1 Introduction

The most conventional production route towards an advanced ceramic material consists of the conditioning, shaping and heat-treatment of dry precursor powders. This procedure is traditionally time-consuming, taking up one or more days per batch of material. Fortunately, this process can be scaled up arbitrarily and considerations of time recede in an industrial environment. For scientific work however, the mentioned time frame is often a hindrance since in contrast to industrial materials production where the emphasis frequently lies on a maximum batch size, the materials scientist seeks to synthesize and learn about as many distinct materials as possible. Thus, the experimental effort scales with the duration of one synthesis cycle.

An opportunity to conduct materials research in a more efficient way is high-throughput experimentation (HTE). The fundamental idea of this scientific paradigm is to maximize the density of information gained from an experiment with respect to experimental time by means of parallelization and automation of synthesis and analysis procedures.

HTE had seen extensive use in pharmaceutical research [MSS07] as well as organic chemistry [Sch04, MSS07], frequently supported by a design of experiments based on combinatorial models as well as elaborate data mining approaches to filter experimental results for valuable knowledge. An adaption to material science with its multi-parameter experimental spaces was obvious and since the 1990s HTE has been common practice also in ceramics research [Sie98, MSS07].

For ceramics however, the vast majority of works reported in literature are based on thin-film technology or use liquid-phase, colloidal processing techniques, both of which allow for an easy, continuous change of composition between samples. Frequently though, samples resulting out of such HTE campaigns fail to allow conclusions with respect to the behaviour of the respective bulk material. Consequently, in this work an attempt is made to implement an HTE setup emulating a conventional powder metallurgical synthesis route that yields ceramic bulk materials.

In the beginning of the work an illustrative part describes the HTE setup as well as the necessary equipment. Requirements leading to the acquisition or adaption of the equipment are illucidated.

Subsequently, the setup is validated by using yttria-toughened zirconia, a well-known ceramic material system. Conventionally produced reference samples are compared to sample libraries from the HTE setup and their difference is evaluated statistically.

Finally, the setup is applied to a novel piezoelectric materials system, namely sodium potassium niobate (KNN). Starting from a well-known subsidiary KNN system, it is shown that the presented HTE-approach allows for an efficient and reliable detection of phase boundaries. Phase boundaries constitute areas of amplified interest in piezoceramics due to the possibility of finding maximum piezoelectric behaviour in their vicinity. The successful employment of a software-based data mining approach for this purpose is demonstrated.

Due to the parallelized handling of small amounts of dry powders the samples from the HTE setup show an inferior composition homogeneity compared to conventionally prepared ceramics. In the course of the work the reasons underlying this effect are closely examined and consequential guidelines for operation and experimental planning are developed.

2 Fundamentals

2.1 Origins

Since its development in the 19th century by Russian chemist Dimitriy Mendeleyev the Periodic Table of Elements has been used for the purpose of classification and comparison of chemical compounds with respect to the positions of their elements in this ingenious tabular arrangement. Few scientists have been capable of perceiving it in addition as a well-ordered catalogue of building blocks to synthesize new and useful substances in a systematic manner. Among these visionaries were people like the German chemist Alwin Mittasch who in the beginning of the 20th century undertook 20000 experimental runs while systematically trying to develop an efficient catalyst for Haber-Bosch-synthesis of Ammonia [Caw03a]. Paul Ehrlich synthesized several hundred trivalent arsenic compounds and finally succeeded in finding Salvarsan, a drug against syphilis [Caw03a]. In the late 19th century US-American inventor Thomas Edison tested several thousand substances until he came up with an optimal material for the filament inside the light bulb. Edison is probably the most renowned of the scientists using this systematic approach and consequently has lent his name to a class of experiments conducted in his spirit [AXZ02, Caw03a].

To understand the scope the Periodic Table offers as a mere record of potential modular blocks one can use the basic models of combinatorics, a subset of discrete mathematics that deals with quantification of combinations of distinguishable and indistinguishable objects. Assuming 50 elements out of the Periodic Table to be useful and stable and, for a start, equimolar compositions of those 50 elements the combinatoric model of a disordered and unreclined sample can be used. The total number of different combinations in this case would be [BB95]

$$N(n_E, n_r) = n_E! / \left[n_r! \, (n_E - n_r)! \right] , \tag{2.1}$$

where n_E is the number of elements (i.e. 50), n_r is the combinatorial range (e.g. 2 for binary) and N is the number of possible combinations. It follows that there are theoretically 1225 possible binary, 19600 ternary and 230000 quaternary molecules or compositions.

Dropping the restriction of equimolarity one can make use of the model of a disordered, reclined sample [BB95]:

$$N(n_C, n_r) = (n_C + n_r - 2)!/\left[(n_C - 1)!\,(n_r - 1)!\right]. \tag{2.2}$$

n_C here is the number of different incremental compositions. Molecules are thus treated as ordered partitions of n_C parts into words of length $n_r - 1$, where the subtraction of 1 is due to stochiometry. Of course equation 2.2 pertains to each of the combinations calculated by equation 2.1. For example for a hypothetical binary combination AB $n_C = 11$ (concentration increments of 10%) would mean A_0B_1, $A_{0.1}B_{0.9}$, $A_{0.2}B_{0.8}$,..., A_1B_0. Hence, the size for this concentration space can be estimated by

$$N(n_E, n_C, n_r) = N(n_E, n_r) \cdot N(n_C, n_r). \tag{2.3}$$

Table 2.1 shows the numbers of some possible combinations.

$\mathbf{n_C}$	$\mathbf{n_r = 2}$	$\mathbf{n_r = 3}$	$\mathbf{n_r = 4}$
6	7350	411600	12.9×10^6
11	13475	1.3×10^6	65.8×10^6
21	25725	4.5×10^6	0.4×10^9

Table 2.1: Estimate of possible molecules from 50 starting elements according to equation 2.3.

It is obvious though that the number of actual experimental runs would be even higher. In addition to formulation factors mentioned so far the experimental space is spanned by all variables in the system [Caw03b]. Thus process factors like for example annealing temperature or mixing time can not be neglected. In fact including these factors will make the experimental space grow geometrically,

$$N(v_{pv}, n_p) = N(n_C, n_r) \cdot n_{pv}^{n_p}, \tag{2.4}$$

with growth factor n_{pv} being the number of parametric values of all n_p process factors. For applications in materials science the numbers resulting from these thought experiments can be put into perspective when one considers the number of known inorganic phases in the late 1980s to be approximately 24000 [AXZ02]. The experimental space mentioned above therefore constitutes both a challenge and a chance for modern materials development. The challenge can be met by combinatorial high-throughput experimentation (CHTE) and high-throughput experimentation (HTE) .

CHTE and HTE can be defined as "*a set of techniques for creating a multiplicity of compounds and then testing them for activity*" [Caw01]. The earliest antecedents of this paradigm fell together with the development of what is known today as Design of Experiments (DOE) [Caw03a] and can be found in the field of agriculture where due to the extreme running times of experiments (typically multiples of years) a parallelization became inevitable. The distinction between HTE and CHTE is not well-defined. In general, the former refers to the parallelized and/or automatized sequential synthesis and analysis of a high number of samples, where preconceptions about the sample behaviour and the analytic results lead to a pre-experimental containment of the experimental space. In the latter this containment does not exist to the same degree which explains the necessity for different procedures for the design of experiments and the evaluation of their results mentioned later in this chapter.

Like many other technologies, HTE and CHTE was only made possible on a larger scale for industry and academia by the advent of affordable and user-friendly computer technology in the 50s of the last century [PM07]. The 60s and 70s brought an interest in the quantitative assessment of biochemical structure-activity relationships and also saw the development of the first autosampling units which effectively introduced robotics into a laboratory work field. Consequently, pharmaceutical companies started putting more and more effort into utilizing CHTE for their needs to lower their time to market [PM07, Caw01]. CHTE-prepared compound sets, so-called "libraries", with up to 10^6 distinct samples are produced

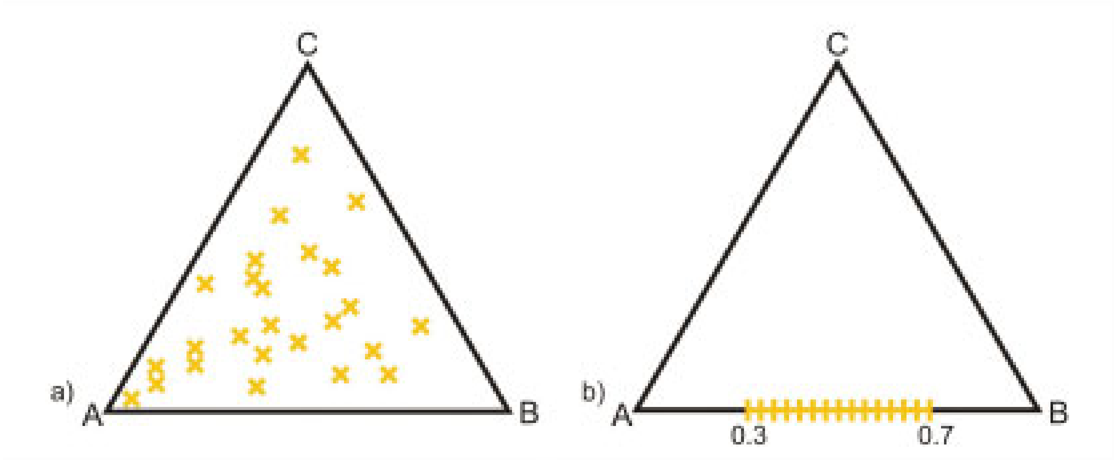

Figure 2.1: Scheme exemplifying the difference between CHTE and HTE concepts with a) showing a typical experimental space in case of a CHTE and b) of an HTE approach.

routinely by most pharmaceutical manufacturers these days [Caw01].

The first works in CHTE of materials science surprisingly go back to the 60s of the last century. Kennedy *et al.* [KSD$^+$65] and Miller and Shirn [MS67] used cosputtering techniques to produce the first multiple-component phase libraries in materials science. Kennedy *et al.* were able to demonstrate agreement between their "proto"-HT phase diagrams and the respective conventional ones by means of electron diffraction. Miller and Shirn succeeded in measuring the electrical resistivity over the full range of composition in the binary Au-SiO_2-system.

In 1970 Hanak published his work on the Multiple-Sample-Concept [Han70] which many authors claim to be the forerunner of modern day CHTE materials science. Hanak made a strong case for dealing with the topic of efficiency in materials development when he wrote "*The present approach to the search for new materials suffers from a chronic ailment, that of handling one sample at a time in the processes of synthesis, chemical analysis and testing of properties*" [Han70]. He suggested to implement a radio frequency sputtering device with two or three different targets that could be sputtered simultaneously onto one substrate. Varying film thickness on the substrate as a function of their position relative to the respective target sections on the substrate was responsible for the varying local compositions. Hanak later blamed a lack of computing power at the time to have prevented his concept from having broad success in the materials community [Han03]. Consequently, the HT-strategy was not implemented on a larger scale until this problem was relieved.

More than two decades later Schultz *et al.* published a paper that marked the beginning of modern combinatorial and HTE materials science [XSB+95]. Catalysed by the developments in biochemistry and pharmaceutical industry mentioned above numerous high-throughput synthesis and screening schemes had been implemented. This newly emerging discipline called combinatorial chemistry also brought the ideas of spatially addressable libraries and gene chips [XT03] and thus the trend to parallelize and minimize experiments. These ideas were taken up by Schultz *et al.* when they deposited metal oxides on top of each other using a masking scheme. The major difference with respect to Hanak's work was the spatial addressability of the samples. The experiments yielded various cuprate superconductors.

CHTE has since developed rapidly spanning the whole field of materials development as it has been applied to all major classes of materials incorporating all possible aggregate states of educts and a plethora of processing and analysis concepts.

2.2 Industrial and academic potential

Industrial HTE originated from academic backgrounds, e.g. at UC Berkeley [Xia98, CTX99, CGT+98], which lead to the foundation of Symyx as the first commercial supplier of hardware and service in the field. Parallely several hundred million US-dollars worth of HT-technologies were being implemented in various projects in large scale industry aiming for the most part at the optimization of known materials and processes. In the US, federal agencies like NIST (National Institute of Standards and Technologies), North Dakota State University or University of Iowa followed. Service providers like Symyx also spawned the interest in the European industrial environment and European start-ups followed in Symyx' footsteps. Examples were hte (Germany), Avantium (Netherlands) and Accelab (Germany). These developments in turn allowed for collaborations between industry and academia which produced among others DPI (Netherlands), FLAMAC (Belgium) and Insight Faraday (UK) [DAHfM06]. At the time of writing it is estimated that by 2010 a yearly turnover of US-$ 400 million will result from sales of HT-equipment in Western Europe alone. The world market for HT-technologies and services is estimated to be at US-$ 1 billion per year with growth rates of 7% [FS03].

The automatized parallel or rapid sequential execution of large numbers of experiments has also remained attractive to academia where money and manpower are traditionally even more limited than in industrial environments. Hence the exceeding presence of HTE- and CHTE-related topics in the respective scientific journals. Potyrailo and Maier [PM07] state that in 2007, the growth-rate of HTE-related publications in materials research has exceeded that of rational materials development publications. About 70% of those publications deal with synthesis and measurement, another 11% with the design of experiments and 8% with the organization and mining of the reaulting data [PT05]. It is obvious from these figures that HTE needs a variety of academic orientations to be impelled.

Indeed the absolute numbers of publications in the field of materials have seen a strong incline within the 10 years leading up to 2004 as can be seen from a search in *ISI Web Of Science* (http://portal/isiknowledge.com/).

Interestingly enough, the search for “High-Throughput” *AND* various materials groups does not sum up to the numbers for “High-Throughput” *AND* “Materials” with the difference increasing over the years. It is possible that workers in the field are actually starting to perceive themselves as “High-Throughput Material Scientists” instead of, say, ceramists using HTE. Although the main reason for this phenomenon is supposedly the rising use of a common terminology of HTE that now reaches back to the sources of HTE, namely various disciplines of what is nowadays termed “life sciences”. Their works would surface under the keyword “Materials” but not under any of the material classes mentioned above.