Summary

In food industry, health care, etc., there is a high need for bio-chemical sensing systems that are sensitive, accurate, selective, and multipurpose. These sensing systems can be used for detection of an analyte concentration in a given sample solution such as pesticides in milk, virus particles such as HIV and SARS in a blood sample, etc. Integrated optical (IO) interference-based sensors offer a good possibility for realization of such sensing systems, being extremely sensitive and offering the prospect for development of multichannel configurations. In this thesis, we describe the design, realization, and characterization of a highly sensitive multichannel IO Young interferometer (YI) immunosensor.

In Chapter 2, a theoretical analysis of the multichannel YI sensor is presented. The principle of a two-channel YI is expanded to a multichannel device by choosing different distances between output channels such that each pair of channels functions as a two-channel YI with a unique distance between its two arms. Calculations show that phase errors of ~ 10% of the phase signal are caused by a mismatch between spatial frequencies of the individual interference patterns and those determined by the pixel distances of the CCD camera used to measure the interference pattern, originating from the Fast Fourier Transform (FFT) algorithm used for signal analysis. A scheme is proposed to reduce this error by a factor of 5.

In Chapter 3, the multichannel IO YI sensing system is designed based on a number of requirements related to the performance such as high resolution, simultaneous readout of all channels, etc., and according to some boundary conditions, e.g. realization of the IO readout system in the Silicon-oxynitride technology. Analysis of the disturbing factors such as temperature difference between channels has introduced some more requirements for the design of the sensor system. The final design of the multichannel IO YI sensor is presented and the process flow for realization of the optical chip is described

Experimental characterization of the multichannel YI sensor devices is presented in Chapter 4. Different glucose concentrations are measured and a good accordance is found with theory. The two-channel YI, which is realized as a first step towards development of the multichannel sensor, shows a phase resolution of ~ $1.5 \times 10^{-5} \times 2\pi$ (refractive index resolution of ~ 3×10^{-9}). Next, it is shown experimentally that the four-channel YI sensor can measure three different concentrations of an analyte, such as glucose, simultaneously and independently from each other. Application of different schemes has reduced the phase errors to ~ 3% of the phase signal. We found that the phase resolution for different pairs of channels is ~ $1 \times 10^{-4} \times 2\pi$, corresponding to a refractive index resolution of ~ 8.5×10^{-8}, and the long-term stability is ~ $5 \times 10^{-4} \times 2\pi \cdot h^{-1}$.

In Chapter 5, the use of the multichannel IO YI as an immunosensor is reported. A pA-modified sensing surface, which promotes proper antibody orientation, is efficiently used to immobilize antibodies at the Si_3N_4 surface, resulting in a

surface coverage of ~ 3 mg/m^2. Next, the YI sensor has been successfully used for detection of Human Herpes Simplex virus. We found that the resolution of the YI sensor can approach detection of a single virus particle. Three different measuring channels are used to monitor proteins and viruses simultaneously and to measure different protein concentrations. The results are in good agreement with predictions for specific interaction and show low non-specific binding.

A new method for correction of the drift in the multichannel YI sensor is demonstrated in Chapter 6. The phase information obtained for different channel pairs is used to correct the drift mainly due to temperature differences between measuring and reference channels. This method is experimentally tested by applying it for sensing applications. We found that the drift in the phase can be decreased by one order of magnitude when the new method is applied. Implementation of this technique is possible because the phase change for each channel pair in the multichannel YI sensor can be simultaneously measured.

In Chapter 7, the development of a microfluidic sensing system obtained by bonding a microfluidic system to an IO four-channel YI chip is presented. The microfluidic system is structured in such a way that after bonding to the IO chip each microchannel addresses one sensing window in the four-channel YI sensor. It is found that the implementation of the microfluidics reduces the response time of the sensor by a factor of ~ 20 as compared to a bulky cuvette and the volume of the sample solution required is three orders of magnitude smaller. Because of this, a better discrimination between the refractive index change of the sample solution and the layer formation can be made in an immunoreaction, resulting into a higher accuracy and offering the prospect for using the kinetics of the immunoreaction.

In Chapter 8, a novel approach, consisting of simultaneous use of three different wavelengths for discrimination of the refractive index change, thickness of a bound layer, and temperature change, is presented.

In Chapter 9, some conclusions that concern the development of the multichannel IO YI sensor and its use for different applications are discussed. A comparison between the multichannel YI sensor and other interferometric sensors, as well as other techniques, is made. This Chapter concludes with an outlook concerning further improvement of the performance of the IO YI sensing system.

Some new approaches for future development of the multichannel interference-based sensors are presented in Chapter 10. Here, attention is paid to the improvement of the resolution and multichannel operation of these sensors. Advantages and shortcomings of the new configurations are discussed.