DOCTORAL CANDIDATE:	Theis Sommer
DEGREE:	Philosophiae Doctor
FACULTY:	Faculty of Mathematics and Natural Sciences
DEPARTMENT:	IBV, NCMM
AREA OF EXPERTISE:	Biochemistry, Structural biology
SUPERVISORS:	Jens Preben Morth, Oddmund Bakke
DATE OF DISPUTATION:	30th of June 2016

DISSERTATION TITLE: *Biotechnological application of the bacterial enzyme Isatin hydrolase AND Structural studies of the regulatory N-terminal domain of the SLC4 bicarbonate transporters*

Part I: describes the characterization of the bacterial enzyme Isatin hydrolase (IH), and describes determinants for substrate binding and conversion. Increased levels of the enzyme substrate – isatin, have been linked to stress in humans and rodents. As a biotechnological extension of the characterization of IH, a fluorescent assay was developed for isatin detection in blood samples. The assay includes a phase extraction step combined with the enzymatic conversion of isatin to isatinate. This utilizes the change in hydrophobicity between the substrate and the product of IH. All steps in the protocol are, in principle, parallelizable which would allow for higher throughput of samples resulting in a better understanding of isatin in human physiology and pathophysiology.

Part II: Control of extracellular and intracellular pH is essential for maintenance of correct cellular function. The bicarbonate buffering system constitutes the main buffering system of the human body. The transport of bicarbonate across the cell membrane is mainly carried out by the SLC4 transporter family two of the ten members include the sodium dependent chloride bicarbonate exchanger (NDCBE) and the electrogenic sodium bicarbonate cotransporter 2 (NBCe2). Here we describe a novel zinc binding site in the regulatory domain of NDCBE and the first crystal structure (2.6 Å resolution) of NDCBE. We describe regions of importance for dimerization and propose a model for the orientation of the regulatory domain with respect to the transport domain. The study is supported by the first low resolution (4.2 Å) crystal structure NBCe2. The novel zinc binding site within the regulatory domain was identified and characterized, by tryptophan fluorescence and isothermal titration calorimetry alongside mutational studies of NDCBE and might pose a novel regulatory mechanism for these essential transporters.