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REAL-TIME MULTISCALE DETECTION OF DEFECTIVE PILLS DURING MANUFACTURING

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Abstract. We explore methods to automatically detect the quality in individual or batches of pharmaceutical products as they are manufactures. The goal is to detect 100% of the defects, not just statistically sample a small percentage of the products and draw conclusions that may not be 100% accurate. Removing all of the defective products, or halting production in extreme cases, will reduce costs and eliminate embarrassing and expensive recalls. We use the knowledge that experts have accumulated over many years, dynamic data derived from networks of smart sensors using both audio and chemical spectral signatures, multiple scales to look at individual products and larger quantities of products, and finally adaptive models and algorithms.

Key words. manufacturing defect detection, dynamic data-driven application systems, DDDAS and integrated sensing and processing, high performance computing, and parallel algorithms

1. Introduction

Diabetes is a problem worldwide. Of the more than 15 million Americans who have diabetes mellitus, about five million do not know it. Nearly 1 million new cases are diagnosed each year. The disease affects men and women of all ages and certain ethnic groups are more greatly affected than other groups [1]. With the more common type 2 diabetes, the body does not make or use insulin properly. Without enough insulin, the glucose stays in the blood system. Having too much glucose in the blood system causes serious problems, e.g., damage to the eyes, kidneys, and nerves. Other side effects of diabetes include heart disease, stroke, and removal of limbs. Pregnant women can also have gestational diabetes [2].

The total annual economic cost of diabetes in 2007 in the U.S. was estimated to be 32% higher than just five years earlier. In 2007, medical expenditures totaled $116 billion ($27 billion for diabetes care, $58 billion for chronic diabetes-related complications, and $31 billion for excess general medical costs). Indirect costs resulting from increased absenteeism, reduced productivity, disease-related unemployment disability, and loss of productive capacity due to early mortality equaled the cost of chronic diabetes-related expenditures. One out of every five health care dollars is spent caring for someone with diagnosed diabetes, while one in ten health care dollars is attributed to diabetes [3].

While U.S. drug products are of generally high quality, there is an increasing trend toward manufacturing-related problems that lead to recalls, disruption of manufacturing operations, and loss of availability of essential drugs. The U.S. Food and Drug Administration (FDA) is combating these problems plus low manufacturing process efficiency (<30%) has also led to increased cost of drugs by emphasizing current good manufacturing practice (cGMP) as the means of controlling drug quality. An unfortunate side effect is that many companies are no

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longer innovating at the same rate as before. The FDAs response is that uses of new sensing technologies will be key to improving the regulation and quality of drug manufacturing using scientifically proven risk-based methods. Near infrared (NIR) is one of the process analytic technologies (PAT) that the FDA has chosen to improve manufacturing process quality [4].

In Section 2, we describe the smart sensors we are designing for use on manufacturing lines and how both offline high performance computing and integrated sensing and processing are involved.

In Section 3, we describe where multiscale techniques are useful and how to construct them.

In Section 4, we describe the process of finding the best frequencies for drug identification considering algorithmical and numerical aspects.

In Section 5, we describe some identification results along with some simple timing information for the parallel computation needed to create libraries for our sensing devices.

In Section 6, we draw some conclusions.

2. Smart Sensors with Integrated Sensing and Processing

Smart sensors are a form of integrated sensing and processing (ISP). ISP optimizes systems that integrate sensing, signal processing, communication, and targeting. Traditional sensing systems lead to high dimensional and prohibitively expensive problems to solve. ISP based methods lead to reduced and low dimensional systems that can be solved through a combination of the on board computing on the sensors and by solving auxiliary problems on highly parallel computers in advance. We convert data directly to knowledge using programmable on demand ISP-based imaging spectrometers that produce detector signals that can be correlated directly to desired samples. Hence, we do not need to do a post collection chemometrics step. Parallel computers produce libraries that are downloaded to the ISPs and include environmentally relevant information that is updated on a regular basis. While these libraries are expensive to create computationally, the use in the ISPs is both inexpensive and fast.

Dynamic data-driven application systems (DDDAS), [5], [6], and [7], place far different strains on high performance systems and centers than traditional applications due to dynamic and unpredictable changes in resources that are required during long term runs. An on demand environment is required that stresses traditional computing centers views on allocating resources. The number of processors, network resources, and location of computing and data can change unpredictably during the course of a long term DDDAS computation [8] and [9].

DDDAS assumes that application components, resource requirements, application mapping, interfaces and control of the measurement system can be modified during the course of the application simulation. Figure 1 provides a schematic of how typical DDDAS applications appear componentwise.

The longest running DDDAS we are aware of began its calculations in 1978 and still runs today even though all of the hardware and software have changed over time, but the application has never been turned off. The application monitors all oil and gas pipelines, storage tanks, wells, and tanker loading in Saudi Arabia.

The devices we are designing for this project are designed to reduce the over abundance of data that is prevalent in most pharmaceutical manufacturing environments today [10]. We envision using similar devices in related fields, e.g., handheld devices to ensure correct pill delivery wherever health caregivers are involved.