PREFACE

Pain, assumed to be the fifth vital sign, is an important symptom that needs to be adequately assessed in health care. Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage.

Pain motivates the individual to withdraw from damaging situations, to protect a damaged body part while it heals, and to avoid similar experiences in the future. Pain is the most common reason for physician consultation in most developed countries [Debono, D. J *et al.*, 2013]. It is a major symptom in many medical conditions, and can significantly interfere with a person's quality of life and general functioning [Breivik, H. *et al.*, 2008]. Psychological factors such as social support, hypnotic suggestion, excitement, or distraction can significantly modulate pain's intensity or unpleasantness [Eisenberger, N.I., & Lieberman, M. 2005]. Pain that lasts a long time is called chronic and pain that resolves quickly is called acute.

In 1994, responding to the need for a more useful system for describing chronic pain, the International Association for the Study of Pain (IASP) classified pain according to specific characteristics: (1) region of the body involved (e.g. abdomen, lower limbs), (2) system whose dysfunction may be causing the pain (e.g., nervous, gastrointestinal), (3) duration and pattern of occurrence, and (4) intensity and time since onset.

The visual changes reflected on the face of a person in pain may be apparent for only a few seconds and occur instinctively. Tracking these changes and assessing

its intensity is a difficult and time-consuming process in a clinical setting. This is why it is motivating researchers and experts from medical, psychology and computer fields to conduct inter-disciplinary research in capturing facial expressions.

Despite the fact that there has been quite a lot of research done in the field of facial expression recognition, not much development has occurred in detecting the intensity of facial actions. In facial expression recognition, the intensity of facial actions is an important and crucial aspect, since it would provide more information about the facial expression of an individual, such as the level of emotion in a face. Furthermore, having an automated system that can detect the intensity of facial actions in an individual's face can lead up to a lot of potential applications from pain detection to smart classrooms. The provided approach includes robust methods for face and facial feature extraction, and multiple machine learning methods for facial action intensity detection.

The facial expressions of children's (0-2 years) in pain and in non-communicative patients need to be recognized as they are of utmost importance for proper diagnosis. The direct measurement of pain is related to the computation approach whereas indirect measurement is by observers ratings. The aim of this study is to correlate the results obtained from the observer, practitioner, and machine. The results showed that the experts often underestimated pain intensity in comparison to the observer and computational approaches used. This will cover both spheres of psychological vulnerability and resilience to pain along with the advanced techniques used in machine learning thereby improving the quality of care by increasing its accessibility to physicians.

Bioinformatics is an interdisciplinary field that integrates computer science and informatics, biology, statistics, applied mathematics, artificial intelligence, etc. to solve the biological problems at the molecular level. The application of advanced statistical and machine learning techniques in the area of bioinformatics help to organize, analyze, and interpret biological data and thereby prediction of pain and no pain genes. Pain genes prediction is a very important task in bioinformatics and has its major application in drug discovery. The knowledge of the functionality of a gene is very important to develop new approaches in any biological process.

Pain, which afflicts up to 20% of the population at any time, provides both a massive therapeutic challenge and a route to understanding mechanisms in the nervous system. Specialized sensory neurons (nociceptors) signal the existence of tissue damage to the central nervous system (CNS), where the pain is represented in a complex matrix involving many CNS structures. Genetic approaches to investigating pain pathways using model organisms have identified the molecular nature of the transducers, regulatory mechanisms involved in changing neuronal activity, as well as the critical role of immune system cells in driving pain pathways. In man, mapping of human pain mutants as well as twin studies and association studies of altered pain behavior have identified important regulators of the pain system. In turn, new drug targets for chronic pain treatment have been validated in transgenic mouse studies. Thus, genetic studies of pain pathways have complemented the traditional neuroscience approaches of electrophysiology and pharmacology to give us fresh insights into the molecular basis of pain perception.

The work presented in this thesis investigates the various available methods in literature for computational intelligence techniques applied to this domain and

proposes new efficient approaches for pain assessment using facial expressions and pain genes.

The major objective of the present work is to develop efficient and robust computational intelligence techniques for prediction of pain based on the intensity level. The success of design and development of efficient and robust computational intelligence techniques relies on the design and development of an appropriate feature extraction, feature selection and pattern classification techniques for the said task.

In this thesis following associated problems of pain, prediction is investigated.

1. A comprehensive review of technologies in the study of facial expression along with its application in pain assessment.
2. Classification of pain using computational intelligence techniques.
3. Classification of facial expressions of pain based on the VAS, observer, and expert ratings.
4. Classification of pain and no pain genes.

To address the above mentioned problem following computational intelligence techniques are proposed.

1. The computational aspects of pain assessment, to acquire knowledge from the clinical data received by patients or experts, are focused in this review. The computer technologies identified were grouped together into following four categories comprising of artificial neural networks, rule-based algorithms, statistical learning algorithms and nonstandard set theory.

2. For binary pain detection and pain intensity estimation, scale invariant feature transform and speeded up robust features are used for feature extraction along with linear discriminate analysis and principal component analysis for dimensionality reduction and support vector machine used for classification.

3. An efficient approach for prediction of pain intensity from facial expressions using facial action coding system by observers along with the self-report of patients provided on a visual analogue scale and computational technique were analyzed and correlated for better accuracy.

4. An efficient and robust approach for the prediction of pain and no pain genes representing amino acid sensing ion channels, machine learning methods in detecting gene-gene interaction and network pathways.