

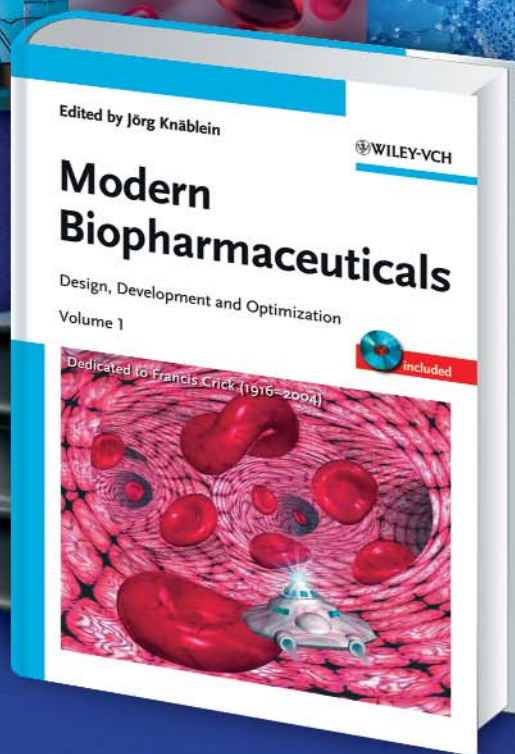
Dedicated to Francis Crick (1916-2004)

# Modern Biopharmaceuticals

The Guinness Book of Biotechnology

Jörg Knäblein,  
Schering AG, Berlin,  
Germany

4 Volumes



2005. 2022 pages with  
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4 | Molecular Imaging and Applications for Pharmaceutical R&D

fore, the improvement of the mechanical design of the gantry, which carries the X-ray tube and the detector, is essential. The final image is reconstructed from the measurements by applying either a filtered backprojection algorithm or more advanced iterative reconstruction techniques. Each pixel contains the averaged attenuation values within the corresponding voxel (the smallest volume unit in the image). This number is compared to the attenuation value of water and displayed on a scale of Hounsfield units (HU), named after the inventor of CT, Sir Godfrey Hounsfield. The scale assigns an attenuation value of zero to water and regular attenuation values range from -1000 to 3000 HU. The attenuation value of soft tissue ranges between 40 and 100 HU.

The spatial resolution in X-ray CT depends on the focal spot of the X-ray tube and the size of the detector elements. The spatial resolution of a clinical CT scanner is less than 0.5 mm in the center of the CT scanner. For pre-clinical imaging, several micro-CT systems have been developed and are commercially available [2]. The spatial resolution of dedicated small-animal scanners is much higher than for clinical scanners, and is in the order of 20 µm. Fig. 4.2 shows high-resolution images obtained with an animal CT scanner. The major advantage of X-ray CT is its ease of use ('push-button-technology') for acquiring large 3D datasets with structural information at a very high spatial resolution. The disadvantage of X-ray CT is the use of ionizing radiation, which can lead to cell death or to cancer due to genetic mutations. For example, the effective dose of a clinical CT scan of the abdomen is about 10 mSv, which is about 400 times higher than the dose of a chest projection X-ray.

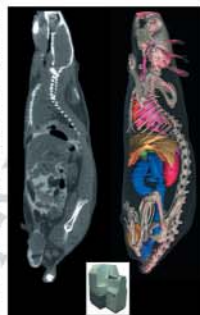
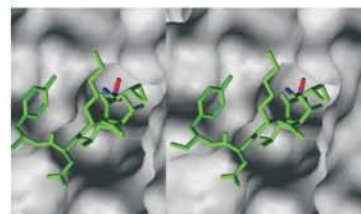


Fig. 4.2 Dedicated animal X-ray computed tomography system that allows high-resolution imaging (up to 18 µm) of rodents. The different attenuation of X-rays in various tissues and bones allows volume rendering of the different structures (right image).

#### 4.2.1.1 X-ray Contrast Agents

X-ray contrast agents are chemicals that are introduced into the body to increase the image contrast. They contain substances with a high atomic number that increase the attenuation value in the regions where they accumulate. A typical X-ray agent used to image the gastrointestinal tract is barium sulfate, a solution of which the patient drinks hours prior to examination. For imaging of the colon, air is also used, which has a high negative Hounsfield value (-1000). Iodine-containing contrast agents are widely used for X-ray-based angiography, and are also ap-

es of Serine Proteinase Activation



prothrombin-2 activation pocket is shown in pink, with the saggan atoms shown in red. The N-terminal hexapeptide of SC is shown in green, while the N-terminal nitrogen is shown in blue.

6-thrombin is essentially unaltered compared to the over-100 crystal of the enzyme deposited with the Data Bank. This observation is consistent with bacterial nucleotide or genomic homology with SK not serine proteinases including also SK modulate the bound enzyme; a new specific surface site for presentation of the substrate(s), shaping the active-site conformation.

#### Nonproteolytic Zymogen Activators

Factor A, a protein from *Streptococcus* whose 251 amino acids show many structure homology to SK, is able for the pathogenesis of botulism, an infection of the udder *pro* uses peptides released from casein from milk casein to meet its amino acid demands [80]. The two-domain protein lacks an equivalent to the SK γ do-

main, leading to faster complex generation, but the complex is less firm and sensitive to inhibition by α<sub>2</sub>-antiplasmin. SUPA does not share significant nucleotide or genomic homology with SK nor serine proteinases including also bovine plasminogen through a SK- and not a SAK-type mechanism. The Ile-Thr-Gly N-terminus of SUPA points towards a molecular sexuality activation mechanism.

Recently, a number of bacterial proteins sharing sequence and apparently secondary structure homology with SK ("ZAAP") could be identified by database searches [77]. Some of them could be already shown to possess at least weak prothrombin activator activity [81]. Whether prothrombin or other host serine proteinases represent the actual targets for these proteins remains to be elucidated.

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