determine sensitivity profiles dependent on the partial optical path lengths in the different types of tissue and source-detector spacing (see fig. 2.8).

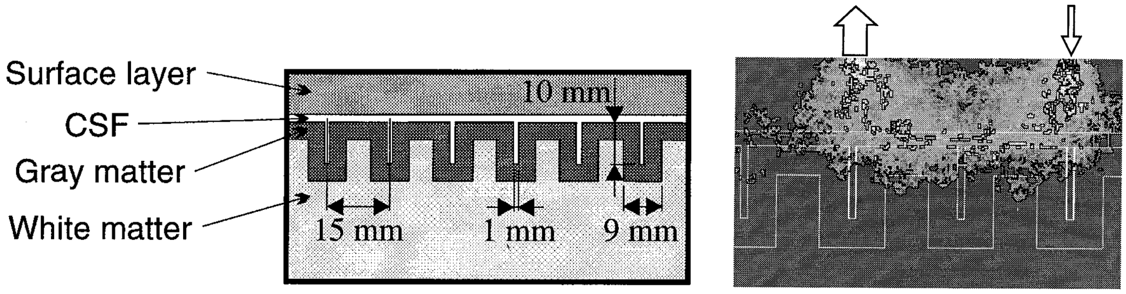

Figure 2.8: Model and spatial sensitivity profile for a source-detection distance of 30mm, fig. taken from [31].

They found that

- at small detection positions ($\leq 15\,mm$), the mean optical path length is approximately equal to the partial mean optical path length of the surface layer (skin, skull) resulting in the spatial sensitivity profile being confined to this surface layer.
- at intermediate positions ($\geq 15\,mm, \leq 25\,mm$), the partial mean optical path lengths of both cerebrospinal fluid (CSF) and gray matter (GM) layers increase with detection position.
- at large detection positions ($\geq 25\,mm$), the partial mean optical path lengths of surface and GM layers remain approximately constant while that of the CSF layer increases with source-detector spacing.

They concluded that for a source-detector spacing of 50mm, light spends approximately 65% of its path in scalp and skull, approximately 35% in the CSF and only approximately 5% in the gray matter of the cortex. Nevertheless, the contribution of the gray matter layer was estimated to be at least 20-30% of the absorption change in the NIRS signal.
In literature, commonly used source-detector distances resulting in a clear brain activity signal are between $3 - 4\,cm$ with the rule of thumb for frequency domain and continuous measurements that the depth of maximum brain sensitivity is approximately half the source-detector separation distance [13].

2.5 Review of existing fNIRS Technology

As a preparation for the CW fNIRS system design, the literature on NIRS instrument development approaches was reviewed. Tab. A.1 and A.2 (see Appendix A) summarize some of the important and comparable features of instruments developed by work groups around the world.
As can be seen, almost all instruments are based on CW technology, about two-thirds using lock-in approaches for improvement of the signal-to-noise ratio [18–20, 30, 44, 45, 48–53]. While some instruments use Time-Division Multiplexing (TDM) techniques, activating only one NIRS channel at a time [15, 32, 38, 45, 49, 52–55], others use frequency-encoded simultaneous emission and band-pass filter extraction or software based demodulation schemes [19], enabling the continuous measurement of all channels.

It should be pointed out that many work groups use external desktop lock-in amplifiers such as from the Ametek series [18, 50] or external ADC/Data Acquisition instruments, e.g. National Instruments or Keithley DAQ USB or PCI devices [18, 19, 49, 50, 53]. Such NIRS instruments dot not work stand-alone and are usually not portable.
Only two stand-alone instruments were found that provide wireless data transmission for mobile deployment [15], [56].

In a review on CW functional Near-Infrared Spectroscopy and Imaging instrumentation and methodology by Scholkmann et al. [11], a comparison of the first commercial instruments on the market can be found (see fig. A.1, Appendix). The variety of these instruments ranges from

- systems with few sources/detectors suitable for local detection of certain brain areas to systems covering the whole head
- a few instruments using sensor patches with integrated components to the majority of instruments using optical fibers and flexible head caps
- most fNIRI devices being larger in size and static to very few being attached to the subject providing wireless data transmission
- some $10,000$ USD to several $100,000$ USD for whole-head imaging systems

In the following, some of the key components of NIRS instrumentation will be discussed.

2.5.1 NIR Light Emitters

The ideal light source provides multiple monochromatic wavelengths in the near-infrared range, each at relatively high power for higher penetration depth [13]. At the same time, the radiation variance should be minimal: If there is no additional monitor for the intensity of the interrogation beam, fluctuations in the radiation intensity cannot be discriminated from changes in absorption due to changes in chromophore concentration in the tissue. At last, the radiation spectrum of the light source should be as sharply peaked as possible, ideally being monochromatic. However, if the emission spectrum is known, weighted averaging approaches can be used to correct the extinction coefficients [11]. Collimation of the input light is less important for the intensity at the detector than the power of the incident light itself, as scattering processes in the first millimeters of the tissue rapidly make the collimated interrogating beam diffuse [21].
For near-infrared light emission into tissue, mainly three types of sources are possible:

- Laser Diodes (LD)
- Light Emitting Diodes (LED)
- White Light Sources (e.g. Xenon flash tube or quartz halogen light) with monochromators/interference filters

The use of white light sources has so far not been documented, as they require filters, they are large and most importantly dissipate much heat. This makes them not suitable to fNIRS instrument applications. The two other options - laser diodes and light emitting diodes - are both often used in NIRS instruments, each having their advantages and disadvantages (see tab. 2.2).
Laser Diodes that have been used for fNIRS instrumentation are, among others, Sanyo DL7140-201 and Hitachi HL8325G [45], Vertical Cavity Surface Emitting Lasers [52] and Laser Diode Labs LA68 and STC LA8 [3]. A table and comparison of commercially available pulsed high-power laser diodes can be found in [21].

LDs	PRO	+ Sharp radiation peak: coherent, almost monochromatic light emission + Pulsatile operation allows ns pulse widths with peak powers of up to 10W [30]
	CON	- Often in large packaging, miniaturizing is more challenging - Higher safety demands to prevent eye damage - Have narrower operating range - Available wavelengths are limited, between $695 - 775\,nm$ expensive [11] - Extreme heating of the semiconductor junction often requires optical fibers to carry light to and from tissue [53]
LEDs	PRO	+ available in packages with 2 or more individually controllable wavelengths + Since the photons are incoherent / uncollimated, a higher emission into tissue is possible than by LD with the same maximum permissible exposure[19] + Easy to adjust, have a broader operating range than LD + Available in greater variations, giving more freedom in wavelength selection + Minimal power consumption and minimal heat dissipation problems
	CON	- Wider emission spectrum: typ. bandwidth $25 - 50\,nm$ - Lower optical power output to consumption ratio than LD

Table 2.2: Comparison of LED and LD for use in fNIRS instrumentation.

Particularly in more up-to-date approaches, Light Emitting Diodes are often used. Work groups chose multi-wavelength LEDs from Epitex [14, 15, 38, 49, 53, 54, 57] such as the Epitex L760/850, different models from Optodiode [19, 20, 58] such as OD-7860, APT-0101 or APT-0010 or from Hamamatsu, e.g. L6112-01 [50] and others.

The selection of the optimal NIR wavelengths is crucial and will be discussed in detail in subsection 3.4.1.

2.5.2 NIR Light Detectors

Mainly three types of detectors can be used to detect the near-infrared light coming from the tissue:

- Photomultiplier Tubes (PMT)
- Silicon p-i-n Photodiodes (SPD)
- Avalanche Photodiodes (APD)

In PMTs, based on the external photoelectric effect, photons free electrons from a photocathode surface, which are then accelerated by a strong electric field, raising their kinetic energy. These high-energy electrons knock out secondary electrons from a cascade of dynodes which themselves are accelerated by the field, thereby multiplying the current which is produced by the incident light by up to 10^6 to 10^7 [11].
In SPDs and APDs free charge carriers are created based on the internal photoelectric effect: Incident photons are absorbed by the semiconductor junction and thereby raise electrons to higher energy, creating drifting electron-hole pairs that result in a detectable photocurrent.
Avalanche Photo Diodes use a similar principle to PMTs: A large electrical field is applied across the APD junction that accelerates free electric charge carriers generated by photon absorption. Those free carriers are again accelerated and generate more carriers through impact ionization, resulting in the so-called avalanche effect. By application of up to several hundred volts, an internal amplification in the range of a few hundred times [11] can be achieved.
Photo diodes have no internal signal amplification. Emerging photocurrents have to be

amplified by external circuitry in one of two possible operation modes: In *photovoltaic mode*, no bias voltage is applied and the generated photocurrent is measured over a large load resistance. The response of the signal to the optical power is logarithmic and much slower than in photoconductive mode but enables a higher dynamic range. In *photoconductive mode*, a reverse voltage is applied over the semiconductor junction, reducing the junction's capacitance, thus the response time, but also increasing dark current. The resulting current is measured across a small load resistance, the output voltage being linear to the incident optical power.
At this point, it should be pointed out that while other photo diode types are available, silicon semiconductors are the most favorable due to their higher sensitivity and better noise characteristics in the NIR spectrum compared to others, e.g. GaAs photo diodes [54].

The detector choice largely determines the resulting sensitivity of the instrument, the maximum sampling rate and the dynamic range [13] and has to include a consideration of the advantages and disadvantages in the context of NIRS application (see tab. 2.3).

PMTs	PRO	+ Gold standard in terms of sensitivity: Allow single photon counting + Large gains up to 10^7 + High speed similar to APDs [11] + Comparable dynamic ranges to APDs, but lower than SPDs
	CON	- Highly vulnerable to ambient light, high light intensities can result in damage to the device - Large, bulky apparatus - Sensitive to magnetic fields - Require high voltage supplies (safety) - Require cooling and voltage stabilization
SPDs	PRO	+ Very small packages + Require only low voltages - can be mounted on the head + Easy to use, no voltage supply stabilization or cooling necessary [13] + Robust to ambient light exposure + Not sensitive to magnetic fields + High dynamic ranges of up to $100\,dB$ [13] + Fast: Support speeds up to $100\,Mhz$ [13]
	CON	- Low sensitivities - Higher trans-impedance gains reduce SNR and bandwidth - No internal amplification, preamplifiers must be low-noise and carefully designed
APDs	PRO	+ Moderate or small packages + Higher sensitivities than PD + Moderate internal gains from 10 to a few 100 + Robust to ambient light exposure + Not sensitive to magnetic fields + Good dynamic ranges of up to $60\,dB$ [13] + Faster than SPDs: Support frequencies $> 100\,Mhz$ [13]
	CON	- Require high voltages of several $100\,V$ (safety) - Require stabilized power supplies - Require cooling due to dependency of internal gain on temperature/bias voltage [13]

Table 2.3: Comparison of PMT, SPD and APD NIR-detectors for use in fNIRS instrumentation.

Photo Multiplier Tubes such as the Hamamatsu R928 or R936 were used mainly in the first publications on fNIRS devices (Cope 1991 [21] and Rolfe et al. 2000 [30]). More recently, PMTs find application in Frequency Division instruments but are all in all rarely

used and have mostly been replaced by Avalanche Photo Diodes.
Avalanche Photo Diodes and Silicon Photo Diodes are both commonly used in today's NIRS instrumentation approaches with the trend of SPDs being preferred. Regarding APDs, most detectors used in literature are fabricated by Hamamatsu, with the Hamamatsu C5460-01 being the most popular [18–20, 45, 50]. For Silicon Photo Diodes, many work groups used Burr Brown sensors such as the OPT101 [14, 53] or OPT209 [44], detectors from Opto Diode Corp. [15, 59] and Siemens [49].

2.5.3 Optical Conduction

While silicon photo diodes and light emitting diodes can be applied directly to the head, white light sources, laser diodes, avalanche photodiodes and photo multiplier tubes traditionally require optical conduction with optical fibers to and from the scalp. Step-index multimode fibers with a core diameter of $\approx 0.5\,mm$ are normally used to guide the light from the light sources to the head. For the conduction from the scalp to the detectors usually fiber optic bundles with larger diameter, e.g. $\approx 2.5 - 3\,mm$ [20, 50] and high numeric aperture maximize the amount of collected light [11].
The fibers have to be attached to the head by fiber holders on straps or caps and add weight, generally decreasing mobility and comfort. Also, good light coupling of the light from the emitting source into the fiber has to be ensured to minimize losses.
When the sources and detectors are placed directly on the head, the geometrical design of the probe is slightly more constrained, and potential heating as well as electric hazards have to be considered. On the other hand, light losses are minimal and the user mobility is less restricted.
As the aim of this work is to design a mobile NIRS instrument, the use of optical fibers and sources/detectors requiring them is not planned and therefore will not be further evaluated at this point.

2.5.4 Signal Amplification

As the functional NIRS signal in the detected optical signal is very weak, low-noise amplification and signal extraction techniques are applied. One often used method is the synchronous (lock-in) detection, which will be discussed in detail in later sections. Using lock-in detection enhances the SNR but also increases system complexity. Using fast light modulation, only photodetectors with an appropriate bandwidth can be used.
To increase the dynamic range of the instrument, variable/programmable gain amplifiers can be used.

2.5.5 Probe Designs

Over the last years, several different approaches for optical probe designs were published. As good coupling of the probes is a significant precondition for high performance and signal quality, many probe designs aim to minimize obstruction of hair and motion effects. Design approaches that were published in literature include

- Conus- and cylinder-shaped single probes for fixation on EEG caps/hair nets and chained patches [15, 49],
- Multiple probes and multidistance probes on flexible PCBs with cushioning material [12, 14, 30, 53, 58, 59],

- Probes integrated into helmets and helmet-like headsets [48, 52] and fixated mechanical mounting structures to sit in [20].

Flexible PCBs with cushioning material bear the disadvantage of laminar resting against the head, thus promoting the obstruction through hair. For this reason, most of the flexible PCB probe designs are applied only to the forehead.

2.6 Fields of Application

The current and future fields of application of NIRS instrumentation for brain activity assessment can be assigned to three overlapping topics: brain research, clinical context and brain computer interface research.

Basic brain research
Brain activation studies were conducted on the visual, the somatosensory, the auditory, the motor and the language system, and on cognitive performance (see [14] for references). In 2003, Izzetoglu et al. conducted functional activity monitoring as a measure of cognitive workload in complex tasks such as aircraft landing situations and warfare management [60]. Psychiatric research is assessed to be still wide open for diffuse optical techniques [13], with the use of fNIRS for brain dysfunction assessment and research [12] and neonatal studies of cognition [48] being further related fields of application. All in all, the interest in the use of fNIRS for basic physiological, biochemical and routine clinical applications has steadily increased since the mid-1970s [30].

Clinical applications
The main clinical interest initially lay in long-term monitoring of cerebral oxygenation in newborn and high-risk infants [3, 21]. More up-to-date neurological applications are the investigation of hemodynamic responses during deep-brain stimulation in Parkinson's patients, brain activation during induced seizures in patients with epilepsy, verbal fluency and cognitive tasks in Alzheimer's patients, prefrontal brain activations of schizophrenic patients (see [14] and [13] for references) and recently inspection of the state in amyotrophic lateral sclerosis (ALS) (see [19] for references). Other potential applications are cortical blood flow monitoring and early diagnosis of cerebral pathologies of vascular origin [51], brain trauma and surgical intervention monitoring [45] and non-invasive monitoring of cerebra ischemia resulting from critical reduction of oxygen and glucose supply [56].

Brain Computer Interfaces
In the last decade, an increasing number of work groups used fNIRS technology for BCI-tasks and proved its applicability in the BCI context (e.g. [20, 50, 61–64]). Experiments were conducted in which motor cortex activity in actual and imagined tasks could be used as BCI control signals for severely paralyzed patients due to stroke, spinal cord injury or ALS [17, 62]. Cognitive workload assessment for the performance output optimization of context-sensitive systems has been done [60] and NIRS technology has been proposed for hybridization with EEG to act as a brain switch for classification performance improvement in hybrid BCIs [16, 64]. The use of fNIRS in BCI applications is promising because of its compact, robust and safe use and long-term applicability. In contrast to EEG, very little training efforts are necessary. As a very young field of research, fNIRS BCIs is assessed as promising new modality [65].