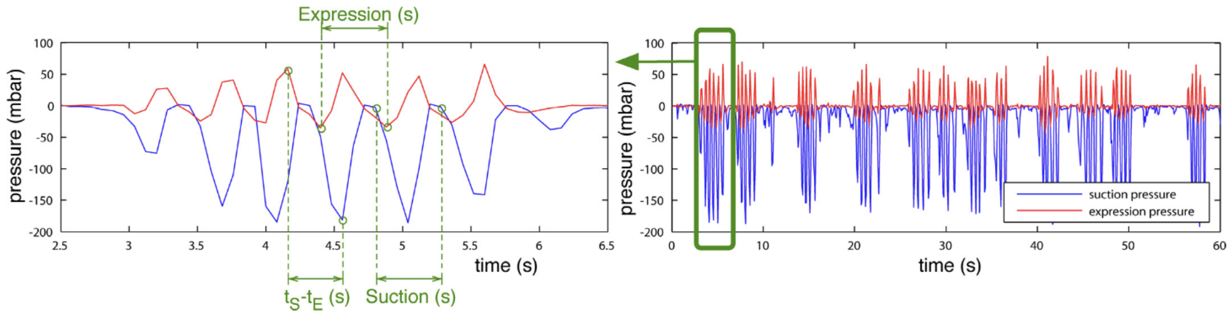


Figure 1.15: Non-nutritive suckling components of expression and suction captured by Grassi et al. measurement system [13].

Figure 1.16: Compact pacifier NNS measurement system proposed by Akbarzadeh et al. [14].

al.'s [57] development of a sensorized pacifier to predict feeding readiness in premature infants, for instance, features a custom 3D printed enclosure to hold a sensitized pacifier and custom electronics. In a clinical study of 137 infants, they collected expression and intra-oral pressures to extract suckling events. Using a logistic regression approach, features from suckling signal were used to determine if preterm infants approached normal ranges in their suckling characteristics. Challenges to their device included: the battery-based system limited the device's sampling frequency, difficulty in sterilization, and the absence of infant pacifier preferences in its design. Ebrahimi et al.'s [15] design featured similar engineering design characteristics with comparable drawbacks. Figure 1.16 and Figure 1.17 show each of the authors' proposed systems, respectively.

With devices and systems in the literature capable of measuring non-nutritive suckling, it is now well understood that non-nutritive suckling plays an important role in understanding infant neurological development and suckling abilities.

Figure 1.17: Compact NNS measurement system devised by Ebrahimi et al. [15].

Collectively, this review so far has established that (1) non-nutritive suckling sets the foundation for nutritive suckling in breastfeeding, (2) infant intra-oral vacuum is a major contributor to milk transfer, (3) devices and systems in the literature still lack the clinical adoptability for screening healthy full term infants, and (4) no objective measurement tool exists for detecting abnormal suckling behavior to determine if infant-focused interventions would likely resolve breastfeeding difficulties.

1.3 Dissertation Objective

The objective of this dissertation is to develop a non-nutritive suckling measurement system that is clinically applicable to evaluating healthy full term infants, particularly as it relates to determining the justification for intervention in infant-focused treatment for breastfeeding difficulties. Studies in this body of work shed light on clinical inconsistencies to better understand the degree of subjectivity in existing clinical assessments that affect diagnosis of infant oral dysfunction to reinforce the need for objective measurement capabilities.

1.4 Organization of Dissertation

Chapter 1 provides background information regarding breastfeeding and establishes the landscape of the technologies used to understand infant suckling.

Chapter 2 describes the proposed system for measuring non-nutritive suckling in healthy full term infants and addresses the translational parameters for clinical adoption.

Chapter 3 studies abnormal infant suckling as identified by outlier detection algorithm. Clinical studies established normative data that enable case evaluations on infant suckling characteristics, particularly those that display abnormal behavior.

Chapter 4 sheds light on clinical subjectivity by comparing clinical assessment against objective measurement data. Subjectivity is a major contributor to inconsistency and lack of accuracy in clinical diagnosis. The study evaluates how clinicians perform in various assessment methods. Additional trends found in non-nutritive suckling as it relates to parameters such as infant age are briefly discussed.

Chapter 5 summarizes the work of the dissertation and provides concluding remarks on the future of the technology and field. Suggestions to further study infant suckling and additional measurement modalities will be discussed.

1.5 Nomenclature

The essential symbols and acronyms used throughout this work are given in Tables 1.1 and 1.2, respectively.

1.5.1 Symbols

Table 1.1: Symbols used in this work.

Symbol	Meaning [unit]
f	Frequency [Hz]
A	Amplitude [mmHg]
T	Time [seconds]

1.5.2 Acronyms

Table 1.2: Acronyms used in this work.

Acronym	Meaning
NNS	Non-Nutritive Suckling
NS	Nutritive Suckling
IP	Intraoral Pressure
EP	Expression Pressure
ROI	Region of Interest
GUI	Graphical User Interface

Chapter 2

Non-Nutritive Suckling System for Real-Time Characterization of Intraoral Vacuum Profile in Full Term Neonates

2.1 Introduction

Early breastfeeding diagnostics to identify poor latch and suck are essential for timely interventions and support for the mother and infant to help reduce breastfeeding cessation. Presently, feeding clinicians and pediatricians assist mothers and infants with breastfeeding challenges, yet are constrained by the absence of instrumentation to objectively quantify suck vacuum, a key aspect of successful breastfeeding [10, 42, 59]. Existing assessment methods are essentially qualitative measurements, such as digital suck assessment using a gloved finger to determine infant suckling vacuum [60]. While more elaborate assessment scales do exist, few clinicians are trained to administer and interpret them. Due to this, both objectivity and consensus among the clinical community are lacking [61], leaving the diagnosis of breastfeeding difficulties in an ambiguous limbo and resulting in a variety of interventions that may be unwarranted (e.g. frenotomy). These difficult circumstances ultimately causes infants to undergo unnecessary surgery, putting them at risk of bleeding, pain, infection, ulceration, and other complications [62, 63].

In recent years, several devices and systems have been developed to quantify the suckling profile and oral-motor coordination of premature infants [7, 11, 13, 15, 36, 44–50]. These systems principally address the challenge of oral feeding readiness in premature infants by measuring their intraoral suction (vacuum) and expression (contact) pressure. While not posed to diagnose breastfeeding problems in full-term infants, some of these systems show promise in doing so. Grassi, et al., for example, developed a sensorized pacifier that measures suction and expression pressures using two integrated pressure transducers, displaying measurement results via a simple graphical user interface (GUI) [13]. Lau, et al., studied pressure measurements from two sensorized catheters attached to a gloved index finger [36, 50]. Ebrahimi, et al., devised a portable compact intraoral pressure measurement system that includes features such as a custom printed circuit board, wireless communication, and a rechargeable battery [15]. The FDA-approved NTrainer by Capilouto, et al., measures the displacement of the tongue (expression pressure) and incorporates pneumatic actuation to help facilitate infant oromotor skills [49, 64]. Geddes et al., utilizes ultrasound along with pressure transducers to correlate vacuum characteristics to milk intake during nutritive sucking [10]. These devices, along with many others [7, 11, 13, 15, 36, 44–50] proposed in the literature, all reflect an effort to provide objective quantification of infant intraoral vacuum.

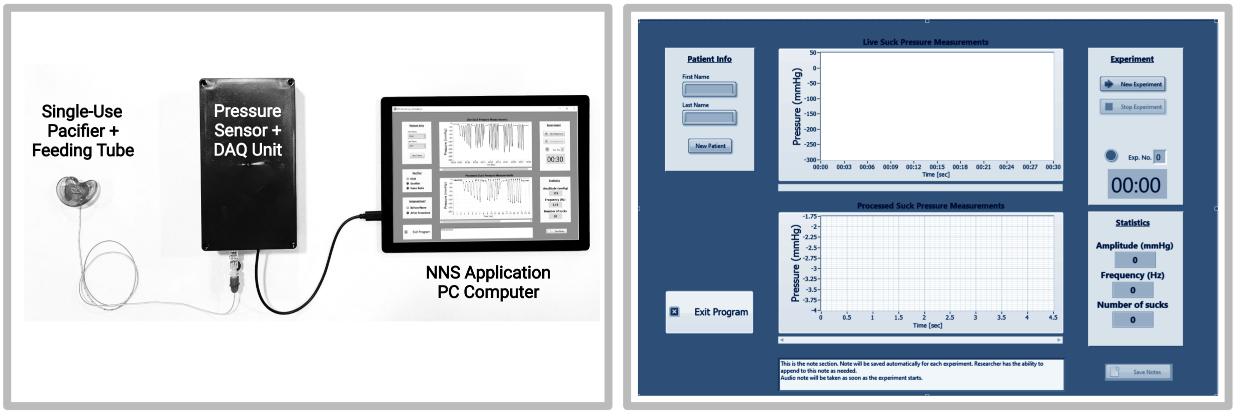
Despite many studies addressing training and coordination of non-nutritive suck in premature infants, very few in the literature have emphasized the development of instrumentation aimed to assess healthy newborn infants experiencing breastfeeding difficulties. While technologies of similar function and purpose dating back over two decades do exist, they have not yet emerged to change medical practices due to their problems with clinical adoptability and measurement reproducibility [36, 65, 66]. As a result, subjective metrics to identify oral dysfunction, such as ankyloglossia, remain widespread and controversial in the clinical community while breastfeeding rates remain low [61]. As intraoral vacuum is well recognized to play a key part in infant suckling and milk removal, our aim is to address the need for screening instrumentation to assess infant non-nutritive suckling (NNS) vacuum) [67].

In this paper, we report on the design of a non-nutritive suckling (NNS) system to measure and analyze intraoral vacuum of full-term neonates in real-time. Our system considers factors important in translation to clinical use, including real-time analysis with immediate feedback to the clinician, ease of use, measurement accuracy and repeatability, and accounting for variability in infant suckling preferences. Our system design provides an objective alternative to the standard digital suck assessment. Specifically, we measure in full term infants the suckling vacuum to extract the following objective micro-structure parameters: the mean and maximum vacuum amplitude, suckling frequency, number of suckling events per burst, burst duration, and number of bursts per minute. Our findings show that the infants' intraoral profile produce distinctive vacuum responses that can in turn be used to identify orofacial issues. We categorize these signals and provide a framework for studying oromotor dysfunctions in future studies.

2.2 Materials and Methods

2.2.1 Clinical and Technical Requirements

To develop a robust system that is feasible for clinical use, our design approach for the NNS system considers its utilization and interaction with both clinicians and infants. Key parameters of the sensing system, described in Table 2.1, and the configuration of the components were considered as a part of the design of the NNS system to ensure clinical feasibility. Table 2.1 also summarizes the design requirements for our proposed system based on the advantages and drawbacks of existing systems reported in the literature.



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Audio note will be taken as soon as the experiment starts.

Figure 2.1: Image of the NNS system design with four major components: a modified pacifier, pressure sensor, data acquisition board, and a custom software interface. The design considers the intended clinical use and ease of adopting the system.

2.2.2 NNS System Hardware

To achieve these design requirements, we developed an NNS system that is comprised of four main components: a single-use modified pacifier, a pressure sensor, a data acquisition unit, and a custom-made software interface (Fig. 2.1).

The pacifier component was fabricated using a commercial teat (Orthodontic Pacifier, NUK) integrated with a 36-inch 5 fr non-collapsible feeding tube (Kangaroo Neonatal & Pediatric Feeding Tube, Covidien). The air in the tubing has significantly affected sensitivity of other devices in the literature that use large volume tubing. We utilize a very narrow tubing (5 fr outer diameter, 1 mm inner diameter) to reduce the total volume of air that can be compressed in the system. This helps us avoid the adverse vacuum measurements seen in other devices: it minimizes the air volume but is large enough to avoid boundary layer losses and drag. Furthermore, 36-inch tubing was the desired length to provide sufficient slack length for clinician and infant during measurements. While this teat was selected for its shape and fit with the infants' oral anatomy [68], the modularity of the system permits quick substitution with any pacifier shape and type preferred by the infant. To integrate the feeding tube with pacifier, a 1-mm diameter biopsy punch was used to create an opening at the tip of the pacifier and the feeding tube was passed through the opening. Next, 0.1 mL

Table 2.1: Design parameters considered in the NNS system to meet clinical and engineering requirements needed for clinical feasibility.

Design Requirements	
Ease of use	Hardware and software must be intuitive for clinicians to use and manage with minimal training
Biosafety	Components in direct contact with saliva, bodily fluids and oral cavity must be sterilized before use and must be sterilized or disposed after each use
Adaptability	Infant pacifier preferences may vary; suckling unit must be versatile in adapting to various pacifier types
Biocompatibility	Components interfacing with infant must meet biocompatibility safety requirements
Electrical Safety	Electrical components must operate within International Electrotechnical Commission (IEC) safety limits
Accuracy	Pressure sensing unit dynamic range must be able to measure physiological range of intraoral vacuum of infants (0 mmHg to -400 mmHg)
Repeatability	System measurements must be repeatable as needed to track infant vacuum over time

of polydimethylsiloxane (Sylgard 184, Dow Corning), a biocompatible and inert non-toxic silicone was used to hold the feeding tube in position at the pacifier's tip. The silicone was mixed at a 20:1 ratio to produce a nearly gel-like elastic material to mimic the pacifier material, and the volume used was the minimum amount required to hold the feeding tube in place at the tip, leaving the majority of the pacifier and its tip empty. This helped us avoid altering the original stiffness characteristics of the pacifier. The silicone was cured in a 50°C oven for 8 hours. Once integrated, the modified pacifier was cleaned with water and mild soap and dried. The unit was bagged and sterilized under 275 nm ultraviolet light (Sterilizer and Dryer, VANELC) for 35 minutes. The bio-compatibility and safety of the modified pacifier was considered in the design. We limit infant exposure to any unknown materials and only consider those that are accepted or widely used. A silicone pacifier (commercially available) integrated with a medical-grade PVC feeding tube are the only materials in contact with the infant, ensuring biocompatibility and safety. In circumstances where the infant rejects the pacifier or has a known allergic reaction to the pacifier material, the pacifier can be substituted for any preferred pacifier such as the Soothie (Philips AVENT, Tucson, AZ), a standard pacifier used in hospitals.

A piezoresistive pressure sensor (MPX5100AP, NXP Semiconductors, Eindhoven, Netherlands) was selected with an operating range of 110–860 mmHg (absolute) to fit the application and system design requirements of neonatal suckling dynamic range. The intraoral vacuum of typical neonates during suckling has been reported to be 375–825 mmHg [13, 59]. The sensor was calibrated against a pressure gauge at various vacuum conditions to verify the manufacturer's reported specifications [69]. Once we verified its accuracy and repeatability, the sensor was electronically configured to begin measurements. To acquire intraoral vacuum measurements, the pressure sensor was directly connected to the modified pacifier and feeding tube. A data acquisition board (myDAQ, National Instruments, Austin, TX) collected the pressure measurements and was sent to a computer with a graphical software interface (LabVIEW, National Instruments) for simple analysis and data visualization by the clinician. The sampling frequency was set to 1000 Hz to sample at a greater rate than the suckling frequency, which is reported in the literature to be within the 1.5 Hz to 2.5 Hz range [13, 70]. The maximum output voltage in the device is 5 VDC, well below the standard limit for contact with a human ($\sim$ 30 VDC). Moreover, the maximum current available in the device is about 2 mA. These aspects make the device intrinsically safe according to IEC standards 61140, 60364, 61010-1, and 60479. The data acquisition board and sensor were entirely contained in an insulated box without possibility of making contact with the infant.

The pacifier and feeding tube unit connected to the pressure sensor through a quick connect luer lock allowing for ease of use. The design considers the clinical workflow as follows. To use the unit, a clinician would (1) connect the hardware to a computer via USB, (2) open the NNS software, (3) open a new pacifier unit, (4) connect the pacifier tubing to the hardware, and (5) press `start experiment` to collect data. All of this can be done in less than a minute with minimal training. Finally, since the components are relatively low cost, we designed the system such that the pacifier-feeding tube unit is single-use (disposable) to minimize both cross-contamination of fluids such as saliva between patients and the need to clean or sterilize the device after each measurement. The disposability and quick connect/disconnect design features helps facilitate the integration of the device into the fast-paced clinical workflow and allows the clinician to quickly test patients as a part of their routine examination schedules.

2.2.3 Hardware Calibration

Each NNS measurement device used in the clinical sutdy was placed inside a vacuum chamber (BACOENG) with a digital pressure gauge (AshCroft) connected. Vacuum inside the chamber was set to twelve levels in the range of -600 mmHg to 0 mmHg (gauge) using a vacuum pump. The calibration range was chosen to reflect the physiological range of NNS and the experiment was used to verify the accuracy within this range. At each vacuum level, pressure measurements from the digital gauge (control) and from the NNS measurement device were recorded. Figure 2.2 shows the calibration line for each device fabricated for the clinical study. The calibration data shows all four NNS devices were ablre to measure sub ambient pressure in the range of -600 mmHg to 0 mmHg with high accuracy. The RMS errors were calculated to be 2.1 mmHg, 3.5 mmHg, 2.9 mmHg, and 3.0 mmHg for each of the devices, respectively.

2.2.4 System Software Design and Signal Processing

The NNS system software is designed to record, process, and display intraoral vacuum measurements for the clinician to see while the data collection is underway. This allows clinicians to utilize information for rapid diagnosis and dynamically adjust to retake measurements as needed. Table 2.2 summarizes the key software features that enable rapid diagnosis in a clinical setting.

The NNS application was designed and built using LabVIEW, a graphical programming environment. The custom program was packaged into an executable application that can be deployed on any PC that is readily available in the clinic without the need of the native LabVIEW software. This allows for ease of adoption and reduces barriers to entry. The NNS app was designed with an intuitive user interface where the clinicians can enter patient

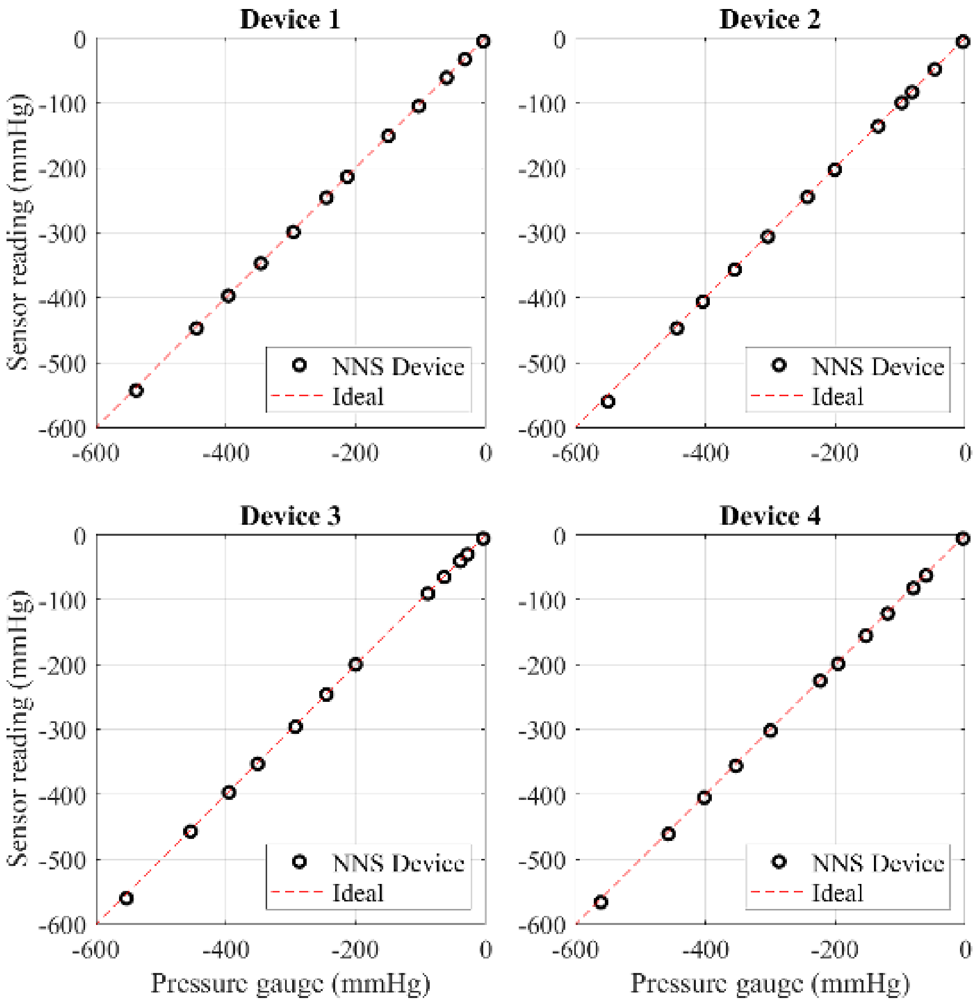


Figure 2.2: Calibration graphs for each of the four NNS devices used in the clinical study. The graphs show a linear relationship between sensor reading and gauge reading.

Table 2.2: Software features and capabilities of the NNS application. Its design focuses on the clinical needs of the medical professional in a clinical breastfeeding assistance setting.

Real-Time Data	Vacuum measurements are collected and shown on the computer screen in real time as the pacifier is used by the patient. Clinicians can adjust and continue measurements, end the experiment, or restart measurements for the same patient.
Immediate Analysis	Once measurements are completed, the software algorithm will automatically compute the characterization parameters such as the max amplitude, frequency, number of sucks, and burst duration for the entire profile.
ROI Analysis	Clinicians can utilize the interface to segment the data for analysis in specific regions of interest (ROI) of the vacuum profile. The characterization parameters are automatically recalculated and displayed.
Note Taking	Audio recording is automatically started for clinicians to record any verbal notes during testing. Written notes are also featured and automatically saved with raw data files corresponding to the patient.

information, start (or stop) experiments, and view the pressure profile and key metrics in real time. Clinicians may also magnify regions of interest for closer inspection and analysis of the shape of the suckling signal. Region of interest analysis is an important feature due to the unpredictability of infant behavior that may be disruptive during vacuum measurements. To isolate abnormalities caused by disruptions, clinicians can perform analysis on specified regions immediately after a test.

2.2.5 Signal Acquisition and Processing

The software begins by calibrating the sensor to remove any baseline drift caused by the sensor. The clinician proceeds to insert the pacifier in the infants mouth to collect NNS data. Should there be difficulty, the clinician can restart the measurement as desired. Once the signal is acquired, characterization is performed automatically by the software.

NNS signal characteristics such as mean suck vacuum, max suck vacuum, frequency, burst duration, bursts per minute, sucks per minute, and sucks per burst can be extracted from the suckling profile. Figure 2.3 shows the flow chart for analysis of the NNS characteristics. Real-time analysis provided by the graphical interface software LabVIEW provides the clinicians with immediate characteristics of NNS signal. Post-processing in MATLAB was

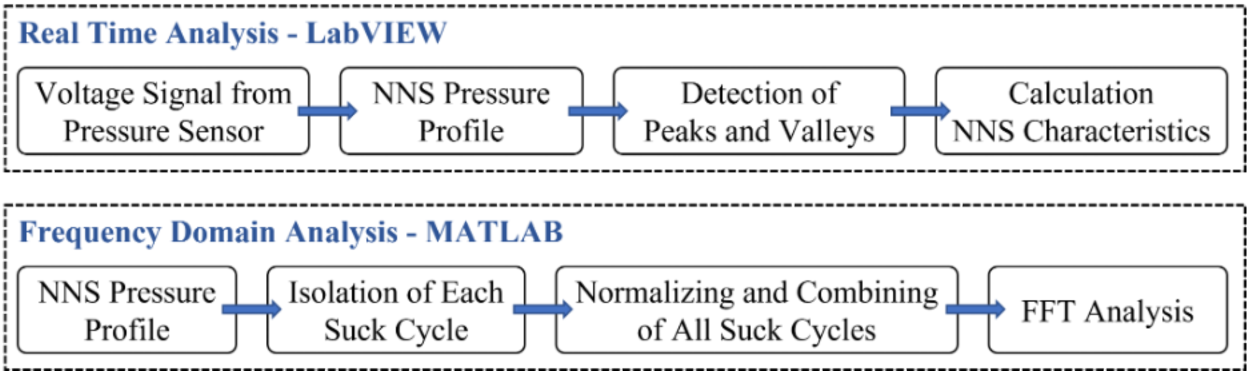


Figure 2.3: Flow chart of NNS characteristic extraction and analysis.

Table 2.3: The features extracted from the suckling signal by the NNS software and which help to characterize the infant's suckling.

Mean Suck Vacuum	Average amplitude within ROI
Max Suck Vacuum	Maximum amplitude within ROI
Frequency	Number of sucks per second
Burst Duration	Duration of a cluster of sucks between rests
Bursts per Minute	Average number of clustered sucks per minute
Sucks per Minute	Average number of sucks per minute
Sucks per Burst	Average number of sucks across all burst events within one recording session

performed to closely analyze additional features such as suckling shape and compile the normative data. Table 2.3 describes the parameters extracted from the NNS signal.

The analysis sequence of the app begins with the detection of peaks and valleys for the full suckling profile. During an experiment, as the infant sucks on the pacifier, the voltage signal from the pressure sensor is collected using the data acquisition unit at a sampling frequency of 1000 Hz and sent to the LabVIEW program on the computer for analysis. This voltage signal is first mapped to a pressure signal, in mmHg, using the sensor calibration information:

$$Pressure = \frac{\frac{V+0.7}{5} - 0.04}{0.009} * 7.5 - 760 \tag{2.1}$$

Next, the pressure data is passed through a peak detector algorithm (Peak Detector.vi) to extract locations and amplitudes of each of the peaks and valleys. Referring to Fig. 2.4, a threshold value of 10 mmHg is set for the minimum amplitudes of the valley, which represents the smallest suck vacuum that would be classified as a suck cycle. Also, a threshold value of 200 ms is set for the minimum distance between two peaks/valleys, which represents the minimum time spam between two consecutive sucks. In other words, the minimum amplitude of a suck cycle is set at 10 mmHg and the maximum suckling frequency is set at 5 Hz. These cut-off values are based off of other systems reported in the literature [71, 72].

The amplitudes of all the peaks and valleys, A_{peak}, A_{valley}, and their locations, t_{peak} and t_{valley}, are next used to determine the NNS characteristics. A burst is defined as two or more consecutive suck cycles with a minimum rest period of one second between bursts [54]. From the NNS profile, other characteristics can be extracted. The suck amplitude is defined by the average measured amplitude of the infant's vacuum placed upon the pacifier over the trial. The time period between two successive valleys of locally maximum suck vacuum are collected over all the suckling events and used to calculate the average suck frequency, both for each burst and for the entire trial. Equations defining the suckling characterization parameters are listed below:

$$Number\ of\ Sucks = n = number\ of\ valleys \tag{2.2}$$

$$Amplitude\ of\ a\ Suck = A_i = A_{peak(i)} - A_{valley(i)} \tag{2.3}$$

$$Mean\ Amplitude = A_mean = \sum \frac{A_i}{n} \tag{2.4}$$

$$Maximum\ Amplitude = A_{max} = max(A_i) \tag{2.5}$$

$$Burst\ Duration = T = t_{peak(n)} - t_{peak(1)} \tag{2.6}$$

$$Mean\ Suck\ Cycle = t_{mean} = \frac{t}{n} \tag{2.7}$$

$$Frequency = f = \frac{n}{T} \tag{2.8}$$

An interactive cursor allows the clinician to extract these features for a specific region of interest (ROI). The application automatically updates values as the clinician selects different ranges of the measured data via the graphical user interface. Figure 2.5 shows the custom interface with NNS signal and analysis displayed. This enables the clinician to focus on specific time points or ROIs in the suck profile for a closer analysis.

2.2.6 Clinical Testing and Protocol

Thirty healthy term newborns (gestational age: 37–42 weeks) under 30 days of age were recruited from both the UC San Diego Health Department of Otolarngology's Center for Voice and Swallowing and the Pediatrics Department. The infant inclusion criteria for the study were: (1) infants 4–30 days old (critical period to establish breastfeeding); (2) healthy; no significant birth or post-partum complications; and (3) no known allergy to silicone or

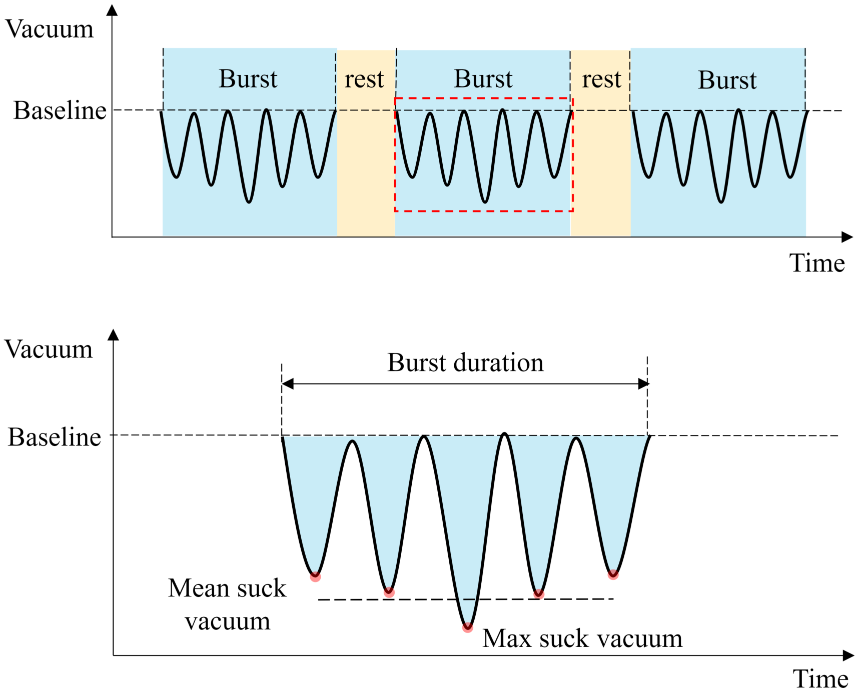
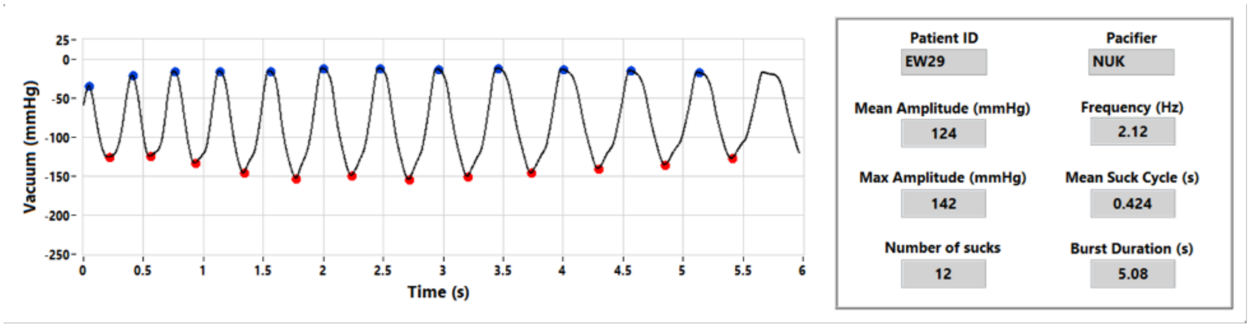


Figure 2.4: Illustration of a typical intraoral vacuum waveform labeled with characterization parameters.



Patient ID	Pacifier
EW29	NUK
Mean Amplitude (mmHg)	Frequency (Hz)
124	2.12
Max Amplitude (mmHg)	Mean Suck Cycle (s)
142	0.424
Number of sucks	Burst Duration (s)
12	5.08

Figure 2.5: Real time analysis of the NNS signal is performed using the custom LabVIEW algorithm and the information is displayed for the clinician. A typical window contains information about suck vacuum, frequency, number of sucks and burst duration.

elastomers typically used for pacifiers and bottle nipples. The study aimed to measure infant suckling vacuum using the NNS system to establish a norm for sucking signal characteristics. Testing occurred during a lactation consultation visit (Center for Voice and Swallowing) and during outpatient pediatric visits (UC San Diego General Pediatrics). Approval from the Institutional Review Board at UC San Diego (IRB 800070 approved 13 September 2021) was obtained before recruitment started. Parents were informed of the nature of the study and consented before the experiment began. Infants underwent a routine weight and physical exam. After an initial routine evaluation, infants were offered the NNS system pacifier. Before the start of measurements, the infant's seal around the pacifier was verified to be secured and established. Inadequate seal can be observed through the infant's contact with pacifier and an observable abrupt loss in vacuum. If the seal was determined to be inadequate, the measurements were repeated. The intraoral vacuum was recorded for a duration of 60 seconds.

2.3 Results

Figure 2.1 shows the final and complete NNS system. The results from the clinical study validate the ability of the NNS system to measure intraoral vacuum. Clinicians utilized the system with minimal training and were able to incorporate the system into their workflow. The characteristics described in Table 2.3 were collected over 60 seconds. Figure 2.6 is a representative snapshot of a typical infant intraoral vacuum profile, including the details of a particular burst event. Table 2.4 summarizes the parameters extracted from the cohort of 30 infants' suckling data. Values extracted are comparable to those previously reported in the literature, both during NNS [13, 66, 71] and breastfeeding [73] as shown in the table, demonstrating the systems' ability to capture intraoral vacuum over time.

Upon closer inspection of the suckling signals by magnifying a suckling burst, we observe subtle differences in the vacuum transducer's signal. Figure 2.7 shows signals representative of the three distinguishable profiles found in the NNS signal of the thirty

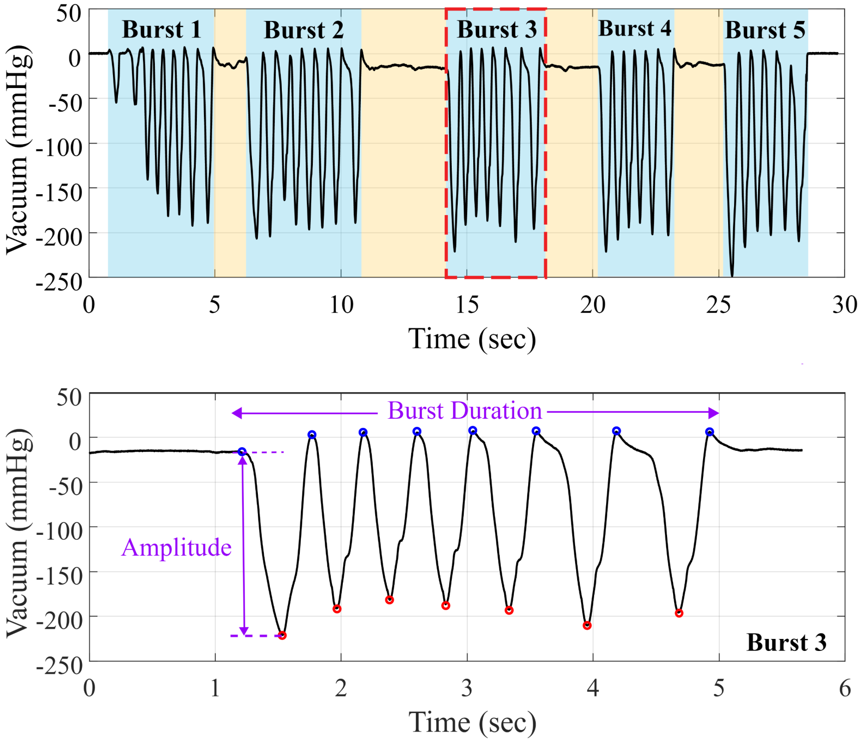


Figure 2.6: An example of a suckling signal generated by an infant utilizing the modified pacifier (left). The figure on the right shows an example of a region of interest (a zoomed in of Burst 3) generated from the NNS software.

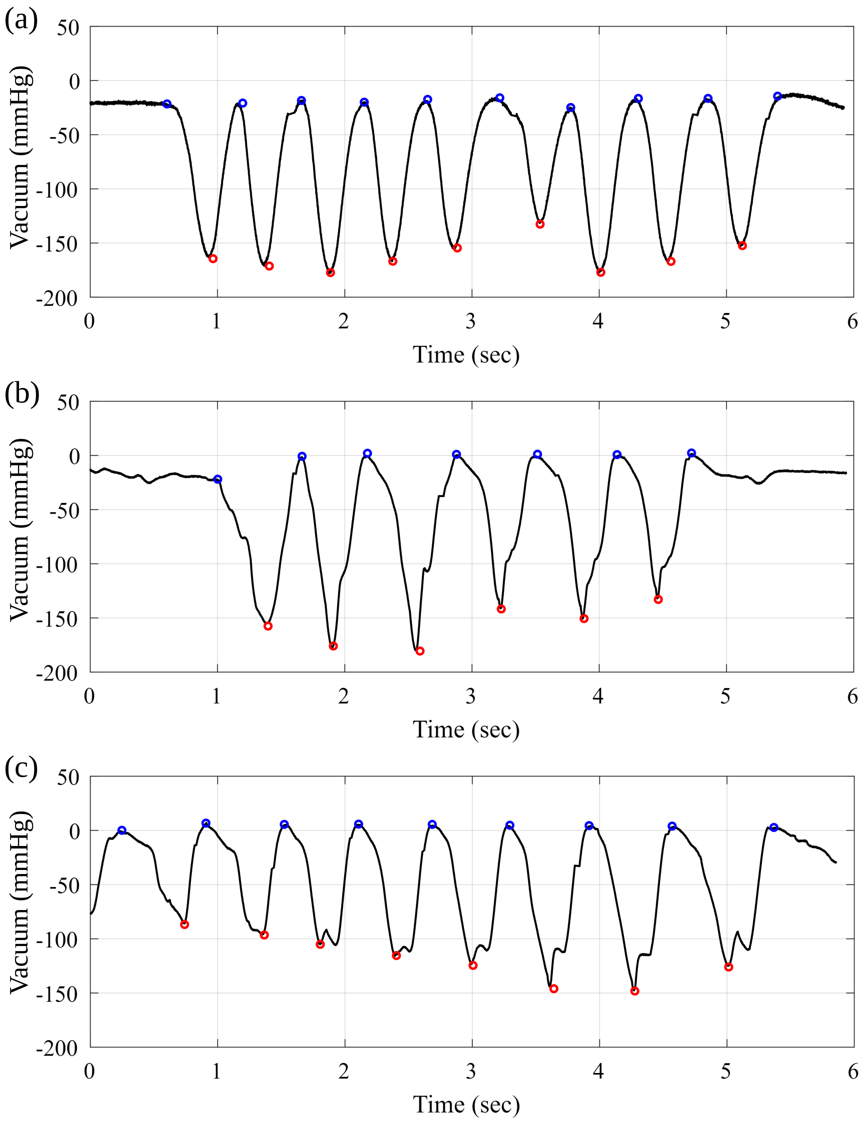


Figure 2.7: Three distinguishable profiles appear in the NNS suckling signal of 30 infants: (a) group 1: smooth sinusoidal, (b) group 2: sharp valley, and (c) group 3: double valley. This figure shows representative examples of NNS signal from each group.

Table 2.4: A summary of results comparing extracted parameter values collected in this study and those reported in the literature.

Parameters	This Work	Grassi [13]	Zimmerman [71]	Prieto [73]
Number of subjects	30	9	16	17
Mean suck vacuum (mmHg)	118.6 (30.8)	-	64.6 (22.9)	50 (5.7)
Max suck vacuum (mmHg)	143.6 (32.2)	164.1 (38.6)	-	197 (10)
Frequency (Hz)	2.01 (0.37)	-	2.16 (0.35)	-
Sucks per burst	8.8 (5.5)	6.9 (1.0)	5.6 (3.1)	-
Burst duration (sec)	4.4 (3.0)	2.9 (0.6)	2.5 (1.4)	-
Sucks per minute	70.7 (16.9)	-	28.1 (25.6)	52 (26)
Bursts per minute	7.2 (3.1)	9.3 (2.1)	4.1 (2.7)	-

infants tested. We classify the three shapes as: smooth sinusoidal, sharp valley, and double valley. While the factors contributing to these varying shapes are not yet known, we group the cohort of infant profiles into three groups corresponding each of the three shapes. Figures 2.8 and 2.9 graphically illustrate the statistical differences between each group based on their characteristics.

In our statistical analysis, classified the shape of the profiles into three main categories: smooth sinusoidal (18 neonates, 106 bursts), sharp valley (10 neonates, 53 bursts), and double-valley (2 neonates, 14 bursts). Histograms of the NNS parameters from the three groups are shown in Figure 2.9. It can be observed in Figure 2.9 (a-c) that the distributions of mean suck vacuum, max suck vacuum, and frequency are normally distributed. This was confirmed using the Shapiro-Wilk normality test. We then performed 2-sample Welch's t-tests, which requires that data to be normally distributed, on the these parameters across the three groups to find any statistical differences between the groups. The results are shown in Table 2.5. There were several statistically significant differences in mean suck vacuum, max suck vacuum and frequency between the three groups. There were no significant differences observed in burst duration and number of sucks per burst. These profile characteristics persist throughout the entire suckling signal of each infant. If the infant displays a signal shape corresponding to a sharp valley, we can observe this pattern throughout the entire suckling profile.

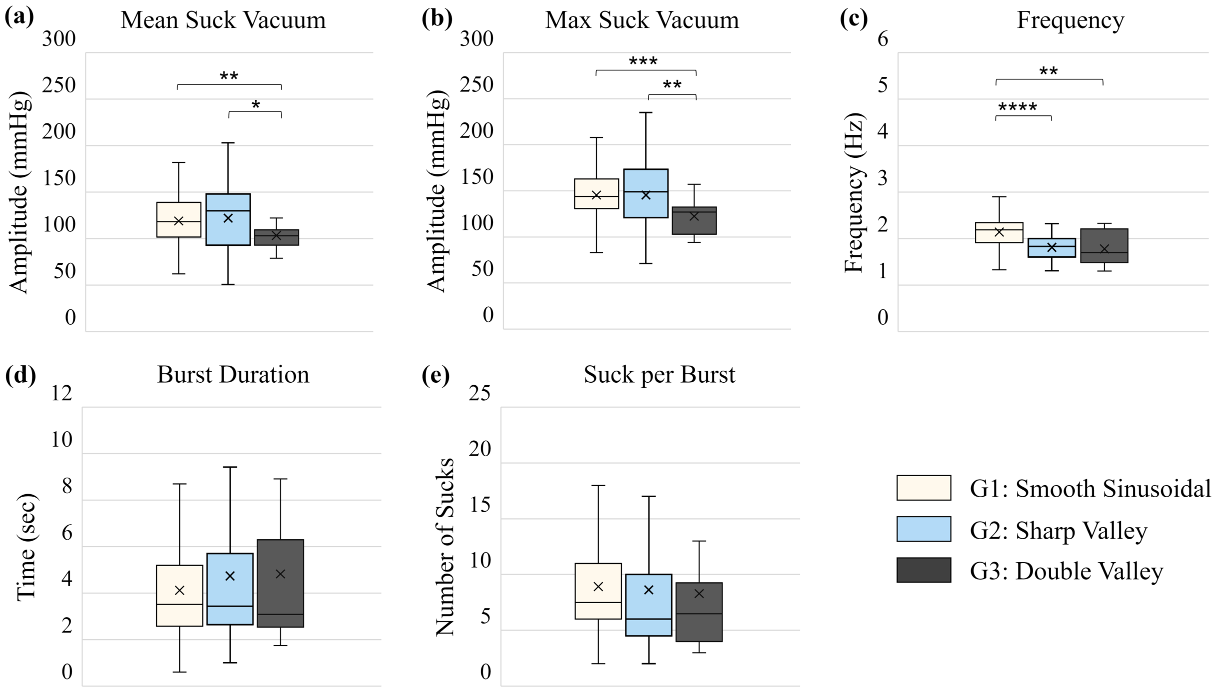


Figure 2.8: Box and whisker plots comparing the extracted parameters from three classified groups. We observe statistically significant differences between groups 1 and 3 across mean suck vacuum, maximum suck vacuum, and frequency.

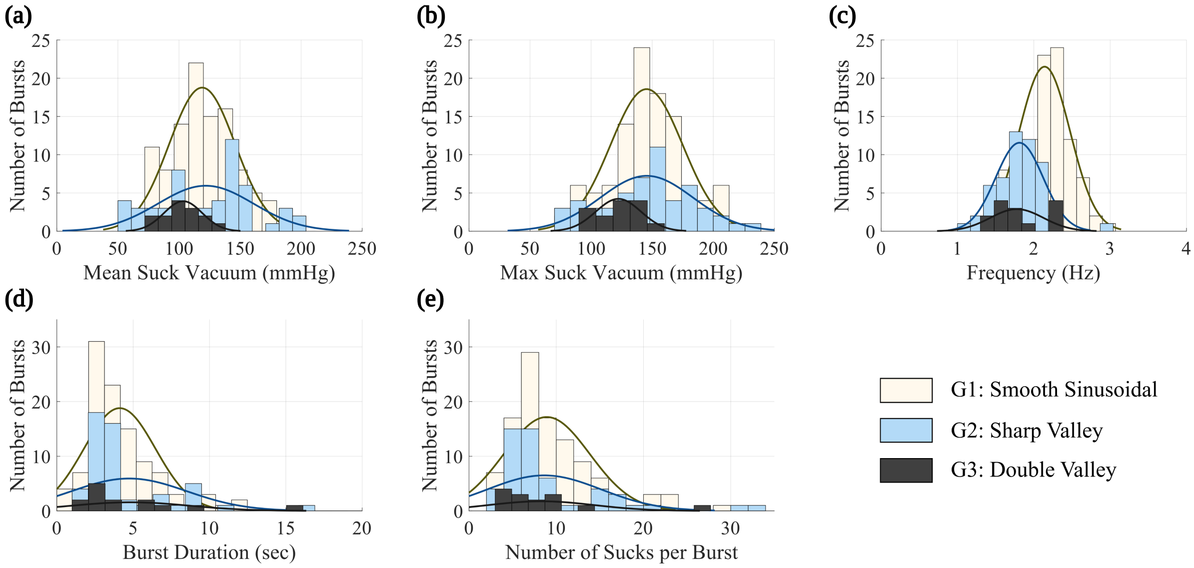


Figure 2.9: Distribution plots of the three classified groups based on signal shape: (a) Mean suck vacuum (b) Max suck vacuum (c) Frequency (d) Burst duration (e) Number of sucks per burst.

Table 2.5: Welch's t-test results comparing mean suck vacuum, max suck vacuum and frequency between the three groups of NNS profile shapes.

Parameters	Groups	t	p
Mean Suck Vacuum (mmHg)	1 vs. 2	-0.49	0.62
	1 vs. 3	3.16	***0.005***
	2 vs. 3	2.72	***0.010***
Max Suck Vacuum (mmHg)	1 vs. 2	-0.02	0.99
	1 vs. 3	4.04	**<0.001**
	2 vs. 3	3.22	***0.003***
Frequency (Hz)	1 vs. 2	6.15	***<0.001***
	1 vs. 3	3.70	***0.002***
	2 vs. 3	0.33	0.74

****Bold values are statistically significant.***

2.4 Discussion

The results from our study show measurements in agreement with values reported in the literature. Our system demonstrates features and capabilities that addresses the clinical needs of an easy-to-use, accurate, and safe system. The immediate feedback of suckling performance allows clinicians to troubleshoot breastfeeding problems with greater accuracy using objective data.

Our region of interest analysis show differences in suckling profile shapes. These may relate to infant oral motor restrictions and function, and therefore are worthy of further study. A detailed burst analysis of the NNS data from the 30 neonates showed that there were statistically significant differences in key NNS parameters between neonates with different suckling profile shapes. These results suggest that the shape of the suckling profile can play an important role in evaluating the suckling mechanics of the infants. To our knowledge, this has not been reported in the literature. As more data from a larger population of neonates becomes available, we aim to further investigate the shape of the infant suckling profile as it relates to oral motor functions or disorders and also map key parameters of the profile, e.g., the sharpness of a given suckling vacuum event, to the severity of certain conditions.

The technical improvements that can be implemented in such a system include reducing the size of the data acquisition unit and incorporating Bluetooth capabilities to eliminate the cable to the computer. While this may further reduce the size of the system, it may also increase the system's operating complexity and cost due to wireless pairing, data security considerations, and biosafety challenges caused by the proximity of the suckling unit to the electronics.

Clinical testing in this study examines a small sample size of infants and will expand further to investigate the system's ability to capture profiles that reflect poor vacuum, coordination, fatigue, respiratory asynchrony, and varying maturation levels. More importantly, we aim to further investigate the shape of the infant suckling profile as it relates to oral motor functions or disorders. We hypothesize that existing systems have not yet demonstrated the subtle changes in the signal due to engineering design problems such as the use of large elastic tubing and the presences of large dead air volumes within the system that may dampen or reduce the sensitivity of the measurements.

Expression pressure is a common measurement capability of systems in the literature aimed at tracking premature infant oral motor feeding readiness. This typically occurs in bottle feeding. Our aim is to target breastfeeding, therefore, future iterations of our system may be modified for an infant's suckling assessment at the breast. The pacifier can be removed and affixed to feeding tubes placed in the mouth while the baby is nursing. This permits comparison of non-nutritive and nutritive suckling skills. Such a system is reported in the literature by Chen et al. [45] and can be further investigated through larger studies with more infants in various clinical environments to better determine the feasibility of the feeding-tube system.

Thermal drift in NNS monitoring devices have been observed in many compact systems [14, 74]. For instance, Akbarkadeh [14, 57] introduced a compact sensorized pacifier that positions the pressure sensor in close proximity to the infant's mouth. As the infant sucks on the pacifier, the small air mass in the pacifier unit is heated causing thermal drift in the pressure sensor. In the design of our NNS device, the pressure sensor is positioned away from the infants mouth, minimizing problems caused by thermal drift. The 5 fr feeding tube ensures minimum air mass in the system while the 36 inch length of tube minimizes heat transfer to the sensor. Analysis of the NNS data shows that the baseline pressure recorded at the end of an experiment returns back to the same level as the start, indicating that thermal drift is not likely an issue for the system reported in this paper.

2.5 Conclusions

In this paper, we report on the design of a non-nutritive suckling system. We demonstrated use and application of the system in a clinical environment: a specialist clinic and a general pediatric facility. Thirty neonates were enrolled in the study and their non-nutritive suckling profile was successfully recorded and analyzed in real time. The proposed system allows for objective measurements and quantitative analysis of an infant's suckling profile. The system software interface automatically extracts features from the profile including the maximum and mean vacuum amplitude, suckling frequency, mean suck cycle, number of sucks, number of bursts, and the burst duration.

Like with all available systems and devices in the literature, the broader adoption of this technology in routine clinical practice will be a key challenge. Our future work will investigate the interpretation of these signals with respect to the norm (e.g., burst duration as it relates to endurance, maximum amplitude as it relates to suck vigor, etc.). As we collect more infant suckling profiles, this will enable us to establish a clear understanding of normal versus abnormal patterns of suckling, perhaps correlated to specific medical conditions at first identified by other means. These subtle suckling deviations can better distinguish infant-based interventions to optimize breast milk intake. Additionally, our study shows that real-time analysis feedback is important in the clinical environment, as measurements can be affected by infant behavior, preferences, and seal. With real-time data, repeating measurements as needed was crucial to obtaining and analyzing data in the clinic to ensure they had sufficient quality.

Ultimately, the challenge of diagnosing breastfeeding issues in mother-infant dyads remains a very complex and multidimensional problem. Our system aims to remove a facet of subjectivity in digital suckling examinations, by providing an objective quantification of suckling, working towards a clinical consensus within the medical and clinical community. This is with the overall goal of helping infants and mothers reach positive breastfeeding outcomes through referral and intervention pathways based on objective measurements. Extended applications of this system can include research of oral-motor or neurological development in infants, at-home intraoral vacuum monitoring system for infants, and as a rapid diagnostics tool in hospitals.

2.6 Summary

Infant breastfeeding diagnostics remain subjective due to the absence of instrumentation to objectively measure and understand infant oral motor skills and suckling characteristics. Qualitative diagnostic exams, such as the digital suck assessment which relies upon a clinician's gloved finger inserted into the infant's mouth, produce a diversity of diagnoses and intervention pathways due to their subjective nature. In this chapter, we reported on the design of a non-nutritive suckling (NNS) system which quantifies and analyzes quantitative intraoral vacuum and sucking patterns of full-term neonates in real time. In our study, we evaluate thirty neonate suckling profiles to demonstrate the technical and clinical feasibility of the system. We successfully extract the mean suck vacuum, maximum suck vacuum, frequency, burst duration, number of sucks per burst, number of sucks per minute, and number of bursts per minute. In addition, we highlight the discovery of three intraoral vacuum profile shapes that are found to be correlated to different levels of suckling characteristics. These results establish a framework for future studies to evaluate oromotor dysfunction that affect the appearance of these signals based on established normal profiles. Ultimately, with the ability to easily and quickly capture intraoral vacuum data, clinicians can more accurately perform suckling assessments to provide timely intervention and assist mothers and infants towards successful breastfeeding outcomes.

2.7 Acknowledgement

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Chapter 3

Identifying Abnormal Suckling Behavior from Non-Nutritive Characteristics

3.1 Introduction

Breastfeeding benefits both mothers and infants by protecting their health and development [75]. Evident from a growing body of literature, breastfeeding infants experience lower rates of diabetes, allergies, cardiovascular disease, and other chronic conditions. Mothers benefit from a decreased risk of breast cancer, ovarian cancer, and postpartum depression [76]. The Center for Disease Control and Prevention (CDC), the World Health Organization (WHO), and the American Academy of Pediatrics (AAP), among many other health organizations, recommend infants exclusively breastfeed for at least six months to attain optimal benefits [3]. Despite the fact that over 80% of mothers attempt to breastfeed, breastfeeding rates fall to a paltry 25% at six months after birth in the United States [23, 77]. While many factors are responsible for breastfeeding cessation, abnormal infant suckling behaviors—such as high intraoral vacuum—are known to contribute to nipple pain and injury, affecting a mother's ability to persistently breastfeed [22, 78, 79]. Other abnormal suckling behaviors, including low intraoral vacuum and suck disorganization, affect latch and milk transfer, causing a down regulation of the mother's milk supply [45, 80, 81]. Thus, infant suckling competency is an essential aspect of successful breastfeeding.

Infant suckling can be described as nutritive sucking (NS) or non-nutritive sucking (NNS). In nutritive suckling, infants coordinate sucking, swallowing, and breathing to intake fluid from a breast or bottle. In non-nutritive suckling, infants do not receive nutrient flow and the suck is from basic instinct when offered an empty or uninitiated breast, pacifier, finger, or object. [32–34]. Prior studies on preterm infants have shown that non-nutritive suckling founds behavior needed for nutritive suckling [33, 35], and that an infant's intraoral vacuum is paramount to effective milk extraction [43]. An analysis of NNS signals can provide infant oral measurement information such as mean oral vacuum, suckling frequency, burst duration, sucks per burst, maximum vacuum, and signal shape, details important in understanding infant suckling behavior [45, 82]. These measurements provide key information on an infant's feeding ability and can be used to screen for infant suckling irregularities. Despite the growth of trained medical assistance for mothers and infants over the last decade, objective screening tools to determine abnormal behavior in infant suckling are only beginning to emerge.

Over the years, there has been considerable work to produce catheter-based NNS, pneumatic and fluid-based sensing for NNS, and compact and portable measurement NNS, all to measure infant non-nutritive suckling [7, 11, 13, 15, 44–50]. However, there has been little consideration of how abnormal non-nutritive suckling shapes could be detected in otherwise healthy full-term infants that may be early indicators of breastfeeding difficulties. Akbarzadeh *et al.* developed a sensitized compact pacifier to measure non-nutritive suckling in preterm infants [57]. Features such as oral pressure, suckling duration, and frequency were used in a predictive algorithm to determine preterm infant feeding readiness. Chen *et al.* proposed a non-nutritive suckling device using pneumatic pressure sensors and performed a comparative study between NNS measurements in bottle feeding versus breastfeeding [45]. Lau *et al.*

introduced a sensitized digital assessment via catheters attached to the index finger that measures intraoral vacuum using a pressure transducer [7, 11, 50].

In this paper, we apply an unsupervised machine learning anomaly detection method using the Mahalanobis distance to detect abnormalities in suckling vacuum signals produced from our real-time NNS system. The machine learning approach is trained upon the collective contributions of 91 infant suckling measurements. From these infants, we establish normative data for eight measurement parameters in non-nutritive suckling shape: mean suck vacuum, max suck vacuum, suckling frequency, burst duration, sucks per burst, and three frequency parameters that affect the signal shape. In a series of case evaluations, we report the identification of normal versus abnormal suckling behavior in healthy newborn infants and infants diagnosed with ankyloglossia, a congenital condition indicated by a shortened lingual frenulum. Our study establishes a foundation for using machine learning methodologies applied to objectively collected data to evaluate infant suckling shapes and patterns, with the hope of developing early screening tools to guide interventions to establish, maintain and improve breastfeeding rates.

3.2 Materials and Methods

3.2.1 Non-Nutritive Suckling Measurement System

In prior work, the authors have demonstrated the application and use of a non-nutritive suckling system in a clinical environment with 30 full term infants. The system shown in Figure 3.1 consists of a modified disposable pacifier with an integrated feeding tube that is connected to a pressure sensing unit. A data acquisition board (DAQ) is used to collect measurements and a custom LabVIEW (National Instruments) software interface was developed to enable clinicians to immediately visualize and interact with the collected NNS signals.

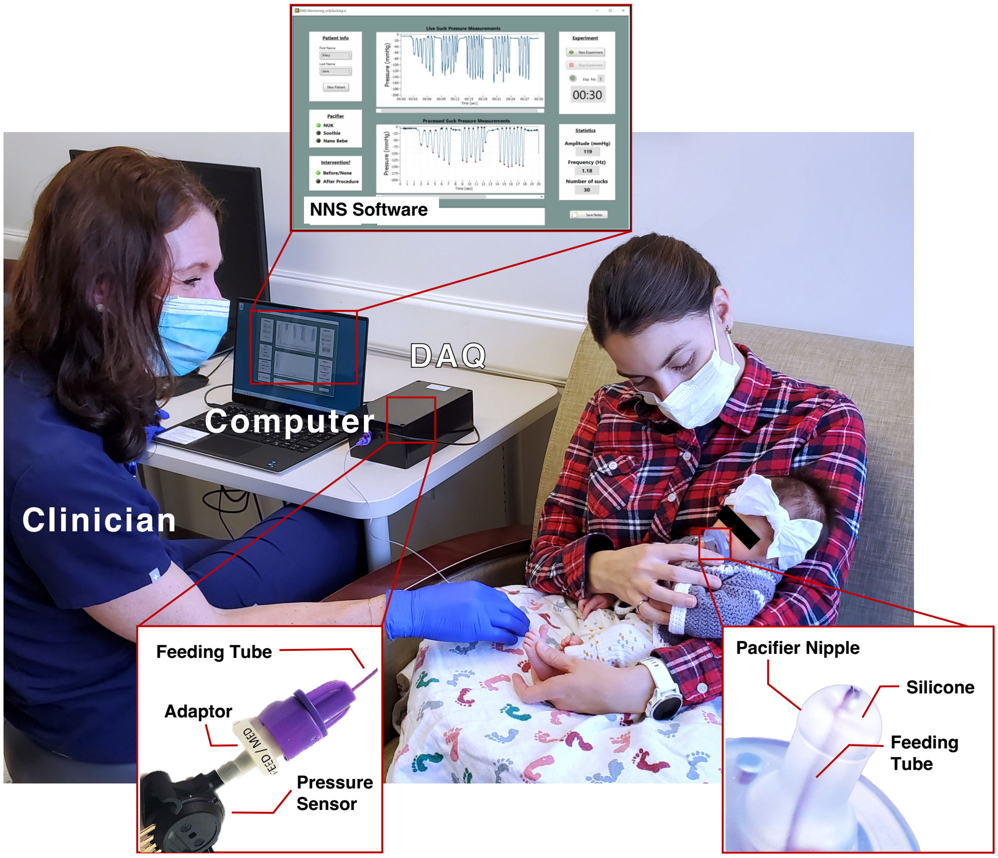

Figure 3.1: An image of the non-nutritive suckling measurement system to measure intraoral vacuum profiles of infants. The system is comprised of an instrumented pacifier, pressure sensor, data acquisition board (DAQ), and computer.

3.2.2 Subject Recruitment

Healthy full-term infants (37 to 42 weeks) under 30 days old and their mothers (n = 91) were recruited from the UC San Diego Center for Voice and Swallowing, UC San Diego Health La Jolla Pediatrics, and the UC San Diego Jacobs Medical Center. Approval from the Institutional Review Board at UC San Diego (IRB 800070 approved 13 September 2021) was obtained before recruitment started. The research aimed to study infant non-nutritive suckling using an objective measurement system. Mothers and infants were recruited to participate in the study during routine postpartum care with their general pediatrician or while consulting with feeding specialists at their respective locations. Infant inclusion criteria included full-term healthy infants establishing breastfeeding and without significant birth or postpartum complications. Mothers provided written and informed consent to participate in the study.

3.2.3 Study Design

Infants were evaluated using standard clinical assessments: a digital (finger-based) suck assessment of their intraoral vacuum, the Hazelbaker Assessment Tool, and the Bristol Tongue Assessment Tool. The Hazelbaker Assessment Tool [**?**] and the Bristol Tongue Assessment Tool [**?**] are both validated clinical assessment scales for evaluating the lingual frenulum's appearance and tongue mobility. Collectively, these assessments are used to identify infants with ankyloglossia and provide metrics for more generally identifying oral dysfunction. Clinicians were blinded to objective data in this study and performed evaluations solely based on standard practice. After clinical assessments, mothers were provided the opportunity to introduce the non-nutritive suckling system to acquire a sixty second measurement of their infant's intraoral suckling vacuum.

3.2.4 Signal Processing

Measurement of the infant's suckling vacuum using our non-nutritive suckling (NNS) device over a period of sixty seconds produces data rich with information. Data was collected on 91 subjects to compute the mean suck vacuum, maximum suck vacuum, suckling frequency, burst duration, sucks per burst, and the *suckling shape*, all for each individual. In prior work [**?**], we explained how the mean suck vacuum, maximum suck vacuum, suckling frequency, burst duration, and sucks per burst were extracted from infant NNS signals. In this work, we provide an additional evaluation: the infant's suckling shape, describing the shape of the vacuum versus time measurement. Normal infant suckling is described as smooth and regular, almost sinusoidal [10, 11, 42, 43]. Deviations in the smoothness and periodicity of this suckling shape may be correlated to irregularities in the infant's suckling and can be detected using frequency analysis.

In prior work [**?**], we showed there were three distinct infant suckling shapes: smooth sinusoidal, "sharp valley", and "double valley". The NNS signals can vary in amplitude and period over the measurement time. To determine contributions caused by the shape of the suckling vacuum signal with respect to time, each suckling event was isolated and normalized in both amplitude (-1 to 0) and period (0.5 sec). The complete normalized NNS signal of typically > 60 suckling events was passed through a fast Fourier transform (FFT) to identify the principal frequencies at 4 Hz, 6 Hz, and 8 Hz in most NNS signal data. These frequencies are known to appear in infant suckling measurements [**?**]. Figure 3.2 and Figure 3.3 show our analysis to isolate the principal frequency components that contribute to the shape of the NNS signal. Consequently, the signal amplitudes produced at these frequencies were recorded and retained as a part of each infant's suckling shape.

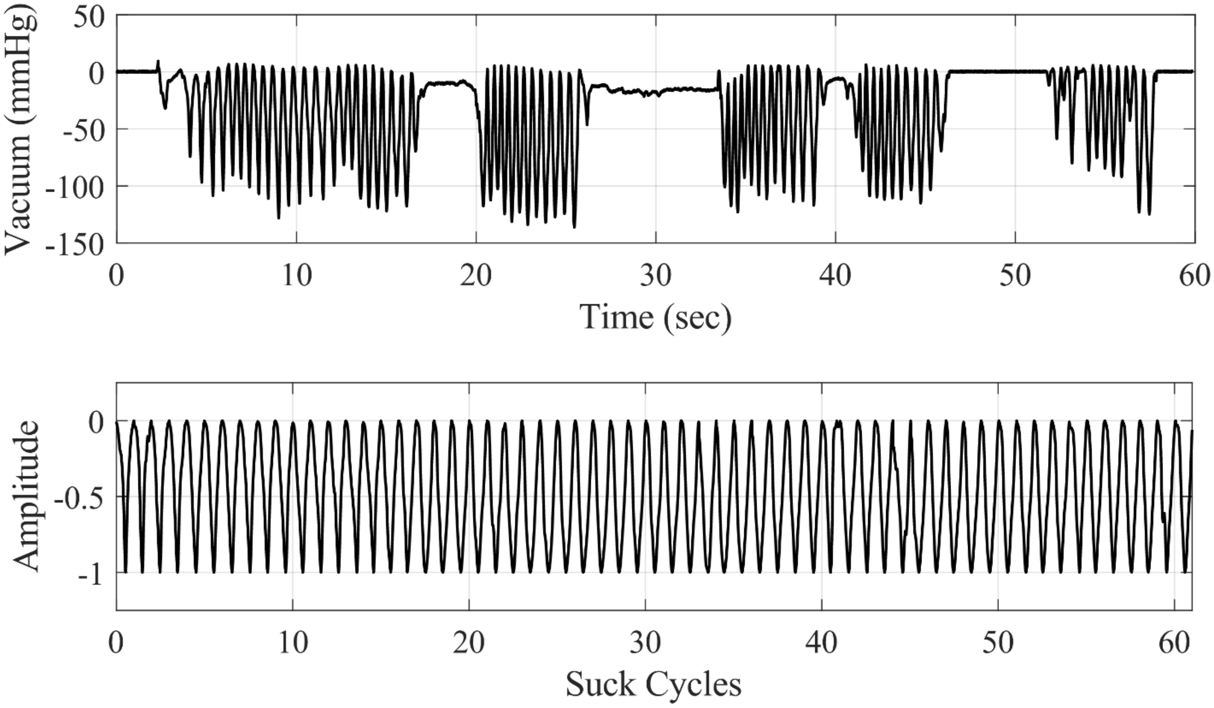

Figure 3.2: An example (top) of a 60-second non-nutritive suckling shape as measured using the NNS shows the irregular nature of suckling by a typical infant.

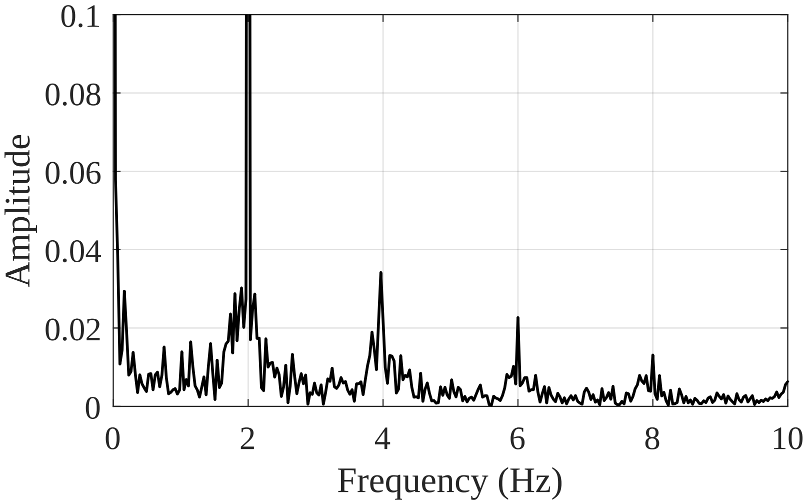

Figure 3.3: A typical example of the FFT-transformed normalized NNS data, indicating the clear appearance of principal frequency contributions at 4, 6, and 8 Hz to the NNS signal. For this reason, the amplitude of the signal at these frequencies was tracked and included in each infants' profile.

3.2.5 Anomaly Detection using Unsupervised Machine Learning based on Robust and Mahalanobis Distance

In this application, we use the Mahalanobis distance to detect and identify a subgroup of neonates that exhibit NNS measurements that appear to be outliers from the majority of the population. The NNS characteristic data collected from 91 neonates were found to be normally distributed and verified using the Shapiro-Wilk test [**?**]. Among many statistical distance measuring tools, the Mahalanobis distance, the distance between a subject and the mean of the distribution in terms of the number of standard deviations, is known for its ability to identify outliers, particularly multivariate outliers in normally distributed data. It and its many variations have been used in applications from finance [83] and neurocomputing [84] to medical diagnosis [85]. The Mahalanobis distance may be determined from

$$\mathrm{MD} = \sqrt{(X-\mu)^T S^{-1}(X-\mu)}. \tag{3.1}$$

In Equation 3.1, the vector X contains all eight NNS measurement parameters, namely, mean suck vacuum, max suck vacuum, suckling frequency, burst duration, sucks per burst, and three frequency parameters affecting signal shape (4Hz, 6Hz, 8Hz), representing the sucking behavior of each neonate. μ is the arithmetic mean vector; and S is the covariance matrix. Neonates with a large Mahalanobis distance are classified as outliers [86]. The robust Mahalanobis distance (RMD) was used in this analysis to reduce effects of outliers on the mean value of the population. The minimum covariance determinant method introduced by [87] of the robust Mahalanobis distance is defined as:

$$\mathrm{RMD} = \sqrt{(X-\mu_R)^T S_R^{-1}(X-\mu_R)}. \tag{3.2}$$

In this equation, μ_R and S_R are the robust estimate of the mean vector and the covariance matrix, respectively.

3.2.6 Outlier Threshold

Neonates whose distance away from the mean exceeded the threshold value, $\Xi = \sqrt{\chi^2_{p,r}}$, were identified as outliers. This threshold value is a function of the number of degrees of freedom (p), eight in this case, commensurate with the number of NNS measurement features. It defines the outliers as separate from the main body of data. In this study, a conservative 7% outlier fraction, r, was used based on the reported prevalence of ankyloglossia in infants [88].

3.3 Results

3.3.1 Normal and Abnormal Suckling Data

We first seek to determine if a simple measurement of the suckling vacuum is sufficient to identify breastfeeding problems, and to explore whether a collection of parameters defined from this measurement may be used to characterize the infant's feeding behavior. We present three exemplary normal and abnormal cases from visual inspection of the suckling profiles and the distributions of the eight NNS parameters in Figs. 3.4, 3.5, and 3.6 in the context of our entire data set from 91 infants. Each figure presents the (a) NNS recording over sixty seconds, a (b) six-second extraction, and a (c) statistical evaluation of eight potentially important parameters. The vertical lines in the statistical plots represent the values obtained for the case under consideration. Figure 3.4 plots data taken from a healthy 12-day old infant exhibiting normal suckling behavior, with the measurements each within one standard deviation from the mean values of the entire population. Moreover, the suckling shape appears to be rhythmic and roughly sinusoidal.

By contrast, Fig. 3.5 provides measurement data from a 6-day old infant that is approximately two standard deviations outside the mean values for at least some of the measurement parameters. Moreover, the suckling shape appears to be irregular over the entire

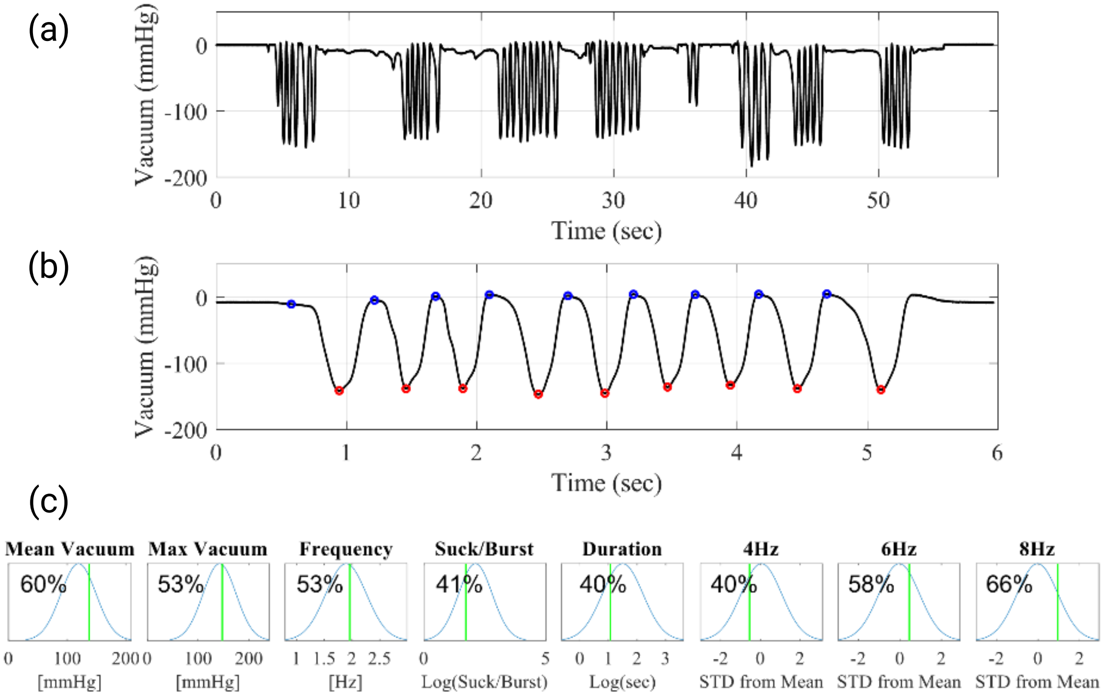

Figure 3.4: Subject 18: a typical infant's NNS suckling response and the results of computing the eight parameters that describe its principal characteristics. (a) Full 60 s NNS measurement, (b) 6-second sample from the third suckling burst, and (c) statistical distribution plots of all eight NNS measurements.

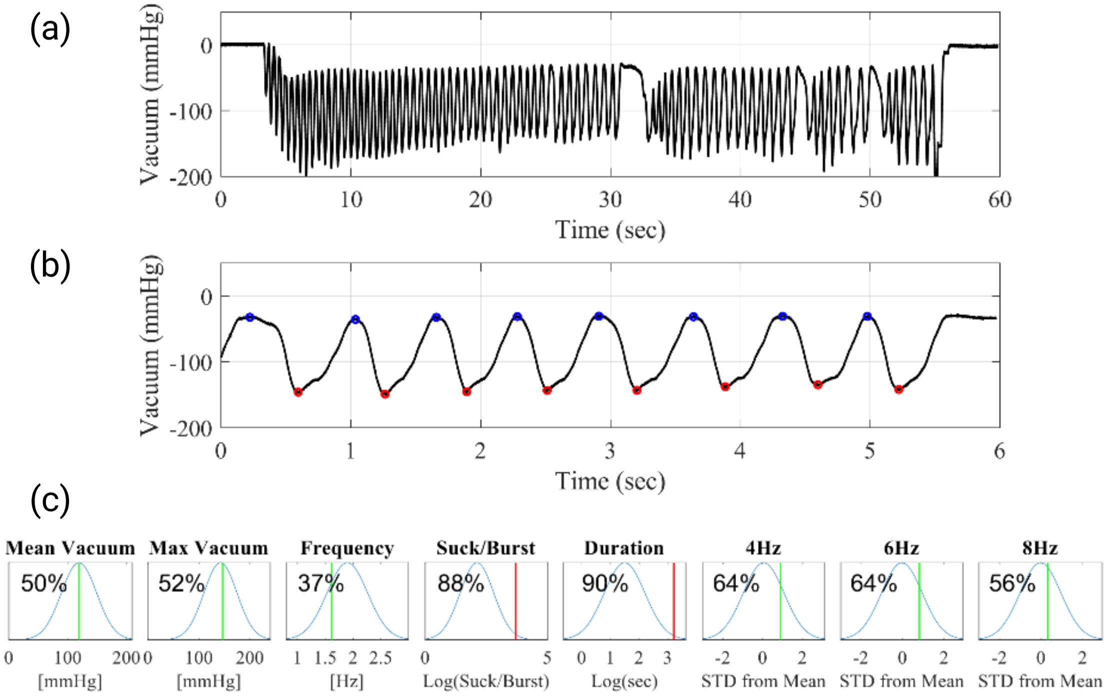

Figure 3.5: Subject 25: an infant with extended bursts of suckling. (a) Full 60 s NNS measurement, (b) 6-second sample from the first suckling burst, and (c) statistical distribution plots of all eight NNS measurements.

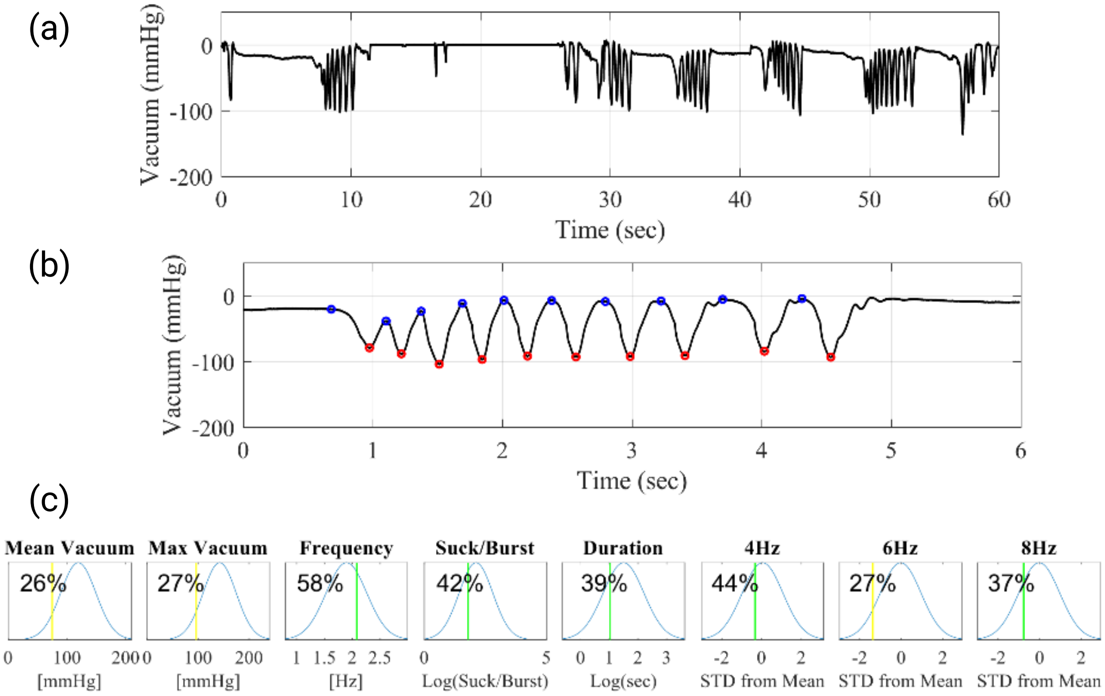

Figure 3.6: Subject 36: an infant with weak and infrequent suckling. (a) Full 60 s NNS measurement, (b) 6-second sample from the fifth suckling burst, and (c) statistical distribution plots of all eight NNS measurements.

data collection period—notice there are three pauses, two of which are exceptionally brief—and each suckling event exhibits a non-sinusoidal pattern, altogether indicating abnormal suckling behavior. In this case evaluation, the clinician reported hemorrhagic nipple lacerations, severe nipple pain, and infant choking caused by poorly coordinated suck-swallow-breathe events. The continuous suckling without rest, evident from the NNS data, may underpin these adverse outcomes.

The third infant's suckling behavior plotted in Fig. 3.6 produces reasonable values from most of the measurement parameters. The NNS data was taken on day 18 of life. The suckling shape itself shows brief suckling bursts separated by relatively long interludes of no suckling; the detail of the fifth burst shows some irregularity near the end. Most importantly, the NNS measured relatively weak mean and max suckling vacuum at 26th percentile and 27th percentile, respectively. This correlates with clinical notes that report poor latch. This infant was fussy and had gastroesophageal reflux; a condition which may cause disengagement during feeding.

There are evident differences between normal and abnormal suckling behavior in the NNS data. Next, we examine NNS data taken from several clinically identified cases of abnormal feeding behavior.

3.3.2 Distance-distance Plot

In this section, we show the results of anomaly detection using the unsupervised machine learning approach. We calculated the Mahalanobis distance and the robust distance for each of the 91 neonates and plotted them together in a distance-distance plot as shown in Fig. 3.7. The outlier threshold was calculated to be 3.8 standard deviations using the expected outlier fraction of 7% and the eight degrees of freedom of the data set. Among the 91 neonates, 81 fall within the normal quadrant (quadrant III of Fig. 3.7). Ten of the 91 neonates were classified to be outliers with either the Mahalanobis distance or the robust distance—or both values—being greater than the threshold.

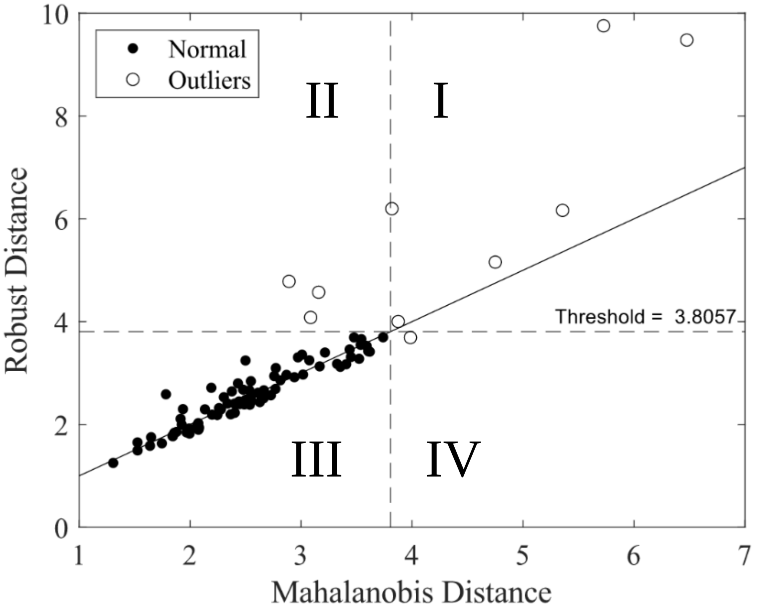

Figure 3.7: Robust distance versus Mahalanobis distance plot for the NNS data from all 91 subjects.

3.3.3 Detecting Anomalies Associated with Ankyloglossia

We now examine NNS data captured from healthy full-term infants that were diagnosed with ankyloglossia, a congenital oral dysfunction caused by a tethered lingual frenulum. A frenotomy is a surgical intervention prescribed to release the lingual frenulum. While the incidence of ankyloglossia is approximately 7% [88], frenotomies have increased tenfold in little more than a decade to improve breastfeeding rates without substantial long-term evidence [89]. The clinical community continues to disagree over the necessity of surgical intervention in ankyloglossia, principally due to a lack of objective assessment tools to serve as a basis for making the decision to pursue a frenotomy. In this context, we seek to explore our NNS data to determine if it provides insight and perhaps a stronger basis to make a decision on frenotomies.

Out of 91 neonates, eight were clinically diagnosed with ankyloglossia and treated with frenotomies. Ankyloglossia was diagnosed based on clinical assessment of persistent nipple pain, inability to maintain latch, feeding fatigue, high feeding frequency, insufficient weight

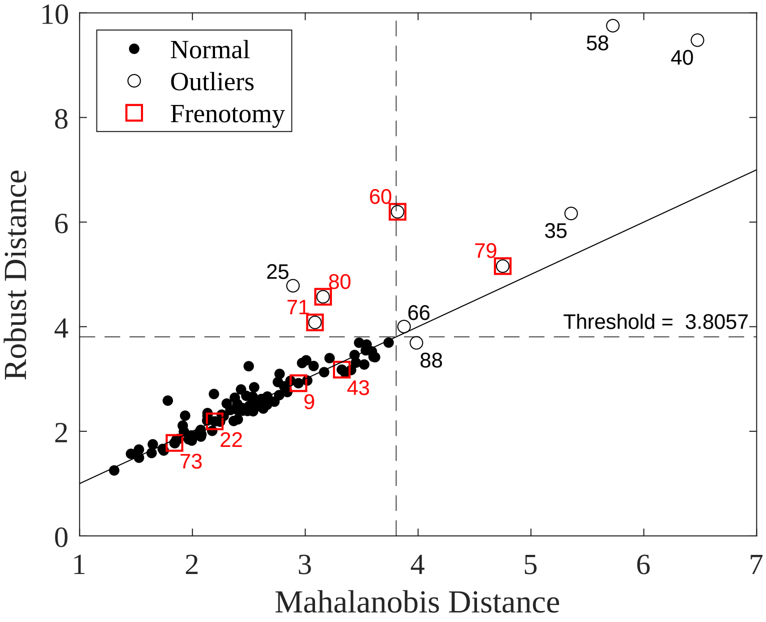

Figure 3.8: Eight of the 91 infants eventually underwent frenotomies, identified with red boxes. Four are outliers in the robust distance versus Mahalanobis distance plot of the NNS data; four are in the normal group.

gain, down regulation of milk supply, and visual inspection of tethered lingual frenulum. NNS data was collected prior to surgical intervention to determine if abnormalities could be detected in their suckling measurements. Clinical evaluation to determine frenotomies was performed blinded to the NNS data. We replot this data in Fig. 3.8, labeling with red boxes all the infants that went on to have a frenotomy. Four cases (9, 22, 43, and 73) were within the normal region while another four cases (60, 71, 79, and 80) were outliers. Frenotomy cases falling within the normal region indicate infants with normal NNS characteristics, but were prescribed a frenotomy. These cases highlight on whether a frenotomy could have been delayed or avoided to remedy breastfeeding struggles. There are six other cases (25, 35, 40, 58, 66, and 88) in the outlier region that are not frenotomy cases. These cases indicate abnormal suckling behavior based on NNS measurements and require further evaluation and follow up with mother and infant to determine causality.

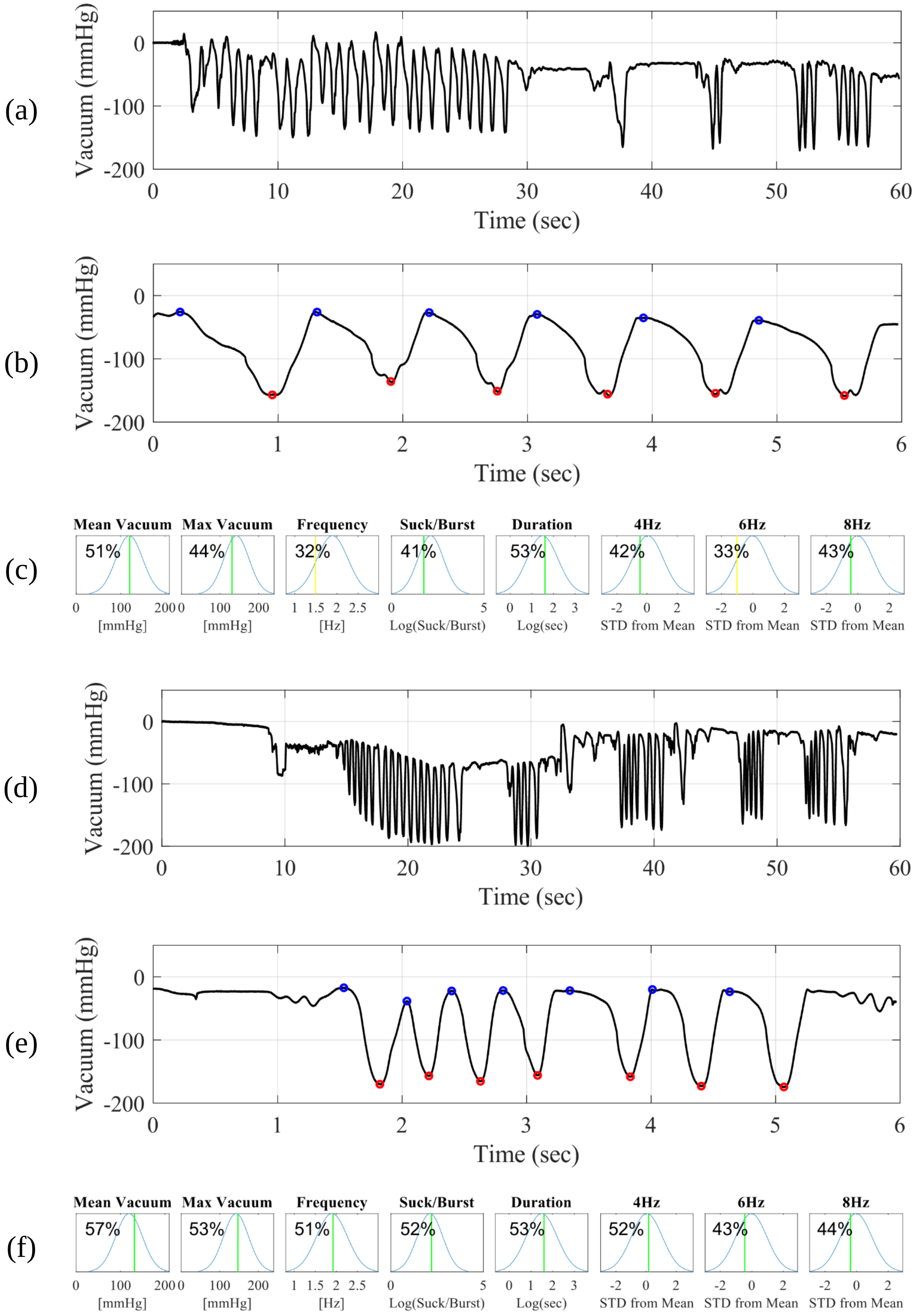

Figure 3.9: The effect of a frenotomy is apparent in subject 71. Plots (a,b,c) and (d,e,f) show NNS data for the full 60 seconds, a 6-second sample, and statistical evaluation of the eight tracked parameters before and after frenotomy, respectively.

3.3.4 The Effect of Frenotomies on the NNS Data

An important part of the controversy regarding surgical intervention in ankyloglossia is whether there is a long-term benefit to the infant from a frenotomy [90]. Here we use the NNS to evaluate the impact of the frenotomy. A pair of complete NNS data sets is provided in Figure 3.9 for case 71: before and after a frenotomy. Before the frenotomy, the subject received a digital suck vacuum score of 3 out of 10, a Hazelbaker score of 5 out of 14 for function and 2 out of 10 for appearance, and a Bristol score of 2 out of 8, indicating tongue restriction caused by tethering of the lingual frenulum sufficient to recommend a frenotomy. The NNS data was captured day 1 of life prior to the frenotomy; the frenotomy was performed on day 1; and the post-frenotomy NNS data was collected on day 18. After the frenotomy, case 71 showed a change in frequency and suck per burst results, with both moving towards the mean of the entire data set as a consequence of the frenotomy. Whether these changes are permanent in the long term was not studied within the scope of this work and will be explored in future studies.

Figure 3.10 shows subject 60 before and after a frenotomy. In this case, the subject received a Hazelbaker score of 9 out 14 for function and 3 out 10 for appearance, a Bristol score of 3 out 8, and a digital suck vacuum score 8 out of 10. The NNS data was captured immediately before and immediately after the frenotomy procedure, all within the first day of life. Before the frenotomy, the magnitude of the suck per burst, burst duration, and the 4 Hz components of the suckling profile in the frequency domain were in the 95^{th}, 97^{th}, and 87^{th} percentiles, respectively. All parameters —except the 4-Hz amplitude parameter—moved closer to the mean, falling within half a standard deviation of the mean after the frenotomy. There were minimal changes to the magnitudes of the three frequency components before and after the procedure, indicating that there were little changes to the shape of the suckling profile. This can be observed in plots (b) and (e) of Figure 3.10.

As indicated by the case evaluations and prior research [90], surgical intervention may help improve infant suckling function in cases in which frenulum restriction is truly

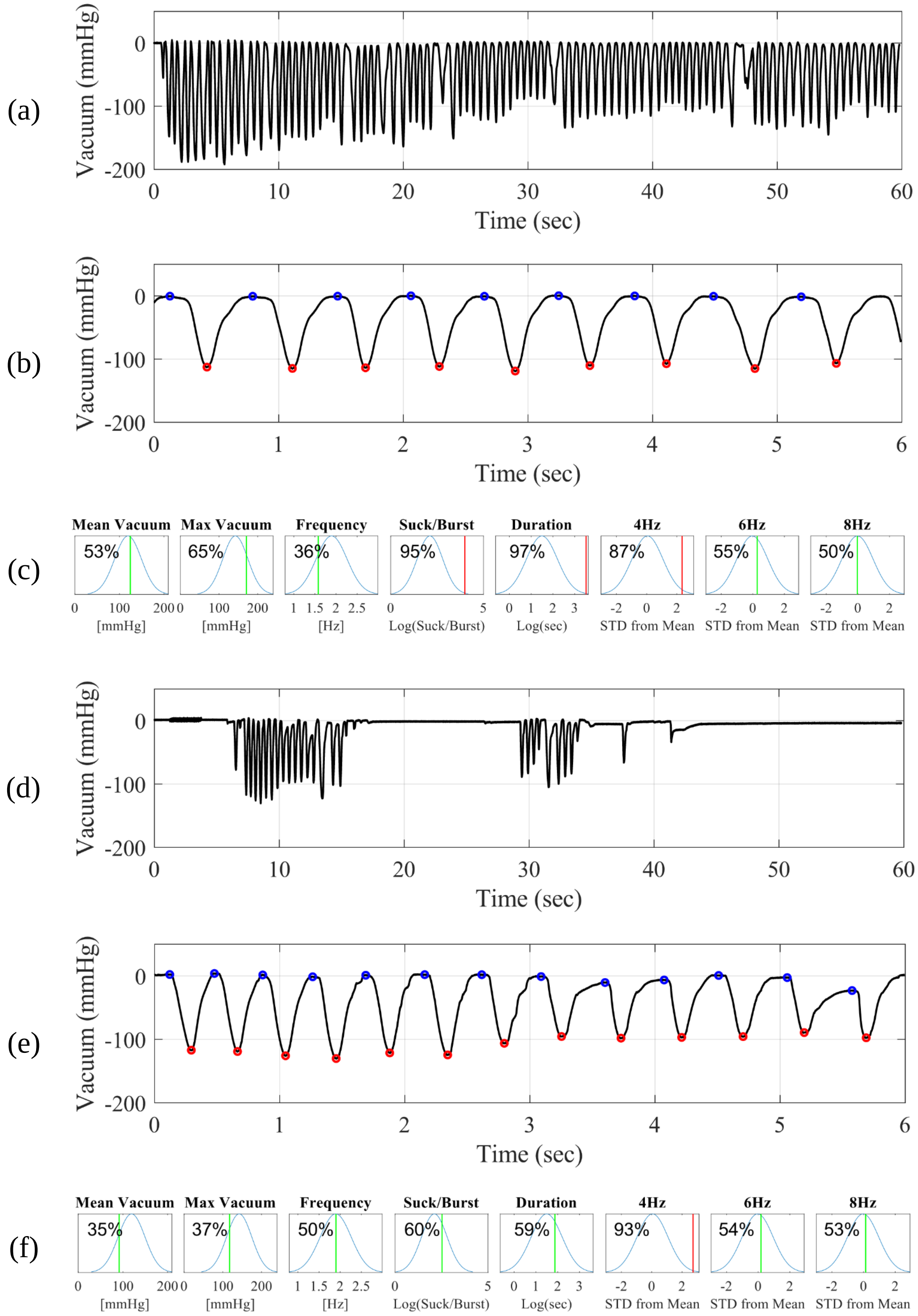

Figure 3.10: The effect of a frenotomy is also apparent in subject 60. Plots (a,b,c) and (d,e,f) show NNS data for the full 60 seconds, a 6-second sample, and statistical evaluation of the eight tracked parameters before and after frenotomy, respectively.

interfering with suckling mechanics. For infants with corresponding clinical evaluation and outlier measurements from the NNS, our results show the abnormal NNS measurements shift to normal ranges post-frenotomy.

We next consider those cases—9, 22, 43, 73—where a clinical decision was made to perform a frenotomy and the NNS indicated normal suckling behavior. We present case 22 in Figure 3.11, where the subject was 8 days old and received a Hazelbaker score of 7 out of 14 for function and 7 out of 10 for appearance, a Bristol score of 6 out of 8, and a digital suck vacuum score 3 out of 10. The NNS-based evaluation was normal based on the distance-distance plot (*see* Fig. 3.8). The suckling shape and most of the statistical data remained statistically similar before and after the frenotomy. The only significant changes in the data were adverse changes in the response amplitudes at 4, 6, and 8 Hz to lie farther from the mean after the surgery. In this case, it would have been possible to recommend breastfeeding without a frenotomy.

More broadly, we next consider the effects of a frenotomy in all eight cases where it was performed in Figure 3.12. The robust distance is plotted with respect to the Mahalanobis distance the same as in Fig. 3.8. The left plot—cases 60, 71, 79, and 80—indicate those cases identified as outliers via the NNS data. In every case, these outliers moved to the normal region (quadrant I) after the frenotomy, indicating that the frenotomy moved their suckling behavior towards the mean of the overall infant population. For those infants possessing NNS results already considered to be in the normal region (quadrant I) before the frenotomy (cases 9, 22, 43, and 73 plotted on the right of Figure 3.12), there were modestly significant improvement for cases 9 and 43 towards the mean of the population in our study and no significant change to cases 22 and 73. Altogether, the effect of a frenotomy was significant on the NNS measurement results for those infants that had adverse NNS results beforehand. For those infants with normal NNS results, the effect was weakly significant to insignificant.

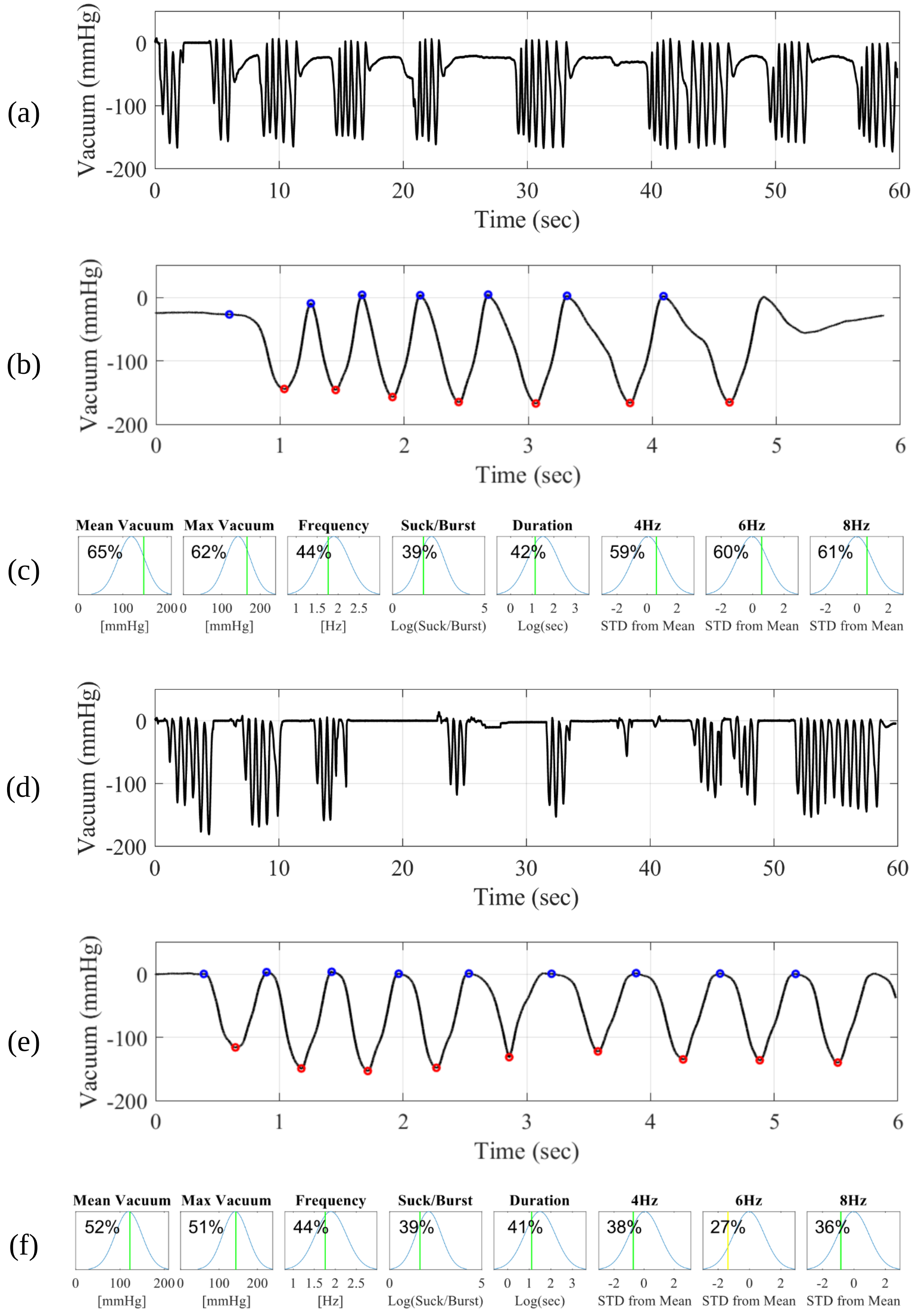

Figure 3.11: The effect of a frenotomy was not apparent in subject 22.

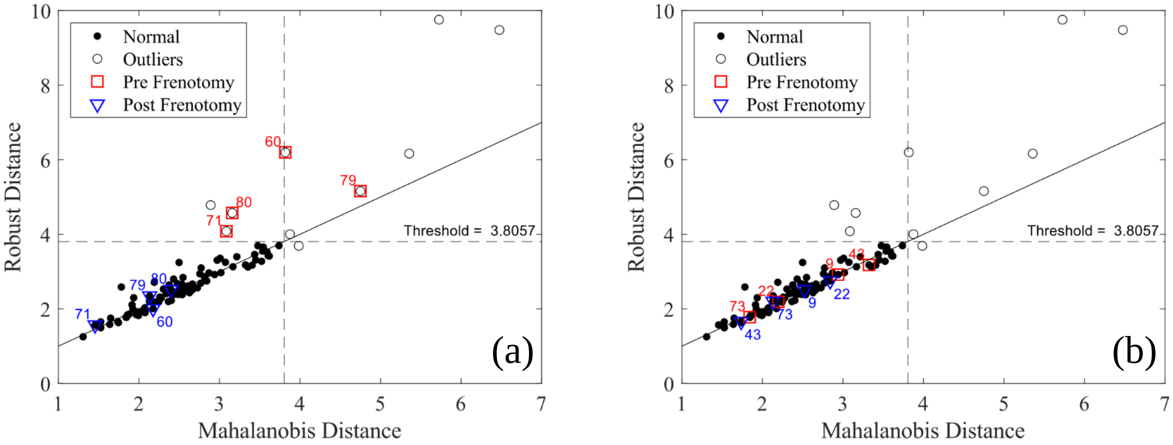

Figure 3.12: Robust distance versus Mahalanobis distance plot of the NNS data for those cases where a frenotomy was performed: before vs. after. (a) shows cases where the NNS measurements were flagged as abnormal. (b) shows cases where the NNS measurements were classified as normal.

3.3.5 Abnormal NNS Measurements with Normal Clinical Evaluation

We finally consider cases in which the NNS identified potential issues but for which the clinical evaluation was normal. Subject 58 shown in Figure 3.13 was clinically evaluated to be normal with Hazelbaker scores of 14 out of 14 and 10 out of 10 for function and appearance, respectively. The Bristol score was 8 out of 8 and the digital suck vacuum was 10 out of 10. However, this neonate was classified as an extreme outlier based on the Mahalanobis distance (*see* Fig. 3.8). The NNS measurements indicated that this subject produced an abnormally long burst duration and a very large number of suckling events per burst: both were in the 100% percentile. Also, in assessing the sucking profile, the 6 Hz component of the signal was two standard deviations away (94th percentile) from the mean value of the whole group. Though the average suckling frequency for this neonate is relatively low at 1.4 Hz, it is within the expected range for infants fewer than 1 day old [57]. This case is an example of an infant identified to need further clinical follow up to determine if suck-breathe coordination improves, identify any early nipple trauma due to sustained suckling, and if

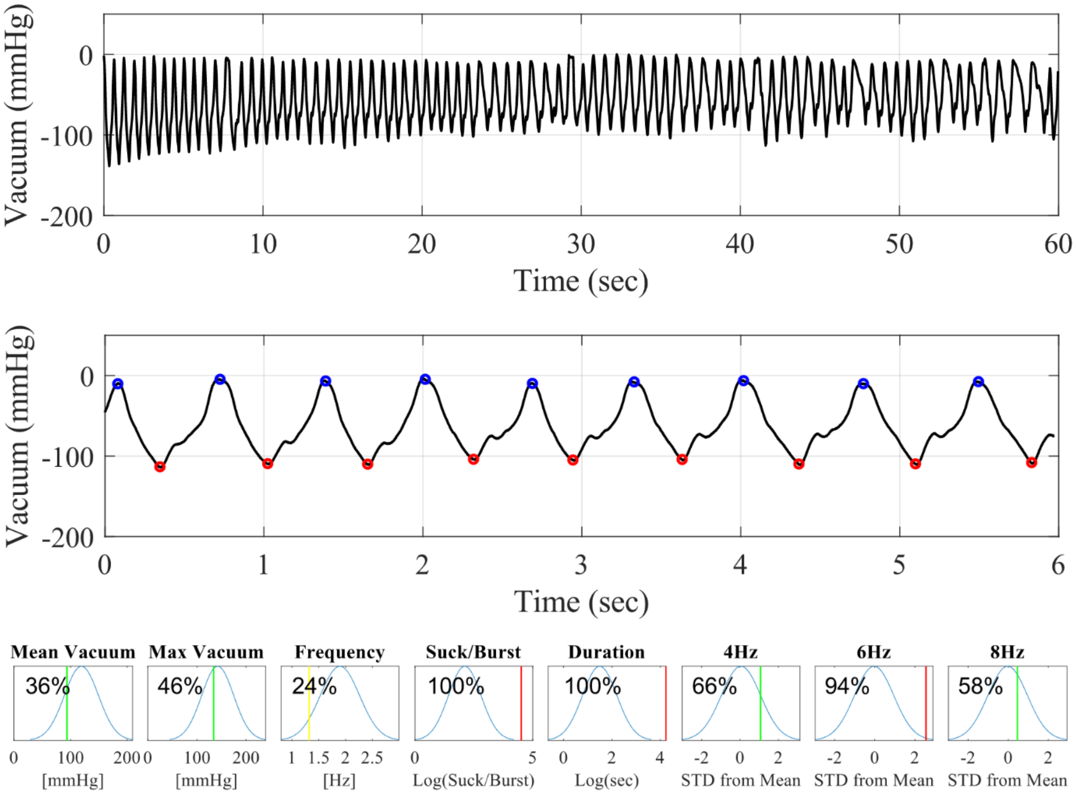

Figure 3.13: This infant, subject 58, was clinically evaluated to be normal, yet objective measurements indicate abnormal suckling behavior.

infant exhibits choking during breastfeeding due to lack of resting in between bursts.

3.4 Discussion

Our NNS device appears to have sufficient sensitivity to identify ankyloglossia and potentially other issues sufficient to affect breastfeeding difficulty. From our NSS measurements, lingual restriction sufficient to cause breastfeeding issues can be sometimes effectively treated with a frenotomy. Our NNS measurements also highlight the controversial nature of current ankyloglossia clinical diagnosis practices with several infants that showed intact suckling mechanics via the NNS that still went on to have a frenotomy with minimal changes to their NNS mechanics. This is a strong representation of the existence of conflicting literature demonstrating certain infants benefiting from frentomies while others do not [89**?**].

Our approach in the use of this technology in the clinical setting has been the following:

- Keep the technology as simple as possible with off-the-shelf cost-effective components to facilitate its adoption in the clinic. Some devices and approaches employ ultrasound, force sensors, arrayed sensors, and cameras, which may improve the veracity of the measurements but at the cost of data complexity, difficulty in use, and expense. By contrast, our approach seeks to make as much use of one quantity—the suckling vacuum—as possible. It may be necessary to later incorporate other sensing methods, but the richness of the suckling vacuum versus time data indicates much can be learned from this single parameter alone.

- Make the measurement results immediately available to the clinician. Measurements are always challenging when using technology, and nowhere more so than with fussy infants in an unfamiliar clinical environment. By having the measurement results immediately available, the clinician can identify faulty measurements, refusal to suckle on a particular pacifier, and problems with the technology, and then overcome these problems by changing the pacifier, repositioning the infant, and so on.

- Present the measurement results in a graphical manner in comparison to the population mean and standard deviation. This helps the clinician to quickly identify outliers that may represent abnormal suckling in a quantitative manner but without the complexity of tabulated data.

From the specific cases demonstrated in the results, we show how these principles can be used to provide quantitative evaluation sufficient to judge whether a frenotomy may be necessary, and whether or not the infant benefited from having a frenotomy.

We then went on to apply unsupervised machine learning using the robust and Mahalanobis distances to identify outliers in Fig. 3.8, with the threshold from normal to abnormal being calculated using a 7% outlier fraction of the overall data in correspondence with the clinical incidence of ankyloglossia. Ten infants produced NNS data that were outliers from the 91 comprising the entire data set. Of these ten, four went on to have frenotomies; these four infants showed significantly improved NNS results as a consequence of having a frenotomy. Of the 81 infants found to have normal NNS results, four had frenotomies. Two—cases 9 and 43—were relatively close to both thresholds defined by the robust and Malahanobis distances and showed modest improvements in their NNS results after their frenotomies. However, two others—cases 22 and 73—were well within the normal NNS data and showed slight adverse change in their NNS results post-frenotomy.

The importance of the machine learning approach is perhaps best exemplified through case 71, with ostensibly normal NNS data provided in Fig. 3.9. Manual interpretations of the suckling shape and the distributions of the eight parameters suggest that the subject's NNS is normal, however, the robust distance placed this infant's NNS data above the threshold, indicating abnormality. Moreover, this infant was clinically diagnosed to need a frenotomy, and the NNS results indicated a significant improvement in suckling behavior in Fig. 3.12 Casual inspection of the NNS data is sometimes helpful, but machine learning-based analysis is necessary to identify the collective deviations of all the measurement parameters that may produce an abnormal classification.

Our study here focused upon the diagnosis of ankyloglossia sufficient to impact breastfeeding outcomes. Improvements in use of the NNS data for other oral dysfunction requires the collection of more clinical evaluation data correlated to NNS measurements to identify and characterize these relatively rare oral deficiencies. Moreover, there is undoubtedly a benefit in pursuing ultrasound studies [43] alongside the clinical and NNS-based evaluations in order to improve the veracity of the diagnosis and interpretation of the NNS data, particularly when including a broader array of possible suckling dysfunction phenomena. It is hoped, however, that the simple NNS-based approach will provide a useful triage tool in the clinical diagnosis of suckling issues.

A limitation with all existing methodologies remains continuous and long-term monitoring of infant suckling maturation. As with any single-point measurement, infants mature and learn beyond the clinical evaluation time that may lead to improvements, regression, or sustained suckling patterns not by the data. Future studies will need to consider multiple time points in infants with and without intervention to determine and distinguish between intervention impact versus infant maturation.

3.5 Conclusions

Infant oral suckling is a highly complex biomechanical process that requires a comprehensive evaluation when problems arise. While ultrasound, force sensors, sensor arrays, and similar methods provide powerful measurements capabilities for understanding of infant oral motor function, it can be challenging to translate this technology to front-line clinical use due to the equipment, training, and ample time required to collect and interpret such data. A simpler approach may be beneficial in the context of early screening, where simple abnormality indicators represent a first step to providing timely intervention and comprehensive care.

With such instrumentation and analytical methodologies, families and clinicians are more informed on objective metrics that may guide next intervention steps. This work provides a methodology via a simple non-nutritive device to quickly assess infant suckling, identify abnormalities, and prescribe careful follow up for mothers and infants. Non-nutritive suckling has long been established as an important foundation to understanding nutritive suckling, and our NNS device supports this perspective. Non-nutritive measurements using our simple pacifier combined with a vacuum sensor and computer interface with a machine learning algorithm is sufficient to provide early and rapid identification of ankyloglossia sufficient to cause breastfeeding issues. It also appears to identify cases where ankyloglossia is not impacting suck vacuum, and cases that might need further evaluation and treatment of suckling problems. Moreover, it does appear to indicate a beneficial outcome from frenotomies in those infants exhibiting outlier NNS results before intervention. Whatever the case, early intervention is necessary during the critical period in which milk supply is being established to prevent damaged tissue and pain that may lead to breastfeeding cessation.

Equally important is the possibility such an NNS device may assist with determining infant-focused interventions versus mother-focused interventions. Clinicians may use these tools to build intuition grounded on objective data as they compare their own tactile feedback with objective measurements. Often, a mother's perception of infant inability to suckle as a result of ankyloglossia may not truly reflect the infant's suckling competence. An objective determination based on NNS measurements and machine learning classification can guide intervention strategies and overcome biases associated with breastfeeding, turning focus to the mother as necessary.

With respect to the diagnosis of ankyloglossia, while tongue tie may be indicated based on current clinical metrics such as Hazelbaker or Bristol Assessment tools, our data shows frenotomies may not be a blanket solution to resolving breastfeeding difficulties in infants with ankyloglossia. As identified by our machine learning classification, infants with normal NNS mechanics exhibit very little changes from such procedure. Future longitudinal studies will follow infants long term to determine the true benefits and changes induced by surgical intervention.

While the exact cause for abnormal suckling cases in this study remains an ongoing research endeavor, the data highlights the need for more objective screening tools that identify abnormal suckling behavior to be addressed with close comprehensive follow up and support for mother and infant. Breastfeeding is an important biological function with important health and developmental benefits and outcomes for breastfeeding mother-infant dyads.

3.6 Summary

While breastfeeding is well established to benefit the health and durability of mothers and infants, breastfeeding cessation by 6 months occurs in 75 percent of dyads. Current standard care lacks objective measurement capabilities for screening infant suckling abnormalities within the first few days of life, a critical time to establish milk supply and successful breastfeeding techniques. A non-nutritive suckling vacuum measurement system, previously developed by the authors, is used to gather data from 91 healthy full term infants under thirty days old. Non-nutritive suckling was recorded over a duration of sixty seconds. We establish normative data for measurement parameters such as mean suck vacuum, maximum suck vacuum, suckling frequency, burst duration, sucks per burst, and signal shape. Based on normative data, we apply machine learning anomaly detection algorithms to identify infants at high-risk for breastfeeding cessation due to abnormal measurement values. We perform case studies of healthy newborn infants and infants diagnosed with ankyloglossia to validate the methodology. In a series of case evaluations, we demonstrate the ability to detect abnormal suckling behavior using machine learning. We evaluate cases of ankyloglossia to determine how oral dysfunction and surgical interventions affect non-nutritive suckling measurements. Machine learning is a viable approach to interpreting infant suckling measurements collectively and can provide a objective approach to identifying abnormal infant suckling biomechanics. More research to apply machine learning to interpret infant oral complexities is crucial to complimenting the emerging technologies aimed to pro

3.7 Acknowledgement

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Chapter 4

Closing Remarks

4.1 Conclusions

The work in this dissertation investigates non-nutritive suckling in infants via a proposed NNS measurement system and studies abnormal behavior based on normative data gathered from the clinical study of 91 healthy full term infants.

The system devised is robust, enabling rapid data collection and real-time analysis considering both engineering and clinical design requirements. Created by simplicity, the device was designed with four off the shelf components: pacifier, feeding tube, data acquisition board, and pressure sensor. The simplistic nature of the device made for minimal training during clinical studies as the use of the device simply involved attachment of the modified pacifier, and opening of the software. Modularity in the design allowed compatibility with any pacifier–a key aspect not addressed in any existing system but very relevant during actual study in which infants reject unfamiliar pacifiers. Real-time analysis was another key element in design that truly impacted clinical workflow. Many systems integrate onboard memory cards, requiring post-processing that hinders immediate feedback to the clinician during the sessions. With the system developed, clinicians can dynamically adjust, provide intervention, and track parameters for improvements within and between sessions. The system was tested with over 90 infants with clinical studies ongoing, showing potential for scaling up in a larger study with more infants or clinicians participating.

With normative data, abnormal suckling behavior can be observed from outlying non nutritive suckling characteristics that may inform or indicate risk for breastfeeding difficulties. While non-nutritive measurement systems are abundant in literature and presented in this work, the challenge remains to correlate specific characteristics to specific abnormalities. As can be observed from the study with tongue tied infants, no specific parameter is found to be exclusive to these infants. This may be attributed by the lack of ground truth–as tongue tie remains a highly controversial diagnosis with surgical implications, our data remains unclear as to the true nature of tongue restriction due to poor clinical classification. In the literature, many if not all NNS evaluation approaches looks at individual parameters with no collective analysis of how all of the abnormalities and normalities of the NNS signal can be collectively interpretted. Machine learning enables multi dimensional analysis of how these parameters collectively determine if an infant exhibits multiple outlying attributes that indicate abnormal suckling. The future of non-nutritive suckling analysis will need to rely on machine learning methods to better understand the overall contributions of suckling characteristics. A key drawback to this approach is the lack of understanding on how each parameter is weighed and whether the parameter is a contributor to NNS behavior. Parameters existing in the literature have long been extracted and accepted without question, and in the application of machine learning, the weight of importance and relevance is significant to the classification methods.

4.2 Future Direction

Future work to expand these investigations include ultrasound studies alongside NNS measurements of abnormal suckling or oral dysfunctions to truly understand dysfunction-specific mechanics. Correlations between movement and mechanics in the oral cavity must be tied closely to NNS characteristics to determine if NNS can indicate a specific oral dysfunction. Interpretation is a key lacking element in the literature as NNS can be captured but not understood enough to make diagnosis.

With respect to the system, improvements to include additional measurement modalities such as a camera unit or expression pressure may be of use to further characterize infant suckling in a comprehensive manner. While NNS is helfpul, visual information, and other physical changes in the oral cavity such as tongue force can be important to understanding oral dysfunction. Wireless features may be added in the future to simplify data transmission and portability of the system.

The technology and area of research presented in this dissertation holds tremendous promise for changes in clinical practice towards data-driven decision-making. Particularly as it relates to a vulnerable population group such as mothers and infants, it can have life-long impact on their health and development during an important time in their lives. Continued advancement to better understand non-nutritive suckling and the application of machine learning can change the landscape of clinical practice in breastfeeding. Ultimately, the hope is to turn the tides on plummeting rates of exclusive breastfeeding by reducing breastfeeding cessation and enabling mothers and infants to reach their breastfeeding goals.

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