Optical Methods for Tympanic Membrane Characterisation
Towards Objective Otoscopy in Otitis Media
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Abstract

Otitis media, which is an upper respiratory tract infection that affect the middle ear, is the second most common disease in childhood, outnumbered in prevalence only by the common cold. Diagnosis of middle ear inflammation is often performed in the primary healthcare where the normal procedure involves anamnesis and physical examination of the tympanic membranes (TM) of the patient, usually be means of otoscopy. The general aim of this thesis was to develop optical methods that enable quantification of TM characteristics associated with otitis media. Diffuse reflectance spectroscopy was applied to quantify TM erythema using previously suggested erythema detection algorithms. Healthy TM:s were significantly distinguished from TM:s with induced erythema ($p < 0.01$) and from TM:s in ears with mucous middle ear effusion ($p < 0.05$). A new technique for surface shape assessment based on an on-axis dual fibre array incorporated in an otoscope was developed and evaluated in ear models and on tympanic membranes from harvested temporal bones. The technique utilises the combined effects of source-detector fibre separation and fibre-to-sample distance on the detected light intensity.

Optical phantoms, both polyacetal plastic solids and latex membranes, were utilised to demonstrate the ability of the surface shape assessment technique to differentiate between convex and concave surfaces – as a bulging tympanic membrane is typically associated with acute otitis media whereas a retracted eardrum is associated with otitis media with effusion. Monte Carlo simulations of the surface shape data were performed in order to validate the experimental results with a theoretical model that are consistent with light transport theory. Retracted and bulging tympanic membranes from harvested temporal bones could be separated with a single measurement, given that variations in measurement distance were accounted for and that measurement from normally positioned tympanic membranes were used for signal normalization. In conclusion, the studies implicate that for individual otitis diagnosis, the hyperaemic tympanic membrane was separated from the healthy by application of erythema indices using diffuse reflectance spectroscopy. Moreover, bulging and retracted positions of the tympanic membrane were separable by means of the source-detector intensity matrix. For further clinical studies it is reasonable to assume that data from both methods are needed for diagnosis.
This thesis is based on the following papers, which are referred to in the text by their roman numerals.


IV. Sundberg M., Peebo M., Strömberg T. In vitro tympanic membrane position identification with a co-axial fiber optic otoscope. In manuscript.

Author's contribution

My contributions to Paper I include the development of the simplified theoretical light scattering model that describes the signals measured by the fibre optic array; part of the instrument and probe design; all measurements and simulations made and the analysis of the experimental and simulated data. In addition, I was the main contributor in writing this paper.

My contributions to Paper II include the majority of the measurements made; the analysis of the experimental data and the main responsibility for writing the paper.

My contributions to Paper III include design, implementation and application of the Monte Carlo software; measurements of optical properties in collaboration with T. Lindbergh (second author) and the main responsibility for writing the paper.

My contributions to Paper IV include design, implementation and application of data acquisition and laser diode control software; design of the ear speculum in collaboration with Dr. A. Johansson and M. Melander; design of the hardware serving otoscope illumination and detection in collaboration with B. Ragnemalm; performance measurements and data analysis and the main responsibility for writing the paper.
Abbreviations and variables

- AOM: Acute otitis media
- EAC: External auditory canal
- ET: Eustachian tube
- FIR: Far infrared (part of the electromagnetic spectrum)
- GP: General practitioner
- Hb: Haemoglobin
- HG: Henyey-Greenstein
- IR: Infrared (part of the electromagnetic spectrum)
- MEE: Middle ear effusion
- NIR: Near infrared (part of the electromagnetic spectrum)
- OM: Otitis media
- OME: Otitis media with effusion
- RTE: Radiative transfer equation
- SCC: Semi-circular canal
- SGAR: Spectral gradient acoustic reflectometry
- SDIM: Source-detector intensity matrix
- TM: Tympanic membrane
- UV: Ultra violet (part of the electromagnetic spectrum)
- VIS: Visual (part of the electromagnetic spectrum)
- VN: Vestibulocochlear nerve
- $\mu_a$: The absorption coefficient
- $\mu_s$: The scattering coefficient
- $\mu_s'$: The reduced scattering coefficient
- $g$: The anisotropy factor
- $g_{HG}$: The Henyey-Greenstein anisotropy factor
- mfp: Mean free path
- mfp': The reduced mean free path
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Recently, the importance of making an accurate diagnosis in otitis media as well as the need for improved diagnostic technology has been stressed [1, 2]. Patients with symptoms of an ear infection are usually subject for examination and treatment within the primary health care, where the status of the tympanic membrane (eardrum) and middle ear are usually assessed utilizing subjective techniques, e.g., otoscopy. It has been reported that the diagnostic accuracy in otoscopy is unsatisfying and that acute otitis media is frequently over-diagnosed. As the standard treatment of acute otitis media involves antibiotic therapy, the implication is unnecessary use of antibiotics. In order to temper the spread of microorganisms resistant to antibiotics, excessive antibiotic prescriptions have to be suppressed.

In this thesis, diffuse reflectance spectroscopy and a novel technique for surface shape assessment have been applied to investigate if the techniques could have potential for objective optical assessment of the characteristics of the tympanic membrane.

In chapter 2-4, the clinical background relevant in otitis diagnosis is reviewed. In chapter 5, an overview of the theory and modelling of light transport are given. This theory is necessary for the Monte Carlo simulations of light transport applied to the surface shape technique which were performed in Paper III. In chapter 6, fundamental diffuse reflectance spectroscopy is presented. Chapter 7 defines the aims of the thesis. Chapter 8-9 summarizes the techniques and methods as applied in the papers. In chapter 10, a review of the papers is given. Discussion and conclusions are found in chapter 11.
Throughout this thesis, *italics* are used for terms that are more thoroughly defined in the glossary of terms and for representations of scalar variables; **bold italics** in representations of matrices and vectors and SMALL CAPS for author names when used for citations.
Chapter 2  
Anatomy and physiology of the ear

2.1 The healthy human ear

Anatomically, the human ear is subdivided into three sections: the external ear, the middle ear and the inner ear (Figure 2.1). The external ear consists of the auricle – an appendage of cartilage, perichondrium and skin – and the external auditory canal (EAC). In the middle ear, the tympanic membrane, the malleus, the incus and the stapes, see ossicles, as well as the Eustachian tube (ET) opening are found. The inner ear consists of the cochlea, the semi-circular canal (SCC) and the vestibulocochlear nerve (VN).

![Figure 2.1: Left: The anatomy of the human (right) ear, which is subdivided into the sections external ear, middle ear and inner ear. The external ear is separated from the middle ear by the tympanic membrane. Right: The structures of the middle ear.](image)

2.1.1 The tympanic membrane

The eardrum (Figure 2.2) is a cone shaped membrane that separates the external and middle ear. The depth of the cone is about 1.5 mm and the di-
ameter is 8–10 mm, approximately the size of the nail of the index finger; it is positioned downward and inward at an angle of about 30 degrees to the vertical axis [3-7].

![Diagram of the tympanic membrane](image)

**Figure 2.2:** The tympanic membrane (right ear) as seen through the external auditory canal.

The tympanic membrane is usually divided into four quadrants: the posterosuperior, posteroinferior, anteroinferior and anteriosuperior quadrant. Structurally, the tympanic membrane can be regarded as a three-layered sandwich. The lateral layer of the tympanic membrane is a continuance of the external auditory canal *squamous epithelium*; the medial layer is an analogous continuance of the middle ear mucosa (*cuboidal epithelium*); and in between, a layer of fibrous tissue, the *lamina propria* which is rich in collagen [3]. The outer border of the tympanic membrane, the annulus or the annular ring, consists of a fibrous and cartilaginous tissue that is thicker and stiffer than the rest of the membrane [3]. The tympanic membrane thickness varies between 55 and 140 µm, being thinnest in the central parts of the posterosuperior quadrant and thickest in the vicinity of the inferior part of the annulus [8, 9]. The triangularly shaped region that is a continuance from the annulus in the superior part of the tympanic membrane is the *pars flaccida*; it is sized to about one ninth of the tympanic membrane. The remaining eight ninths of the eardrum is the *pars tensa*.

### 2.1.2 The middle ear

The middle ear is the space between the tympanic membrane and the inner ear. Here the smallest bones in the human body reside, the *ossicles*: the malleus, the incus and the stapes. The depth of the middle ear, as viewed from the external auditory canal, varies between 2 and 6 mm, [3], in the different subspaces; the *hypotympanum*, i.e., the lower part of the middle ear,
being the deepest and the *mesotympanum*, i.e., the middle part of the middle ear, the shallowest. Two openings are found in the bony part separating the middle ear and the inner ear, the oval and round window; the former being occupied by the footplate of the stapes and the latter closed by a thin membrane. A continuous mucous membrane, the middle ear mucosa, covers all structures in the middle ear.

The middle ear is connected to the *nasopharynx* via the *Eustachian tube*. The ET helps protect the middle ear from secretions and pressure from the nasopharynx as well as it serving as a canal for drainage of fluids from the middle ear into the nasopharynx. It also functions as a pressure equaliser, maintaining atmospheric pressure in the middle ear [3, 10, 11]. As the ET is closed most of the time, the gases in the middle ear are absorbed by tissues with lower gas partial pressure such as the bloodstream. This causes a subatmospheric pressure in the middle ear that retracts the tympanic membrane and instigates establishment of middle ear fluid if the middle ear pressure is not equalised. Fortunately, the ET opens occasionally as part of its normal function, e.g., when swallowing, yawning or sneezing [3, 11]; it can also be forced open, e.g., during the Valsalva manoeuvre [3]. In infants, the ET is tilted 0–10 degrees from the horizontal plane, whereas in adults the tilt is around 45 degrees [3]. Moreover, the infant Eustachian tube is shorter than the adult ET, making the width-to-length ratio higher in infants than in adults. This, in combination with the fact that infants are frequently in a supine position, increases the risk of otitis media [3].

### 2.1.3 Ossicular landmarks

Upon visual inspection of the tympanic membrane, some structures of the middle ear should be seen through the transparent eardrum. In the healthy ear, part of the *ossicles* should be seen; especially, both the long and short process of the malleus should be clearly visible. Individual variations occur in the visibility of the long process of the incus and the *chorda tympani*; these structures can be seen in individuals with highly transparent tympanic membranes. Deviations from what landmarks that are normally visible indicate abnormalities; e.g., in a retracted tympanic membrane, the long process of the incus and the joint between the incus and the stapes can be visible.
A complete description of otitis media pathology and pathophysiology is beyond the scope of this thesis. However, an effort has been made to clarify the terminology in this field as well as to some extent describe the different diseases and stages of the diseases.

Otitis media is inflammation of the middle ear. The inflammation is either chronic or acute. Accumulation of fluid in the middle ear, i.e., a *middle ear effusion*, is typically associated with both conditions.

The terminology is confusing and inconsistent in distinguishing different types of otitis media. In the literature, chronic otitis media are also referred to as *otitis media with effusion*, serous otitis media, non-purulent otitis media, secretory otitis media and glue ear. All are names for the same condition but none manage to grasp the essence of the condition without being too wide or too narrow or even false. The term serous otitis media implies that the *middle ear effusion* is serum, which it obviously is not, whilst non-purulent otitis media suggest that there are no bacteria present, which is true in general but not universally. Secretory otitis media can be considered inappropriate as it insinuates that the middle ear is secretionary. In order to temper this confusion, the term otitis media with effusion will be adopted throughout this thesis for otitis media without signs or symptoms of an acute infection. In 1976 at the First International Symposium on Recent Advances in Middle Ear Effusions, it was agreed to classify otitis media into: (1) Acute purulent otitis media, in this thesis called acute otitis media; (2) serous otitis media; and (3) mucoid secretory otitis media [10, 12, 13].

The *middle ear effusion* can be one of, or a combination of, four types: serous, mucoid, bloody and purulent. The serous fluid is a waterlike, pale
yellow-coloured transudate which resembles serum. A transudate is a fluid that originates from transudation, which is the passing of liquid from the body's cells outside the body. Upon removal and exposure to air, the liquid will clot within minutes. The mucoid effusion originates from cell secretion in the middle ear mucosa – where the *cuboidal epithelial cells* in the middle ear mucosa to some extent becomes *mucus-producing goblet cells*, adding to the fluid filling in the middle ear [12]. The colour of the secretion is yellow or grey and it becomes tenacious with time, hence the expression glue ear is frequently used for this condition. The purulent effusion contains pus and is associated with acute otitis media [11].

Traditionally, many authors have attributed the pathogenesis of *middle ear effusion* to the *hydrops ex vacuo theory* [14], hypothesising that the effusion is a transudate due to a negative pressure in the middle ear caused by e.g., Eustachian tube dysfunction [15-19]. There are, however, other authors who suggest that otitis media is primarily a disease of the middle ear mucosa caused by infections or allergies rather than by Eustachian tube dysfunction [20-22].

### 3.1 Acute otitis media

The mucous membrane that coats the middle ear is continuously connected to the mucous membrane of the nasopharynx, Eustachian tube and the mastoid. Hence, microbes can be transported from the nasopharynx, via the ET and into the middle ear and cause infection. For the same reason, inflammation of the middle ear mucosa can have an impact on the *mastoid air cells* as well as the ET.

Acute (bacterial) otitis media, *AOM*, is an infection that develops in the *middle ear cleft* and occasionally spreads into the mastoid air cells. By definition, acute otitis media is recognised by an effusion in the middle ear in combination with acute symptoms and signs of infection [23, 24]. The incidence of *AOM* is more frequent in the autumn and winter as well as more common in young children than in youngsters and adults [12].

Acute otitis media undergoes three phases (*SHAMBAUGH et al.* [12] identify five phases): the *erythematous phase*, the *exudative phase* and the *suppurative phase* [25]. In the erythematous phase – which is the early stage of *AOM* that is associated with hyperaemia of the middle ear mucosa, Eustachian tube and the mastoid cells. The mucous membrane continuously connect the nasopharynx, the Eustachian tube, the middle ear and the mastoid air cells; hence, an infection of the mucosa potentially affects the
whole membrane [12] – the short process of the malleus and the umbo are still visible. In the exudative phase of AOM, the infectious process causes closure of the Eustachian tube, and the middle ear cleft rapidly becomes fluid filled because of the active production of pus. As the infection proceeds into the suppurative phase, the exudate changes from serous to purulent; this causes blurring of the tympanic membrane, and the ossicular landmarks cannot be recognised through the membrane. Bulging of the membrane usually occurs in all stages, but severe bulging is commonly associated with the suppurative stage. As a consequence of increased middle ear pressure, i.e., bulging of the tympanic membrane, spontaneous rupture of the tympanic membrane can occur. Tympanic membrane rupture usually comes about in the suppurative phase and is easily recognised by findings of secretion in the external auditory canal. The self-induced perforation of the middle ear occurs in the pars tensa of the tympanic membrane and is limited in size, sufficiently to admit spontaneous drainage of the middle ear fluid.

3.1.1 Epidemiology

Acute otitis media is, by far, the most frequently diagnosed disease in children that involves antibiotic treatment. In the United States, more than 20 million antibiotic prescriptions are registered annually due to AOM alone [26-28].

One of the most cited studies in otitis media epidemiology is the Greater Boston study by Teele et al. [29]. They followed children from birth to approximately 7 years of age in order to determine the epidemiology of acute otitis media and the duration of middle ear effusion. 877 children were included in the study, and it was concluded that 62 % of the children had at least one episode of AOM in their first year in life. 17 % had more than three episodes before their first birthday. 83 % of the children had at least one episode of AOM in their first three years, whilst 46 % had three or more. In the Greater Boston study, acute otitis media was defined as “effusion in one or both ears accompanied by one or more signs of acute illness including ear ache, otorrhoea, ear tugging, fever, irritability, lethargy, anorexia, vomiting, or diarrhoea”.

Pukander et al. [30] performed a similar study in the early ‘80s. They studied 37 570 Finnish children under the age of 15 years, in order to determine AOM occurrence and recurrence in that population. The children were studied for one year, and 4 337 (16.6 %) of them experienced 6 249
episodes of AOM. Among the infants, 75.5 % had at least one episode of acute otitis media during their first year in life.

3.1.2 Complications

Whenever the bacterial infection propagates into tissues surrounding the middle ear and the middle ear mucosa, a complication is present. Unresolved AOM can cause complications such as mastoiditis, meningitis, labyrinthitis, facial palsy and bacteraemia [12].

Chronic otitis can develop from AOM. In this disease, the tympanic membrane is perforated, which fails to heal spontaneously, and myringoplasty (surgical closure of the perforation) is usually required. Otorrhoea, i.e., a discharge from the ear, is in general observed in chronic suppurative otitis media. Moreover, chronic suppurative otitis media frequently causes irreversible pathological changes to the tissues in the middle ear [11].

Unresolved acute otitis media can also result in persistent middle ear effusion (OME), which if not resolved can cause a hearing impairment. Recurrent AOM and retraction pockets can cause cholesteatoma, i.e., a cyst containing cholesterol which can develop in the middle ear, which can spread into the mastoid air cells and cause mastoiditis, i.e., a spread of the inflammation from the mucous membrane of the middle ear into the mastoid air cells. In mastoiditis, the bony parts of the mastoid air cell system are subject to degeneration and the condition can, if left untreated, spread into the brain having, in the worst case scenario, a fatal outcome. The process is, however, reversible, as the bone erosion stops as soon as the pus in the mastoid air cells is cleared out [12].

3.1.3 Symptoms

Primarily, acute otitis media is associated with otalgia, i.e., earache, which can occur within hours, days or weeks from the onset of the disease [25]. In addition, a raised temperature usually is present. These symptoms are sensitive, but not specific [23, 24]; hence, additional observations must be included to ensure diagnostic accuracy.

3.1.4 Signs

Certain deviations from the normal appearance and function of the tympanic membrane, such as abnormal colour, position or mobility, are the most frequently mentioned signs of acute otitis media. An infection in the middle ear usually causes hyperaemia locally, which can entail increased vascularisation of the tympanic membrane, resulting in an erythematic ap-
Acute otitis media

pearance. Moreover, a bulging tympanic membrane, i.e., an increased middle ear pressure is commonly associated with AOM, whereas a retracted membrane is related to otitis media with effusion (OME). Thus, the tympanic membrane position is a key in differentiating AOM from OME. An impaired mobility of the tympanic membrane is frequently present in otitis media; partly as a consequence of the fluid-filled middle ear, and the incompressible nature of water-like fluids, and partly due to membrane thickening commonly occurring in AOM. Impaired tympanic membrane mobility usually is present in both AOM and OME. Hence, proving abnormal mobility alone does not help in distinguishing the one disease from the other.

3.2 Otitis media with effusion

Otitis media with effusion is fluid in the middle ear in absence of acute signs and symptoms [10]. The condition can, if not resolved, cause pathological changes to the tympanic membrane. Frequently, a retracted eardrum is seen in OME, making the ossicular landmarks more visible. More complicated pathologies involves tympanosclerosis, atelectasis and fibrosis.

OME is a disease that is caused by a multitude of factors. Even though it is not clearly understood what is causing OME, Eustachian tube dysfunction, mucosal changes, presence of microorganisms and the effect of inflammatory cells and mediators are frequently mentioned [11]. It also commonly occurs as a sequel to acute otitis media, successfully treated with antibiotics [12].
A typical investigation of the ear involves inspection of the tympanic membrane and the middle ear structures via an otoscope or other visualisation devices. A prerequisite for adequate performance is cleaning of the external auditory canal, i.e., removal of cerumen, purulence, debris and epithelial flakes obstructing partially or completely [31]. Upon examination of the tympanic membrane and middle ear structures, an ear speculum is utilised in order to straighten and, to some extent, stretch the external auditory canal to obtain a better visualisation of the eardrum. It is important that the ear speculum is not inserted further into the EAC than two thirds of its length, the flexible cartilaginous part, as the inner third is a bony part with superficial nerves that are very sensitive to pressure [31].

4.1 Acute otitis media

The golden standard in otitis diagnosis is to perform tympanocentesis in order to demonstrate the presence of a middle ear effusion. This confirms otitis media. Secondly, in order to distinguish a bacterial infection from a non-bacterial one, the presence of bacteria in the effusion has to be confirmed. Unfortunately, this procedure is difficult to motivate by its invasive nature and the associated discomfort for the patient.

Otitis media diagnostics instead rely upon anamnesis and observations of symptoms, such as earache and a raised temperature, in combination with observations of signs, such as tympanic membrane colour, shape and mobility, which is revealed by the physician during the otoscopic examination. In addition to otoscopy, the pneumatic features of the otoscope can be utilised in order to determine whether tympanic membrane mobility is impaired or not. An impaired tympanic membrane mobility suggests the pres-
ence of a *middle ear effusion* [12] or tympanic membrane thickening due to inflammation. Quantitative measures of tympanic membrane mobility can be assessed with tympanometry and acoustic reflectometry [12, 32-36].

As an alternative to otoscopy, signs of an acute infection in the middle ear can be exposed by examining the nose and *nasopharynx*, which, in the case of such infection, usually demonstrates vascular congestion and oedema [25]. However, cultures from this site do not correlate with bacterial findings in the *middle ear effusion*; even though the pathogens present in the middle ear usually travel into the nasopharynx.

### 4.1.1 Pathogens and inflammatory cells

The most frequently occurring bacteria in acute otitis media are Streptococcus pneumoniae, Haemophilus influenzae, Group A Streptococcus, Staphylococcus aureus, Moraxella catarrhalis (aka Branhamella catarrhalis), Gram-negative enteric bacilli and Staphylococcus epidermis [10, 12, 13].

Inflammatory cells are present in both the middle ear mucosa and the *middle ear effusion* in AOM. In an early stage of the disease, polymorphonuclear leukocytes predominate; as the disease progresses, lymphocytes and macrophages typically occur [10]. Moreover, the *middle ear effusion* contains inflammatory mediators, such as histamine, prostaglandin and leukotriene, causing e.g., vasodilatation [10].

Some strains of the bacteria found in AOM are β-lactamase producing, meaning that the pathogen is resistant to certain types of antibiotics, e.g., phenoxyethyl penicillin (pcV), amoxicillin and ampicillin that are frequently prescribed in AOM [12, 37].

### 4.1.2 Treatment and recommendations

Acute otitis media is frequently treated with antibiotics. Recommendations in Sweden are that children younger than two years and patients with a perforated eardrum with presented discharge of pus in the external auditory canal should be treated with antibiotics, whereas the watchful waiting approach could be used for children older than two years [37]. However, some individuals are more susceptible to acute otitis media than others, e.g., because of a subnormal flora of α-haemolytic streptococci in the nasopharynx [38]. For these otitis-prone individuals, antibiotic treatment can have a negative effect as the treatment is likely to affect the, already altered, homeostasis of the nasopharynx. If the α-streptococci flora is further
weakened, the probability of succeeding episodes of otitis media is increased as well as the likelihood of complications, such as otitis media with effusion, as the α-streptococci is known to inhibit colonisation of pathogens that are associated with AOM [38]. Hence, it has been suggested that AOM should be left without antibiotic treatment, as it is likely to resolve spontaneously [12]. This requires watchful monitoring however, as an unresolved AOM can have complications. Antibiotics are normally administered in order to restrict the infection to its early stage, shorten the febrile illness and minimise the risk of complications [12]. Recently, Pichichero reported on potential way to vaccinate against acute otitis media [39, 40].

In the US, administration of a high dose of Amoxicillin (90 mg/kg/day) for 10 days is the recommended treatment for AOM patients [41]. In Sweden, Penicillin V (phenoxymethyl penicillin, 50 mg/kg/day) for 5 days is the first choice recommended if antibiotics are decided necessary [37]. In complicated AOM cases, Amoxicillin (50 mg/kg/day) is recommended in Sweden as well [37]. It is commonly thought that the Swedish V-Penicillin model partly explains why antibiotic resistance has not developed to the same extent in Sweden as it has in the western world in general [42].

4.2 Otitis media with effusion

In the physical examination, preceding OME diagnosis, the physician seek proof of one or more of the visual characteristics of OME (from [10]): (1) abnormal colour or increased capillary vascularity of the tympanic membrane; (2) a chalky-appearing malleus handle; (3) tympanic membrane retraction, e.g., as indicated by visibility of the joint between the incus and the stapes; (4) fluid levels or bubbles in the middle ear, seen though the tympanic membrane; and (5) a bluish tympanic membrane or haemotympanum, which indicates the presence of blood in the middle ear cavity due to several causes. In addition, examination of the mobility of the tympanic membrane is frequently performed by means of pneumatic otoscopy or tympanometry. An impaired mobility of the eardrum suggests the presence of a middle ear effusion, occlusion of the Eustachian tube or thickening of the tympanic membrane.

4.3 Diagnostic accuracy

Asher et al. [43] evaluated the diagnostic accuracy in a study including 590 children. 73 paediatricians provided referral letters, and AOM was con-
firmed by myringotomy. It was found that the paediatricians were right in 62% of the cases and that the accuracy rate was higher for patients with recurrent AOM, i.e., more than three or four episodes of AOM during the last 6 or 12 months, than for the other patients. It was also concluded that diagnostic accuracy was not related to the speciality of the physician.

BLOMGREN and PITKÄRANTA posed the question if it is possible to diagnose AOM accurately in primary healthcare [24]. They compared the diagnoses of a general practitioner and those from a specialist in otorhinolaryngology in a group of 50 children with caregiver-suspected AOM. Acute otitis media was diagnosed in 64% by the GP and in 44% by the otorhinolaryngologist. The discrepancies were explained by the authors as being correlated to what observations the examiners paid attention to in deciding their diagnoses. Apart from symptoms, the GP paid attention to the colour of the tympanic membrane, whereas the specialist focused more on the position of the membrane and its ability to move, utilising tympanometry. The tympanic membranes of the examined ears were photographed by the otorhinolaryngologist and viewed and evaluated by a specialist in paediatric infectious diseases and by an experienced paediatric otorhinolaryngologist. The evaluation was performed in two steps, first diagnosis was decided based on the photographs alone, secondly the photographs were combined with the tympanograms acquired by the specialist examiner. Using the photographs alone, the specialist and the paediatric otorhinolaryngologist diagnosed AOM or OME in 38 children (76%). When the results from tympanometry were included, the numbers were reduced to 48% and 58% respectively. Diagnose discrepancies between examiners ranged from 18–40%.

ROSENFELD, [44], investigated the diagnostic accuracy of AOM when applying the United States Agency for Healthcare Research and Quality (AHRQ) criterion for acute otitis media: “middle-ear effusion plus onset in the past 48 h of signs or symptoms of middle-ear inflammation”. 135 children were included in the study and the clinicians were asked to express their degree of diagnostic certainty. The clinicians reported a certain AOM diagnosis in 90% of the examined children whereas only 70% were consistent with the AHRQ criterion. In 35/122 patients, diagnosed with AOM, middle ear effusion was recorded as being absent.

JONES AND KALEIDA, [45], reported that by using pneumatic otoscopy, the accuracy of identifying MEE was significantly approved as compared to static assessment.
4.4 Technology in otitis diagnostics

Traditionally, otitis diagnosis relies on findings from otoscopic examinations. There are, however, technological means that facilitates and, as it is argued by several authors, improve the diagnostic accuracy.

4.4.1 Otoscopy and pneumatic otoscopy

An otoscope is an endoscope with a design to optimally function as a tool for ocular inspection of the tympanic membrane through the external auditory canal (Figure 4.1). An otoscope consists of a handle, a light source, an instrument head containing the necessary optics for visual inspection and a disposable or reusable tip. Usually, an otoscope incorporates pneumatic features, [3], where the mobility of the tympanic membrane can be observed through the otoscope (with subjective quantification of tympanic membrane mobility made by the eye of the observer) by applying pneumatic pressure to the external auditory canal. To achieve a pressure difference between the external auditory canal and the middle ear, an airtight seal between the speculum and the EAC has to be accomplished. Alterations of the pneumatic pressure will alter the position of the tympanic membrane and the ability of the tympanic membrane to move upon pressure change is dependent on the presence or absence of middle ear effusion. Hence it is of great importance for the clinician to know to what extent a healthy tympanic membrane responds to pneumatic stimulus in order to determine whether the mobility is impaired or not. Pneumatic otoscopy is applied to decide the presence or absence of middle ear effusion. It has been reported that application of pneumatic otoscopy is increasing diagnostic accuracy [45].

Figure 4.1: An otoscope is a diagnostic instrument that allow for visual inspection of the ear. Inserting the ear speculum into the external auditory canal of a patient allow for ocular inspection through the lens of the eyepiece in the otoscope head. Normally, the handle is equipped with rechargeable batteries that empower the light source, which is normally located between the handle and the head.
4.4.2 Video otoscopy

In video otoscopy [46], endoscopic technology is utilised to monitor the structures of the ear, as seen through the external auditory canal. This technology is well suited for simultaneous inspection by several observers, making it appropriate in educational settings. The most frequent users of video otoscopy are found among otolaryngologists, otitis researchers, audiologists, veterinary surgeons and in telemedicine.

One advantage with this visual inspection technique is the possibility of post examination, i.e., image analysis that can be performed at any time subsequent to image acquisition. This allow for, e.g., quantification of the extent of tympanosclerosis or retraction pockets [47].

4.4.3 Otomicroscopy

A better visualisation, as compared to otoscopy and video otoscopy, of the tympanic membrane and the structures of the middle ear, is accessible through an otomicroscope. Due to magnification and limited ear speculum diameter, generally a portion of the tympanic membrane can be viewed. Usually, this devise offers an opportunity to record and document the field of view by means of a video camera or comparable equipment; it also allows for binocular vision.

4.4.4 Tympanometry

A tympanometer is utilised to acquire an indirect measure of MEF presence by quantification of the compliance of the EAC and tympanic membrane. As in pneumatic otoscopy, an airtight seal between the ear speculum and the external auditory canal has to be obtained for tympanometry to function properly. A typical tympanometer broadcasts a tone at a constant frequency and measures the absorption of that sound as a function of the external pressure applied by the tympanometer into the sealed auditory canal. Tympanometry is an indirect method of measuring the functionality of the Eustachian tube. The tympanogram, which is the output from the tympanometer, is a graph showing the compliance of the sealed system as a function of the applied pressure. Tympanometry on a healthy tympanic membrane shows a compliance that increases with pressure to a certain point (where the applied pressure is equal to the atmospheric pressure, and hence equal to the middle ear pressure) where it starts to decrease with additional pressure. If an effusion is present in the middle ear, the peak in the tympanogram is flattened. Tympanograms without a peak suggest a non-compliant tympanic membrane due to a middle ear effusion and a positive
pressure in the middle ear (a pressure above the atmospheric pressure) [48, 49]. Due to increased canal compliance, tympanometry cannot be applied reliably in children younger than seven months [34]. The increased compliance is caused by lax skin and cartilage in the external auditory canals. Hence, even if the middle ear of such a young child is filled with fluid, the tympanogram frequently indicates compliance within a normal range, giving rise to false negatives. Moreover, as the tympanometer measures the volume of the external auditory canal, cerumen occurrence, as well as tympanic membrane perforations, will prohibit accurate measurements as the calculated volume will be too low and too large respectively. For the same reason, tympanometry cannot be utilised efficiently in children having a tympanostomy tube placed through their tympanic membrane.

### 4.4.5 Acoustic reflectometry

Spectral gradient acoustic reflectometry (SGAR) was developed by John Teele as a diagnostic method that fulfilled the demands on safety and accuracy in children of all ages, speed and freedom from pain [32]. In acoustic reflectometry, it is not necessary to accomplish an airtight seal between the speculum and the external auditory canal, as it is in tympanometry. Instead, an acoustic reflectometer utilises sound waves. A typical device consists of a signal generator that sweeps through some spectrum of tones, a loudspeaker, a microphone and processing electronics. The device is placed at the distal end of the auditory canal and the microphone records both the direct sound and the sound originating from reflections on tissues and cerumen in the external auditory canal and the tympanic membrane. The mix of direct sound and reflected sound interferes constructively and destructively as a function of the tone frequency, motivating the sweep over a tone spectrum, as the distance from the loudspeaker to the tympanic membrane is constant. An acoustic reflectometer records and processes the response of the tympanic membrane to sound stimuli. The intensity variation as a function of tone wavelength is utilised to predict the likelihood of the middle ear containing an effusion. With an effusion present in the middle ear, the difference, in the acoustic signal, between constructive and destructive interference is greater than when no effusion is present. In SGAR, the slope of the frequency-dependent total reflectance is utilised to differentiate MEE from non-MEE.

### 4.4.6 Ultrasound

Since the 1970s, efforts employing ultrasound for diagnostics of middle ear diseases have been made [50]. The relevance to otitis diagnostics is obvi-
ous when ultrasound is applied in order to detect *middle ear effusion*. This technique has not, however, reached common clinical practice.

A simple A-scan can be utilised to detect fluid in the middle ear cavity. If an effusion is present, echoes are seen from the tympanic membrane and from the tissues in the middle ear. In case of an air filled middle ear, only echoes from the tympanic membrane are apparent from the ultrasound scan [50].

### 4.4.7 Moiré interferometry

In straight line ruling Moiré interferometry, the contour of a surface can be imaged by projecting coherent and monochromatic equidistantly spaced fringes of light onto the surface and observing the reflections from that surface at an angle oblique to the projection angle. As seen from the observation angle, the reflected fringes are bent as a consequence of the shape of the surface. By observing the image of bent fringes through a grid of equidistant lines, an interference pattern arises. The surface topography is derived from this interference pattern.

Several studies, utilising Moiré interferometry, have been performed to image the tympanic membrane in the gerbil [51-56]. *In vivo* applications in the human ear have most likely proven to be difficult to implement. This is, probably due to the fact that traditional Moiré interferometry requires an angle between the incident light and the monitored reflected light; additionally, as the human tympanic membrane is very thin and fairly transparent, reflective coating of the membrane or light polarization techniques are most likely required in order to record a high qualitative topogram. Therefore, this technique is preferably used *in vitro* where the temporal bone has been harvested and the tympanic membrane uncovered. In this way, Moiré interferometry has been employed in human tympanic membrane shape acquisition [4, 7]; but to the best of my knowledge, *in vivo* applications have not yet emerged.

### 4.5 Drawbacks with current techniques

As for the visual inspection techniques, they are subjective in nature, depending on the experience of the examiner and suffer from standardisation difficulties. As a consequence, the otoscopic diagnostic accuracy is unsatisfying [35, 36, 57-59]. Other limiting factors in otoscopy are the absence of binocular vision, inability to use instruments through it, insufficient illumination and inadequate handling [31].
In tympanometry and pneumatic otoscopy, an airtight seal has to be accomplished between the instrument and the external auditory canal. Apart from moderate discomfort for the patient, this requires extensive cooperation from the patient, hence making the technique inadequate for use in young children. Acoustic reflectometry also has been reported to be operator dependent [60], which undermine its objectiveness and makes it less appealing for use in clinical practice. Malfunction of tympanometers and acoustic reflectometers is common in young patients due to their natural inability to collaborate [60, 61]. However, the major drawback of tympanic membrane mobility assessment techniques is their incapability of distinguishing AOM from OME as they aim for detection of middle ear fluid, occurring in both AOM and OME [34]. Hence, a positive outcome from such an examination does not, in itself, aid in deciding appropriate treatment, whereas a negative outcome virtually rules out the possibility of otitis media. This does not mean that acoustic reflectometry and tympanometry are inefficient methods in otitis diagnosis. Proof of middle ear fluid in combination with the presence or absence of symptoms of an acute infection is helpful in deciding treatment.
In the new setting of ideas the distinction has vanished, because it was discovered that all particles have also wave properties, and vice versa. Neither of the two concepts must be discarded; they must be amalgamated. Which aspect obtrudes itself depends not on the physical object but on the experimental device set up to examine it.

Erwin C. Schrödinger

Chapter 5

Light transport theory

5.1 The nature of light

Light can be regarded as the visual or nearly visual range of electromagnetic radiation; and on the other hand, light can be regarded as particles or energy quanta, i.e., photons. This is known as the wave-particle duality of light. Both approaches can be utilised separately to model light theoretically, both suffering from limitations. In the middle of the 17th century, Christiaan Huygens presented a wave theory of light, which described wavefront interference. His theory was rejected, however, when Sir Isaac Newton presented his corpuscular theory of light. Newton showed that light could be regarded as small particles, which easily explained light reflection, and, with a more extensive explanation, light refraction. Even though Newton’s theory of light was undisputed for more than 100 years, it failed to explain how light interference could occur. It was in the beginning of the 19th century that the wave property of light, previously postulated by Huygens, was again subject for scientific evaluation when Thomas Young and Augustin-Jean Fresnel showed, that light sent through a grid...
showed constructive and destructive interference. The wave perspective of light was, in a way, completed in the late 19th century when James Clerk Maxwell presented his theory of electromagnetic wave propagation and identified light to be electromagnetic waves, [62, 63]. The concept of light having both wave and particle properties arose from Max Planck's work on black body radiation [64] and Albert Einstein's theory of the photo-electric effect [65]. Planck's work implied that light was in fact discrete energy quanta, something that Einstein identified and described mathematically. Even though Einstein's description could be verified in experiments, the idea of light being energy quanta was subject to massive resistance from other physicists and scientists, as it was considered to contradict Maxwell's theory of light – a theory that was well-known and accepted. Einstein predicted that the energy of photo-electrons (electrons emitted due to photon absorption, i.e., the photo-electric effect) was proportional to the frequency of the incident light. This prediction was experimentally verified in 1915, by the work of Robert Andrews Millikan.

As the intensity of the incident light, generating a photo-electric effect, did not affect the kinetic energy of emitted electrons, wave theory could not explain this phenomenon. Hence, as light seen as particles could not explain polarization and interference, the wave-particle duality of light was born.

In 1924, Louis-Victor de Broglie postulated a relation between wavelength and momentum, a relation between a wave property and a particle property, implying that everything that hitherto had been explained from particle properties, i.e., all matter, also had wave properties [66]. Well-known examples of experiments on particles showing wave-like properties are the independent electron diffraction experiments by George Paget Thomson and Joseph Davisson, which they were rewarded for by their sharing the 1937 Nobel Prize in Physics. An explanation of the wave-particle duality is offered within the field of quantum physics, which is beyond the scope of this thesis.

5.2 The transport equation and Beer-Lambert's law

Light transport in turbid, i.e., scattering, media can be modelled utilising the light transport equation. In this section, a heuristic derivation of this equation based on obvious assumptions will be given [67-69].

Assume that during the time $\Delta t$, at a position $r$, within a small volume $dV$, there are a number of photons, $N$ [m$^{-3}$sr$^{-1}$], that are travelling in a direction
The transport equation and Beer-Lambert’s law

\[ \hat{s}, \text{ within a solid angle } d\Omega \text{ (Figure 5.1). The following observations can be made:} \]

![Figure 5.1: N photons per volume, } dV = c \Delta t \, dA, \text{ and solid angle, } d\Omega, \text{ are assumed to be positioned in } \mathbf{r} \text{ with a direction } \hat{s}.

From the number of photons per solid angle (SI unit steradian, [sr]) in \( \mathbf{r} \) travelling in the \( \hat{s} \) direction (1), the energy per solid angle (2) and the power per solid angle (3) can be expressed by multiplication of the photon quantum energy, \( h \nu \), and subsequent division by \( \Delta t \).

\[
N(\mathbf{r}, \hat{s})dV = N(\mathbf{r}, \hat{s}) \, c \, \Delta t \, dA \quad [\text{sr}^{-1}] \quad (1)
\]

\[
E = h \nu \, N(\mathbf{r}, \hat{s}) \, c \, \Delta t \, dA \quad [\text{Jsr}^{-1}] \quad (2)
\]

\[
P = \frac{E}{\Delta t} = h \nu \, N(\mathbf{r}, \hat{s}) \, c \, dA \quad [\text{Wsr}^{-1}] \quad (3)
\]

The power per solid angle, (3), is also called the radiant intensity, denoted by \( I \). [69]. Utilising equations (1)-(3), the photon density (4), \( \rho(\mathbf{r}) [\text{m}^{-3}] \); radiance (5), \( L(\mathbf{r}, \hat{s}) [\text{Wm}^{-2}\text{sr}^{-1}] \); fluence rate (6), \( \phi(\mathbf{r}) [\text{Wm}^{-2}] \), and the net flux vector (7), \( F(\mathbf{r}) \), can be expressed. The net flux vector is useful when the net flux through a surface element is sought, as the net flux is equal to scalar product between the surface normal and the net flux vector [69].

\[
\rho(\mathbf{r}) = \int_{4\pi} N(\mathbf{r}, \hat{s})d\Omega = \oint_{S} N(\mathbf{r}, \hat{s})dS \quad (4)
\]

\[
L(\mathbf{r}, \hat{s}) = N(\mathbf{r}, \hat{s})c \, h \nu \quad (5)
\]

\[
\phi(\mathbf{r}) = \int_{4\pi} L(\mathbf{r}, \hat{s})d\Omega = c \, h \nu \int_{4\pi} N(\mathbf{r}, \hat{s})d\Omega = c \, h \nu \, \rho(\mathbf{r}) \quad (6)
\]
Chapter 5 - Light transport theory

\[ F(\mathbf{r}) = \int_{4\pi} L(\mathbf{r}, \hat{s}) \hat{s} \, d\Omega \]  \hspace{1cm} (7)

In an illuminated turbid sample, \( dV \), around a point in space, \( \mathbf{r} \), a number of events can occur (Figure 5.2).

**Photons can:**
1) enter,
2) exit,
3) be absorbed inside,
4) scatter away from (4a) or into (4b) a specific direction,
5) and originate from internal sources within the volume.

*Figure 5.2: The events of photon-sample interaction within \( dV \).*

The net flow through the sample is the difference between photon entry and photon exit. Radiative transport in turbid media is described by the events 1-5 through the time-dependent radiative transfer equation (RTE),

\[
\frac{\partial L(\mathbf{r}, \hat{s}, t)}{\partial t} = -\hat{s} \cdot \nabla L(\mathbf{r}, \hat{s}, t) - (\mu_a + \mu_s)L(\mathbf{r}, \hat{s}, t) \\
+ \mu_s \int_{4\pi} p(\hat{s}, \hat{s}')L(\mathbf{r}, \hat{s}', t) \, d\Omega' + S(\mathbf{r}, \hat{s}, t),
\]  \hspace{1cm} (8)

or in steady-state, the time-independent RTE, [69]:

\[
\hat{s} \cdot \nabla L(\mathbf{r}, \hat{s}) = -(\mu_a + \mu_s)L(\mathbf{r}, \hat{s}) + \mu_s \int_{4\pi} p(\hat{s}, \hat{s}')L(\mathbf{r}, \hat{s}', t) \, d\Omega' \\
+ S(\mathbf{r}, \hat{s}).
\]  \hspace{1cm} (9)

Equations (6) and (7) can be expressed in \( N \) by application of equation (5). The terms of the right-hand side of equation (8) and (9) are described by events 1-5 in Figure 5.2. Hence, during \( \Delta t \), the number of photons per volume and solid angles in the \( s \)-direction altered according to

\[
\Delta N_{tot} = -\Delta N_{(2)-(1)} - \Delta N_{(3)} - \Delta N_{(4a)} + \Delta N_{(4b)} + \Delta N_{(5)},
\]  \hspace{1cm} (10)
where the subscripts denotes events 1-5.

5.2.1 Photons entering and exiting $dV$

During $\Delta t$, the difference between the number of photons, per unit volume and solid angle, entering and exiting $dV$ is

$$\Delta N_{(2)-(1)} = c \Delta t \nabla N(r, \hat{s}) \cdot \hat{s}. \quad (11)$$

5.2.1 Photons absorbed in $dV$

The third event, i.e., photon absorption is expressed by means of probability theory. It is assumed that photons are absorbed as described by the Poisson process, and that the intensity of that process is equal to a parameter called $\mu_a$. Hence, the probability that a photon is absorbed within the time $\Delta t$ is, [69]:

$$P\{\text{absorption within } \Delta t\} = 1 - e^{-c \Delta t \mu_a} \approx c \Delta t \mu_a \quad (12)$$

The frequently occurring simplification made only uses the first term of the Taylor series expansion of the expression. The number of photons, per unit volume and steradian in direction $\hat{s}$, that are absorbed is

$$\Delta N_{(3)} = c \Delta t \mu_a N(r, \hat{s}) \quad (13)$$

5.2.1 Photons scattered in $dV$

The event of photons scattering away from the direction $\hat{s}$ is also governed by a Poisson process (with intensity $\mu_s$), hence the number of photons, per unit volume and steradian in direction $\hat{s}$, that are absorbed is

$$\Delta N_{(4a)} = c \Delta t \mu_s N(r, \hat{s}) \quad (14)$$

The event of photons scattering into the $\hat{s}$ direction, from another direction ($\hat{s}'$) is shown in Figure 5.3. The probability that a photon is scattered from one direction into another is described by the phase function of scattering $p(\hat{s}', \hat{s})$ multiplied by the solid angle, $d\Omega$. Hence, the number of photons scattered into the $\hat{s}$ direction from the $\hat{s}'$ direction, per unit volume and unit steradian, is
\[ \Delta N_{(4b)} = c \Delta t \mu_s \int_{4\pi} p(\hat{s}', \hat{s}) N(r, \hat{s})d\Omega', \]  
\tag{15} \]

where integration over all solid angles is performed to account for contributions from all directions.

**Figure 5.3:** Illustration of scattering events. During \( \Delta t = (t_2 - t_1) \), photons 1-3 are scattered at \( r \). At \( t = t_1 \), photons 1-3 travel in the \( \hat{s}' \) direction, i.e., within \( d\Omega' \). At \( t = t_2 \), photon 1 and 3 have been scattered into the \( \hat{s} \) direction whilst photon 2 has been scattered into the \( \hat{s}' \) direction.

### 5.2.1 Photons generated in \( dV \)

The fifth event, i.e., photons per unit volume and solid angle that originate from sources within the sample, can be expressed as

\[ \Delta N_{(5)} = \Delta t \ s(r, \hat{s}), \]  
\tag{16} \]

where \( s(r, \hat{s}) \) describes the internal sources.

### 5.2.2 The radiative transport equation

By combining equations (10)-(16), \( \Delta N_{\text{tot}} \) can be expressed as

\[
\Delta N_{\text{tot}} = -c \Delta t \nabla N(r, \hat{s}) \cdot \hat{n} - c \Delta t (\mu_a + \mu_o) N(r, \hat{s}) \\
+ c \Delta t \mu_s \int_{4\pi} p(\hat{s}', \hat{s}) N(r, \hat{s})d\Omega' + \Delta t c \ s(r, \hat{s}). \]  
\tag{17} \]
To arrive at the time-dependent rate, describing events 1-5 in a volume $V$, division by $\Delta t$, letting $\Delta t \to 0$ and integrating over the volume is performed on equation (17):

$$
\lim_{\Delta t \to 0} \frac{\Delta N}{\Delta t} = \frac{\partial N}{\partial t} \Rightarrow
$$

$$
\frac{1}{c} \int_V \frac{\partial N}{\partial t} dV = -\int_V \nabla N(r, \hat{s}, t) \cdot \hat{s} dV - \mu_t \int_V N(r, \hat{s}) dV
$$

$$
+ \mu_s \int_V dV \int_{4\pi} p(\hat{s}', \hat{s}) N(r, \hat{s}) d\Omega'
$$

$$
+ \int_V s(r, \hat{s}) dV
$$

(18)

The right hand side of the equation is the net flow into the volume in the $\hat{s}$ direction plus the added photons from scattering events from other directions into the $\hat{s}$ direction, minus the loss due to absorption and scattering from $\hat{s}$ into other directions plus the contribution from embedded sources. Different expressions of the transport equation occur in the literature, e.g., in terms of fluence rate or radiance; but all of them are described by means of the events presented here.

The derivation of the transport equation was made to accentuate the importance of the optical parameters of absorption and scattering, as well as the phase function of scattering. Hence, if no internal sources are present, the light transport within the turbid medium is dependent solely upon these parameters.

Moreover, in a steady state situation with no scatterers or embedded sources in a homogeneous sample, the transport equation reduces to:

$$
\int_V c\hat{s} \cdot \nabla N(r, \hat{s}) dV = \{\text{homogeneity}\} =
$$

$$
\int_V c \frac{dN(r, \hat{s})}{ds} dV = \int_V c\mu_a N(r, \hat{s}) dV \Leftrightarrow
$$

$$
\frac{dN}{ds} = -\mu_a N \Leftrightarrow \frac{dL}{ds} = -\mu_a L
$$

(19)
The latter expression being a first order differential equation, with the solution:

\[ L = L_0 e^{-s \mu_a} \]  

(20)

which is known as the Beer-Lambert’s law. Steady state allows for termination of the time derivative term in the transport equation; absence of scatterers removes all terms linearly dependent on the scattering coefficient; analogously, the absence of embedded sources eliminates that term; and finally, the assumption of homogeneity reduces the direction derivative to depend merely on the norm of the direction vector.

The transport equation is derived under the assumption that light is considered as particles, i.e., photons. Hence, wave properties of light are not encountered when the transport equation is applied. To include wave properties, such as interference, polarization etc., modifications have to be made or other fundamental theories be applied, e.g., the Maxwell equations in a finite element model. These issues are not covered here as they are beyond the scope of this thesis. For the same reason, approximations of the transport equation are left out, e.g., the diffusion theory; as they have not been applied in any work presented here.

5.2.3 Photon scattering phase function

The probability density function for a photon being scattered into direction \( \hat{s} \) from the \( \hat{s}' \) direction, \( p(\hat{s}, \hat{s}') \), is also called the (normalised) phase function of scattering. For isotropic scattering the phase function is uniform, whilst for anisotropic scattering a non-uniform phase function has to be applied. In this thesis, the Henyey-Greenstein (HG) phase function has been adopted:

\[ p(\hat{s}, \hat{s}') \triangleq p(\hat{s} \cdot \hat{s}') = p(\cos \theta) \]  

(21)

\[ p(\cos \theta) = \frac{1}{2} \left( 1 + \frac{1 - g_{HG}^2}{g_{HG}^2 - 2g_{HG} \cos \theta} \right)^{3/2}, \quad g_{HG} \in [-1, 1] \]  

(22)

where \( \theta \) is the angle between the \( \hat{s} \) and \( \hat{s}' \) directions and \( g_{HG} \) is the Henyey-Greenstein anisotropy factor for light scattering. If the medium is homogeneous, the probability density function for light scattering from \( \hat{s} \) to \( \hat{s}' \) depends solely upon the angle, \( \theta \), between \( \hat{s} \) and \( \hat{s}' \), (21). An anisotropy factor equal to zero implies isotropic scattering (i.e., all scattering direc-
tions are equally probable), whilst an anisotropy factor equal to 1 or -1 implies that light is scattered in the forward or backward direction, respectively. Equation (22) is the Henyey-Greenstein phase function of light scattering.

5.3 Monte Carlo modelling of light transport

5.3.1 Light transport in turbid media

The Monte Carlo technique is a statistical model that describes stochastic processes, first suggested by Metropolis and Ulam in 1949 [70]. In light transport theory, the Monte Carlo method is suitable for tracking photon interaction with scattering and absorbing media, e.g., tissue [71]. The model can simulate photon paths as a combination of many linear fractions where each photon is subject to interaction within (absorption) and between the fragments (scattering). The length of each linear fragment, i.e., the step size of the photon, can be set as variable or fixed. As both absorption and scattering are governed by Beer's law, the probability of a photon being absorbed or scattered, when interacting, is determined by Poisson processes with intensities of $\mu_a$ and $\mu_s$ respectively, i.e., the absorption and the scattering coefficient; and that an anisotropy factor of the material describes the average cosine of the scattering angle, i.e., the diversion angle from the previous linear fraction of the photon path. By storing the path history of a large number of photons, including photon injection and exit, a photon distribution in time and space can be achieved with this method. The accuracy of Monte Carlo simulations, as compared to photon distribution in a physical medium with the specified optical properties, is proportional to $1/\sqrt{N}$, where N is the number of injected photons [72]. Hence, the simulated result will converge to true values as the number of injected photons approach infinity.

5.3.2 The Monte Carlo method

A Monte Carlo model is as much dependent upon the geometry of the medium as upon the optical properties of the medium, as internal reflections affect the result. The simplest, non-trivial, geometry is the semi-infinite model, which is limited in the z-direction but unlimited in the horizontal plane. Wang and Jacques presented a thorough survey of the semi-infinite multiple layers Monte Carlo in their MCML documentation [73]. It is possible to implement complex geometries into a Monte Carlo model.
In its simplest form, the Monte Carlo method utilises a fixed step size approach. Each photon is initialised and injected into the medium to a depth of $\Delta s$ in the $\mathbf{s}$ direction. From its new position, $\mathbf{r}$, a check to see if it is still in the medium is performed, and a probability calculation for scattering and absorption is carried out. If the photon is scattered, it is assigned a new direction, which depends on the scattering phase function of the medium, and the procedure is repeated by moving the photon $\Delta s$ in the scattered direction, $\mathbf{s}'$. If the photon is absorbed, a new photon is injected. This scheme is repeated until an exit criterion is fulfilled, such as $N$ photons being injected. Scattering events, absorption events etc., can be logged and stored for off-line analysis or recalculation.

![Figure 5.4: The flowchart for the scheme of a Monte Carlo simulation.](image)

In the fixed step size approach, the step size is chosen so that it is much smaller than the distance within which the photon is expected to interact with the medium once, on average. That distance is called the mean free path (mfp), and is determined by the absorption and scattering properties of the medium.
\[ mf = \frac{1}{\mu_a + \mu_s} = \frac{1}{\mu_t} \]  

(23)

The demand that \( \Delta s \) should be much smaller than the mean free path arises from the fact that the event of a photon being both absorbed and scattered within \( \Delta s \) is not included in the fixed step size model, and should therefore be highly unlikely.

The probability for a photon being absorbed or scattered is stipulated by Beer's law as: \( P\{\text{absorption}\} = 1 - e^{-\Delta s \mu_a} \) and \( P\{\text{scattering}\} = 1 - e^{-\Delta s \mu_s} \) which is approximated by truncation of the Taylor expansion of the exponentials. Hence, \( P\{\text{absorption}\} \approx \mu_a \Delta s \) and \( P\{\text{scattering}\} \approx \mu_s \Delta s \) for small step sizes.

If a photon is not scattered nor absorbed, it is considered to not interact with the medium it travels in. Moreover, if it is assumed that a photon cannot be both absorbed and scattered within the distance \( \Delta s \), the probability of the events "absorbed", "scattered" and "no interaction" sums to unity, and a random number between zero and unity can be utilised to separate between the events. This is achieved by introducing a dimensionless random number, \( \xi \), with uniform distribution strictly between 0 and 1. Between each step of the photon, \( \xi \) is generated and an event decided [72]:

\[
\begin{align*}
0 < \xi < \mu_a \Delta s & \quad \text{Photon is absorbed} \\
\mu_a \Delta s \leq \xi < \mu_t \Delta s & \quad \text{Photon is scattered} \\
\mu_t \Delta s \leq \xi < 1 & \quad \text{No interaction}
\end{align*}
\]

(24)

If the sample is below the probability for absorption, the photon is absorbed; if it is between the probability for absorption and the probability for scattering or absorption, the photon is scattered; otherwise no interaction takes place and the photon is moved another \( \Delta s \) in the same direction.

Using fixed step size causes slow execution, as many photons have to be moved several times before they are either scattered or absorbed. The use of a variable step size solves this problem as the step size can be designed so that either an event of absorption or of scattering occurs after each step. From Beer's law, the probability of a photon being absorbed or scattered within a pathlength \( \Delta s \) is \( 1 - e^{-\mu t \Delta s} \); hence, the probability density function for photon-medium-interaction, \( p(\Delta s) \), is \( \mu_t e^{-\mu t \Delta s} \). By sampling \( p(\Delta s) \), a variable step size with interaction after each photon move can be achieved. The random number \( \xi \) is utilised in a mapping procedure for this
purpose. The variable step size, $\chi$, is calculated using the random number, $\xi$, according to the sampling procedure illustrated in Figure 5.5. By using variable step size, the scheme for Monte Carlo simulations, Figure 5.4, is modified by introducing a new process "set step size" between the processes "inject photon" and "move photon".

![Figure 5.5: Mapping of a random number to a sample from a non-uniform distribution. The shaded areas of the probability density functions (lower left and lower right) are equal.](image)

In variable step size Monte Carlo, a one-to-one mapping from the random number to a non-uniformly distributed variable is made by setting the probability of a step being shorter than a certain length equal to the probability of a random number being below a certain number between zero and one. This is the same as setting the cumulative distribution function of the uniform variable at the point of interest equal to the cumulative distribution function of the non-uniform variable at the same point. The variable step size can thus be decided from:

$$\xi_1 = \int_0^{\xi_1} ds = \int_0^{\chi_1} \mu_t e^{-\mu_t s} ds$$

By solving this integral equation for $\chi_1$, a relation between the random number and the variable step size is obtained:

$$\chi_1 = -\ln \left(1 - \xi_1\right) = -\ln \xi'_1$$

The second equality follows from the fact that there is no difference between the distribution of $\xi$ and $1-\xi$ when $\xi$ is uniformly distributed between
Monte Carlo modelling of light transport

0 and 1. Hence, the relationship between the random number and the variable step size is, i.e., sampling of a non-uniform distribution, made by:

\[
\chi = \frac{-\ln \xi}{\mu_t}
\]  \hspace{1cm} (27)

In an analogous way, sampling from the Henyey-Greenstein phase function of scattering, utilizing a random number, is performed by [72]:

\[
\cos \theta = \frac{1}{2g_{HG}} \left\{ 1 + g_{HG}^2 - \left[ \frac{1 - g_{HG}^2}{1 - g_{HG} + 2g_{HG}\xi} \right] \right\}
\]  \hspace{1cm} (28)

where \( \theta \) is the angle between \( \mathbf{s} \) and \( \mathbf{s}' \), \( g_{HG} \) the Henyey-Greenstein anisotropy factor of light scattering and \( \xi \) the random number between zero and one.

As \( \theta \) is the angle between \( \mathbf{s} \) and \( \mathbf{s}' \), i.e., the zenithal angle, an assumption for the azimuthal angle has to be made for direction uniqueness. If the phase function of scattering does not have an azimuthal dependence, the distribution of the azimuthal angle, \( \varphi \), is set uniform and the relation between the random number, \( \xi \), and \( \varphi \) becomes:

\[
\xi = \frac{1}{2\pi} \int_{0}^{\varphi} d\varphi' \Rightarrow \varphi = 2\pi\xi
\]  \hspace{1cm} (29)

where the uniform probability density function for \( \varphi \) has been normalized by multiplication of the factor \((2\pi)^{-1}\) as \( \varphi \) lies in the interval \([0, 2\pi]\).

Now, as a relationship between random numbers and probability distributions of the variable step size, the longitudinal and azimuthal angles of light scattering have been established, the scheme for a Monte Carlo simulation (Figure 5.4) can be implemented. However, the events of internal reflection must be processed. There are different ways for doing that; for instance, the photons can be allowed to carry a weight that is reduced when a photon path crosses a boundary between two media with different refractive indices; or, a roulette can be adopted in order to, in a statistically correct way, decide whether a photon is reflected or transmitted at a boundary. Irrespective of the method, internal reflection and transmission are governed by Fresnel's laws of reflection (31)–(32), whilst the relation between the incident angle and the transmission angle is decided from Snell's law:
\[ n_i \sin \alpha_i = n_t \sin \alpha_t \]  

where \( n_i \) is the refractive index of the medium from which the light is incident, \( n_t \) the refractive index of the medium into which the light transmits, \( \alpha_i \) the incident angle and \( \alpha_t \) the transmission angle. When light passes from an optically denser medium into an optically less dense medium, the transmission angle will be greater than the incident angle.

\[
R(\alpha_i) = \begin{cases} 
1 & \alpha_i \geq \alpha_c \\
\frac{(n_i - n_t)^2}{(n_i + n_t)^2} & \alpha_i = \alpha_t = 0 \\
\frac{1}{2} \left[ \frac{\sin^2(\alpha_i - \alpha_t)}{\sin^2(\alpha_i + \alpha_t)} + \frac{\tan(\alpha_i - \alpha_t)}{\tan(\alpha_i + \alpha_t)} \right] & \text{otherwise} 
\end{cases}
\]

\[
T(\alpha_i) = 1 - R(\alpha_i),
\]

Photon absorption can be handled in different ways in a Monte Carlo simulation scheme. One way is to assign a weight to each photon and reduce the weight, according to the absorption coefficient specified, in each interaction and, if the weight becomes too small decide whether the photon survives the interaction or not. The decision for photon survival is necessary for the conservation of energy. Another way of handling photon absorption is to store the total path length of each photon and post process photon absorption by applying Beer Lambert's law to each photon. Both methods are easily implemented, but the latter allows for application of multiple values for \( \mu_a \), utilising only one Monte Carlo simulation.
6.1 Background

Diffuse reflectance spectroscopy has been widely used to study skin colour. In 1939 Edwards and Duntley, [76], utilised the method to characterise the colour of living human skin in objective quantities for the first time. In 1952 Kuppenheim and Heer, [74], compared the diffuse reflectance spectra from Caucasian and Black subjects and were among the first to observe the light absorption of water. In 1981 Anderson and Parrish, [75], explained the difference of spectra between normal and erythematous human skin. Numerous studies using diffuse reflectance spectroscopy in diverse fields of scientific research have emerged over the years.

In diffuse reflectance spectroscopy, a sample is illuminated by light from a light source, and the backscattered light from the sample is collected by a photo-detector. The total optical power of the detected light is decomposed by the spectrometer into spectrally resolved optical power. The measurements result in spectra that depend on the scattering and the absorption properties of the sample. By fitting the absorption characteristics of chromophores to the resulting spectrum from a measurement, the concentration of these chromophores can be deduced [77, 78]. Besides the absorption characteristics of a certain sample, the scattering characteristics play a major role in diffuse reflectance spectroscopy. Without scattering, only the specularly reflected light or transmitted light is detectable. On a macro-
scopic level, light travelling from one medium to another is reflected at the boundary separating the two, if the refractive indices of the media are different. Upon macroscopic light reflection, the incident angle is equal to the reflection angle (angles between optical axis and surface normal). Microscopic reflection (scattering) is governed by particle and bulk refractive index mismatch and interference. Scattered photons change direction and the new direction of a scattered photon is decided by particle size, wavelength and the refraction index mismatch. Photon scattering is more prominent in the ultraviolet than in the visual and near infrared range [79, 80].

6.2 Theory

No matter if light is regarded as electromagnetic waves or energy quanta (photons), it has the ability to interact with its surroundings. In the electromagnetic representation, these interactions can be described by Maxwell’s equations (usually in a finite element model), Mie theory or Rayleigh theory; whereas in the energy quanta representation they can be described by the transport equation, diffusion theory or Monte Carlo simulations.

In optical spectroscopy, the interaction between light and matter is analysed, e.g., by studying the intensity-to-wavelength distribution of light that has interacted with a sample as compared to the intensity-to-wavelength distribution of the light source. Hence, the ability of the sample to scatter and absorb light will affect the wavelength distribution of the light that travels in the sample, as a function of the optical properties of the sample and the spatial position of interest.

The energy of a photon is proportional to the frequency of the light (or inversely proportional to its wavelength):

\[ E = h\nu = \frac{hc}{\lambda} \]  

(33)

where \( h \) is Planck's constant, \( \nu \) the frequency of the light, \( c \) the speed of light and \( \lambda \) the wavelength. As energy is conserved, energy from a photon that is absorbed by matter must undergo conversion and/or be remitted as a photon. When an atom or a molecule absorbs a photon, it is excited to an energy level that is higher than the ground state energy level. For the atom or molecule to return to its ground state, the absorbed energy must be re-
leased. This energy transition can be radiative or non-radiative. In radiative transitions, light emission is part of the energy conversion.

### 6.2.1 Photon absorption

When energy from a photon is transferred to another physical system, e.g., an atom or molecule, photon absorption has occurred. A molecule that absorbs photon energy changes its quantum energy state via electronic, vibrational or rotational transitions. Electronic transitions can occur in both atoms and molecules whereas vibrational and rotational transitions take place in molecules, exclusively. Absorption via electronic transitions involves excitation to an excited singlet state, from which the atom (or molecule) is decayed, as it strives to maintain equilibrium. The absorbed energy can be released in different forms, e.g., by emission of a new photon (see section 6.2.4) or heat. Vibrational transitions invoked by photon absorption alter the distribution of the vibrational stages of the atoms in the molecule. Less energy is required to achieve vibrational transition as compared to electronic transitions. Rotational transitions are changes to the quantum rotational state, and are associated with even less energies than vibrational transitions. In the visual range of the electromagnetic spectrum, biological species are, mainly, subject to electronic and vibrational transitions. Electronic transitions are associated with absorption in the UV-VIS part of the spectrum, whereas vibrational transitions are associated with absorption in the VIS-NIR part.

Molecules or parts of molecules that are responsible for light absorption are called chromophores. In biological media, haemoglobin is a major chromophore also absorbing light via electronic transitions. Haemoglobin is the molecule that carries oxygen in the red blood cells. Oxygenated haemoglobin (HbO₂) has different absorption characteristics than reduced haemoglobin (Hb). Hence, HbO₂ and Hb are two different chromophores. Melanin is a pigment that is present in human skin. A high concentration of melanin makes the skin darker as compared to a low concentration. Water is a chromophore absorbing light via vibrational transitions. Absorption characteristics of reduced and oxygenated haemoglobin are shown in Figure 6.1.
6.2.2 Elastic light scattering

In elastic scattering events, photons do not lose energy, nor do they gain energy. In other words, light that undergoes elastic scattering preserves its frequency (wavelength). Hence, photons travelling in elastic scattering media are subject to energy loss merely due to absorption. Rayleigh and Mie scattering are both elastic.

![Jablonski diagram of elastic and inelastic scattering](image)

*Figure 6.2*: A Jablonski diagram of elastic and inelastic scattering.
6.2.3 Inelastic light scattering
When photons gain or lose energy in scattering events, they are subject to inelastic scattering. In Figure 6.2, the inelastic scattering process, along with the elastic scattering process, is illustrated in a Jablonski diagram. When the excitation energy is larger (arrow of greater length) than the energy of the inelastically scattered photon, the photon is subject to a Stokes' shift, as opposed to when the scattered photon gains energy (anti-Stokes' shift). Stokes' and anti-Stokes' shifts are studied in Raman spectroscopy where the vibrational energy distribution of molecules is measured.

6.2.4 Photoluminescence

Some chromophores have the ability to absorb photons and remit the energy as photons of lower energy than the absorbed energy. Those chromophores (fluorophores) have an energy level distribution that allows for molecule excitation to the singlet state upon photon absorption. The return to the ground state involves vibrational energy conversion, i.e., generation of heat, and radiative energy conversion, i.e., the photon emission, see Figure 6.3. The wavelength of an emitted photon corresponds to the energy gap between the vibrational levels of the singlet state and the ground state, between which the radiative transition occurred. In the excited state, a spin conversion through an intersystem crossing can occur, leaving the system in a triplet state from which a return to the ground state is forbidden by the selection rules of the standard model. Hence, transitions from the triplet state to the singlet ground state (phosphorescence) are associated with longer life-times than are transitions from the single excited state to the singlet ground state (fluorescence).

Figure 6.3: A Jablonski diagram of the photoluminescence. Straight-line arrows involve photons (radiative transitions) whilst curled arrows do not (non-radiative transitions).
6.2.5 Measuring wavelength distribution

The phase velocity of electromagnetic waves depends on the optical frequency. Hence, refraction is frequency (wavelength) dependent. This can be verified easily by focusing a beam of white light onto a triangular prism and observing the light decompose to its spectral components in the form of a rainbow (Figure 6.4). This effect is called chromatic dispersion and can be utilised to measure the wavelength distribution of light. Another way to separate light into wavelength components is by utilising the effect of diffraction. In spectroscopy, this is frequently done by the use of a diffraction grating, which acts in a similar way as a prism. However, the effect of diffraction is much more prominent than the effect of dispersion, making the diffraction technique more suitable for precision measurements. A grating can be, e.g., an assembly of many, closely spaced slits. When a plane wave of light passes through the grating, destructive and constructive interference results in a diffraction pattern. The pattern is predictable as the spatial positions of the intensity maxima and minima, relative to the grating, are decided by the wavelength of each component.

![Figure 6.4: White light incident on a triangular prism, left side, disperses and creates a rainbow pattern as it exits the prism on the right side.](image)
The general aim of this thesis was to develop optical methods that enable quantification of tympanic membrane characteristics associated with otitis media. The specific aims were to:

1. Investigate whether diffuse reflectance spectroscopy can be utilized to differentiate the healthy, the hyperaemic and the OME tympanic membrane.

2. Develop a new fibre-optic technique for non-contact assessment of surface shape that can be incorporated in a standard otoscope.

3. Develop a method for Monte Carlos simulations of light transport in solid tissue phantoms with curved surfaces based on the surface shape assessment technique.

4. Evaluate the surface shape assessment on membranes in an ear phantom and on tympanic membranes.

5. Suggest methods for calibration and signal normalisation for the surface shape assessment technique.
In Paper II, spectroscopy was applied for assessing the diffuse reflectance spectra from 18 children, where eight of the children were scheduled for tonsillectomy and ten scheduled for tympanostomy tube placement (the OM group). An ear, nose and throat specialist examined the children in the tonsillectomy group by means of otoscopy. Children with healthy ears were included and served as healthy references. In the tympanostomy placement group, the children were examined by means of otomicroscopy where the ears were classified according to the characteristics of the middle ear effusion (MEE) into the groups: absent, serous and mucous. After examination and MEE classification, a first diffuse reflectance spectrum was recorded. Next, myringotomy was performed as needed for tympanostomy tube placement. Prior to grommet placement, the MEE, if present, was removed (and classification confirmed) from the middle ear by suction and a second diffuse reflectance spectrum recorded. When performing myringotomy, the tympanic membrane is traumatised and hyperaemia develops. This was utilised to simulate the tympanic membrane erythema frequently observed in AOM. Examination and spectroscopic recordings were performed during general anaesthesia. In Figure 8.1 the procedure is illustrated.

Figure 8.1: An illustration of the procedure for assessing the first and second diffuse reflectance spectrum from the tympanic membranes in the OM group. First, cerumen was removed from the external auditory canal; second, a first diffuse reflectance spectrum was recorded from the intact tympanic membrane; third, myringotomy was performed and MEE was drained; fourth, a second diffuse reflectance spectrum was recorded from the hyperaemic tympanic membrane.
The diffuse reflectance spectra were acquired by means of a modified Hopkins® telescope from Karl Storz where a metal tube was placed around the telescope rod and optical fibres was embedded inside the metal tube but outside the rod. Half the embedded optical fibres guided light from a tungsten halogen arc lamp to the tip of the modified telescope, allowing for tympanic membrane illumination; the other half served for guiding back-scattered photons from the tympanic membrane to the spectrometer. The design of the modified telescope is more thoroughly described in Paper II.

8.1 Signal processing

8.1.1 Normalising spectra

To compare spectra from two or more measurements, the spectra have to be compensated for the spectral characteristics of the light source and the contribution from background radiation. Light source influences were compensated for, by introducing a standard, which all measurements were related to. The standard should be white, with high reflectivity in the wavelength range of interest. In Paper II, a white diffuse polytetrafluoroethylene based reference tile (WS-2, Avantes, Eerbeek, The Netherlands) was utilised as standard. The output from the standard measurement was depicted as having 100 % reflectance throughout the wavelength range. Normalisation was performed as in (34), where $R$ is the normalised reflectance spectrum, $I$ the measured spectrum, $I_{ref}$ the standard spectrum and $I_b$ the spectrum of the background radiation, which was recorded on site with the light source obstructed.

$$R[\lambda] = \frac{I[\lambda] - I_b[\lambda]}{I_{ref}[\lambda] - I_b[\lambda]}$$  (34)

When the measuring distance is not constant, as in Paper II, further normalisation has to be performed to allow for inter-spectra comparisons. The energy of the reflected light can serve as such a normalisation factor. Hence, the sum of all components in the spectrum can be used for normalisation; this approach was applied to achieve a normalised diffuse reflectance spectrum $R_N[\lambda]$, (35).

$$R_N[\lambda] = \frac{R[\lambda]}{\sum_{\lambda} R[\lambda]}$$  (35)
8.1.2 Erythema indices

In order to quantify the redness of the tympanic membrane from acquired diffuse reflectance spectra, two erythema detection indices were applied (36)-(38), previously suggested by DAWSON et al. [82] and FEATHER et al. [83]. The melanin correction in the index suggested by DAWSON et al. [82] was omitted as the tympanic membrane can be regarded as melanin free.

\[ L_\lambda = -\log_{10} R_N[\lambda] \tag{36} \]

\[ E_D = 100[L_{560} + 1.5(L_{540} + L_{575}) - 2(L_{510} + L_{610})] \tag{37} \]

\[ E_F = 100 \left[ \frac{L_{544} - L_{527.5}}{16.5} - \frac{L_{573} - L_{544}}{29} \right] \tag{38} \]
There are many ways to perform optical assessment of surface curvature. In situations where the object of interest is easily accessible, methods such as shape from shading, triangulation and fringe projection can be suitable. However, when the object of interest is not that easily accessible and an angle between the optical axis of the detector and the optical axis of the source cannot be created, those methods fail to perform. Therefore, a technique for optical characterisation of the shape of a surface, where the optical axis of detector and source are parallel, was developed and evaluated.

9.1 Principle

Consider two parallel optical fibres, one that is emitting light onto a surface and one that is guiding the backscattered light from the surface to a detector (Figure 9.1). The cross section of the emitting cone of the source fibre, the cone of acceptance of the detector fibre and the surface of the object depend on the separation between the source and detector fibres, the distances from the fibres to the surface, the effective area of the fibres and the numerical apertures of the fibres. Consider also, a fibre arrangement where the fibres are parallel with the normal of a semi-infinite plane. Place a coordinate system so that the plane is the x-y plane, i.e., with the normal (0, 0, 1), the centre of the fibre ends in positions (0, 0, h) and (d, 0, h) for the source and detector, respectively; where \( h \) is the distance in z-direction from the fibre ends to the surface plane and \( d \) the separation between the source and detector fibres.
Figure 9.1: The separation (d) between the source fibre (left) and the detector fibre (right) along with the measuring distance (h) determine the intersection of the emitted cone, the cone of acceptance and the surface.

Given that the optical power of the light source is constant, the backscattered optical power depends upon fibre separation, d, and the measuring distance, h. Apart from the geometrical factors; material optical properties and surface structure affect the total backscattered power. However, the principle is easier to grasp if the effects of multiply scattered photons and surface structure are neglected.

The conceptual idea of this technique is to combine the effects from fibre separation and measuring distance variations in a device that measures at multiple source-detector separations and, when applied to a non-flat surface, measures at multiple measuring distances as the surface itself is responsible for the variations in measuring distance. Figure 9.2 illustrates the idea as applied to a spherical cap.
By activating one source fibre at a time and detecting the backscattered optical power simultaneously, but individually, with the detector fibres then the effects from variations in fibre separations and average measuring distances are measured for each source-detector combination. Thus, the measured signals can be sorted into a matrix where each row is depicted as the detected signals from all detectors when a specific source was activated, and each column is depicted as the detected signal from a specific detector for all light source activations (Figure 9.3). As the matrix represents the backscattered intensity for different combinations of source and detector fibres, the matrix was named the source detector intensity matrix referred to as the SDIM.

![Flowchart](image)

**Figure 9.3:** Flowchart for the collection of surface curvature data in a fibre array set-up.

### 9.2 Signal processing and fitting

As there are differences in sensitivity between the light sources and the detectors due to, e.g., variations in coupling efficiencies and light source output power, the raw SDIM was normalised by array division with the SDIM from a reference surface.

In the diagonal of SDIM the backscattered intensity for the source detector pairs with the smallest separations ($d_{\text{min}}$) is found. The separation is constant and thus the signal depends on variations in the measuring distance
and not variations in source-detector separation. The anti diagonal of the matrix is defined as the backscattered intensity as detected by detector $i$ when light source $N-i+1$ is active ($i = 1, 2, ..., N$). In the anti diagonal, the sequence of source detector pairings with the largest range of source detector separations is found, $d_{\text{min}} < d < d_{\text{max}}$, and the signal depends on variations in both source-detector separation and variations in measuring distance. Hence, the largest signal dynamics is expected for the anti diagonal.

In Paper II, the $SDIM$ from convex and concave surfaces was normalised by array division of the $SDIM$ from a plane surface (39). A discrimination index, $D$, was defined as the difference between the $SDIM$ diagonal average and the $SDIM$ 5th off-diagonal average (40).

$$d_{\text{norm}}^j(i) = \frac{d_j(i) - b_j(i)}{d_{\text{flat}}^j(i) - b_j(i)} \quad i, j = 1, 2, ..., N$$

$$I_{\text{norm}} = \begin{bmatrix}
  d^\text{norm}_1(1) & \cdots & d^\text{norm}_5(1) \\
  \vdots & \ddots & \vdots \\
  d^\text{norm}_1(N) & \cdots & d^\text{norm}_5(N)
\end{bmatrix}$$

where $d_j(i)$ is the backscattered optical power as detected by detector $j$ when light source $i$ is active; $b_j(i)$ the corresponding background and $N$ the number of light sources and detectors. The superscript flat denotes reference from the flat surface and the superscript norm emphasizes that the element is normalised with respect to the reference surface.

$$D = N^{-1} \sum_{k=1}^{N} d_{\text{norm}}^k(k) - (2N - 10)^{-1} \sum_{l=1}^{N-5} [d_{\text{norm}}^l(l + 5) + d_{\text{norm}}^{l+5}(l)]$$

In Paper III, the dynamic nature of the anti diagonal was utilised, and a curve fitting algorithm applied to measurements and simulations. The anti diagonal was defined as in (41) and is also illustrated in Figure 9.4:

$$ad[k] = \frac{d_{\text{norm}}^k(N - k) + d_{\text{norm}}^{k+1}(N - k + 1)}{2}$$

The anti diagonal was arbitrarily fitted to a discrete Gaussian function (42), centred at $k=5.5$, using least squares.
Signal processing and fitting

**Figure 9.4:** A SDIM and the diagonal elements (black circles) where source detector fibre distance is 0.75 mm and the 2nd anti diagonals (white circles) consisting of SDIM elements corresponding to source-detector separations ranging from 1.1 mm, in the two most central anti diagonal elements to 7.5 mm, in the first and last elements.

\[
\hat{a}_d[k] = Ae^{-(k-5.5)^2/(2\sigma)^2} + C
\]  

where \(k\) is the element number of the anti diagonal, i.e., \(~\)proportional to the source-detector separation for the corresponding pairings; \(A\) the Gaussian amplitude, \(\sigma\) the standard Gaussian width and \(C\) the offset. Pearson's product-moment correlation coefficient, \(r\), for \(ad\) and \(ad_{fit}\) was calculated and \(r^2\) served as a measure of the goodness of fit.

### 9.3 The Lambertian surface approach

In Paper II, the theoretical model for simulating the SDIM was derived by assuming that the surfaces of the optical phantoms were Lambertian, meaning that a beam of light with an infinitesimal width is backscattered from the incident point in all directions with equal probability. The optical power output from the source fibres was set constant and the surface reflectivity to 100 \%, i.e., every photon incident on the surface was assumed to backscatter from the surface.

The surface was discretized into a mesh, representing a finite number \(N = 10^6\) of surface elements (Figure 9.5). Each source-detector pairing was associated with an intersection of the cone of illumination from the source fibre \((L)\), the meshed surface and the cone of acceptance of the detector fibre \((D)\), (43)–(44). The size of the intersection depends on the surface shape, the source-detector separation and the distance from the fibres to the surface. For all \(S_k\) in the intersection \(L_s \cap D_d\), the fraction \(g_k\) of the backscattered optical power \(P_k\), as seen by detector \(d\), was calculated. In Figure 9.5, surface element \(S_j\) fulfils the requirements to be included as contributing to the signal, whereas the elements \(S_i, S_m\) and \(S_n\) do not. As the surface was modelled as Lambertian with 100 \% reflectivity, the backscattered optical power was equal to the optical power incident on \(S_k\). The scheme for the formation of the simulated source-detector intensity matrix \((SDIM)_L\) is shown in Figure 9.6.
Figure 9.5: Discretization of the optical phantom was performed by applying a mesh to the shape. Each intersection in the mesh was regarded as a point source. Left (side view): Light that is illuminated (left cone) from a source fibre onto the meshed surface and the cone of acceptance (right cone) for a neighbourhood detector fibre. The gradient fill illustrates the angular distribution of the illumination and of the detection effectiveness. Right (view from above): The dashed circles show the NA limit for the source and detector and the solid outline, the intersection of the illuminated surface and the surface within the cone of acceptance for the detector. Coordinates in the mesh belonging to the intersection of the illumination cone and the cone of acceptance for a source-detector pairings were identified and processed individually.
The Lambertian surface approach

Figure 9.6: Scheme of the Lambertian simulations. Each surface was discretised to a mesh, $S$, so that $S \equiv \bigcup_k S_k$ and $\bigcap_k S_k \equiv \emptyset$. For each source-detector pair, the detected backscattered optical power was calculated. $L_s$ is the conic optical output volume for source fibre $s$, $D_d$ the cone of acceptance for detector fibre $d$, $N_s$ the number of source fibres, $N_d$ the number of detector fibres and $N$ the number of surface elements (the number of $S_k$).
Chapter 9 - Surface curvature assessment

The photon flux volume, $L$, from the illumination fibre, positioned at $l = (x_{lc}, y_{lc}, z_{lc})$, was defined as in (43). The detectable back-scattered photons were assumed to be within the volume $D$ (44), with the detector fibre positioned at $d = (x_{dc}, y_{dc}, z_{dc})$. $NA$ in (43)–(44) is the numerical aperture of the fibres. In the measurements, fibres with $NA=0.5$, giving a full acceptance angle of $60^\circ$, were applied. The illumination profile was set so that the intensity on the surface decreased from the centre and out (45).

Figure 9.7: Illumination profile of the source fibres.

\[ L \equiv \text{all x, y, z so that} \]
\[ (x - x_{lc})^2 + (y - y_{lc})^2 \leq \tan(\arcsin(NA))^2 (z - z_{lc})^2 \]  
(43)

\[ D \equiv \text{all x, y, z so that} \]
\[ (x - x_{dc})^2 + (y - y_{dc})^2 \leq \tan(\arcsin(NA))^2 (z - z_{dc})^2 \]  
(44)

\[ I_k = I_c \cos \alpha \begin{cases} x, y, z \in L \cap D \cap S \\ x', y', z' \in L \cap S \end{cases} \]  
(45)

\[ P_k = \int_{S_k} I(x, y, z) dS_k \approx I(x_k, y_k, z_k) \cdot A_{S_k} = A_{S_k} \frac{\cos \alpha}{r_k^2} \]  
(46)

where $I_k$ is the intensity in the centre of surface element $S_k$; $I_c$ the intensity in the centre of surface element, $S_\infty$ that intersects with the optical axis of the source fibre (see Figure 9.1 and Figure 9.5) and $A_{S_k}$ the area of $S_k$. Photons incident on $L \cap S$, was reflected from the surface with an angle of reflectance that was uniformly distributed in the upper hemisphere, i.e., the centre of $S_k$ was regarded as an isotropic point source emitting spherical waves. Hence, the fraction of detectable reflected photons was proportional to the ratio between the detector fibre area and the area of the upper hemisphere with radius ($r_d$) equal to the

Figure 9.8: The detectable fraction of the optical power of light reflected from $S_k$. 

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distance between the incident point and the detector fibre. The function \(g(x,y,z)\) was defined to calculate this fraction.

\[
g_k = \frac{\cos \beta}{r_d^2}
\]  

(47)

where \(\beta\) is the angle between the optical axis of the detector and vector from \(d\) to \(S_k\) (see Figure 9.1). The detectable fraction is proportional to \(\cos \beta\) as the effective area of the detector is proportional to \(\cos \beta\). Hence, the elements of the \(SDIM_L\) were calculated as:

\[
SDIM_L(l,d) = \sum_k g_k P_k
\]  

(48)

9.4 Monte Carlo simulation of surface curvature assessment

9.4.1 Assessing the optical properties of Delrin

In Monte Carlo modelling, the photon distribution inside the medium depends on the ability of the medium to refract, scatter and absorb light. Hence, simulations of light transport require knowledge of the optical properties for the sample.

The refractive index for Delrin was measured by utilising a waveguide method, previously described by BOLIN et al. [84]. An optical fibre with core refractive index of 1.495 and a diameter of 1.3 mm was stripped from its cladding and the cladding replaced by Delrin by drilling a hole through a piece of Delrin and inserting the fibre core into it. The diameter of the drilled hole was slightly smaller (1.2 mm) than the core diameter in order to maximise the contact area between the fibre core and the Delrin cladding and hence minimise the occurrence of air pockets. Three additional waveguides – using water, whole blood and the original cladding as cladding material – were assembled and utilised for calibration. The optical power distribution with respect to the photon exit angle, \(P(\theta)\), was measured by means of goniometry (Figure 9.9) and the refractive index of the cladding calculated according to (38).
Figure 9.9: The goniometer set-up. An aperture stop allows detection of photons on a specific ray, defined by the angle \( \theta \) (adjustable between \(-60..60^\circ\)). With sample A, laser light from the HeNe gas laser illuminated a diffuser (a thin slab of Delrin) to ensure mode filling of the waveguide and the goniometer was utilized to measure the numerical aperture of the waveguide. With sample B, the scattering profile of Delrin was measured.

\[
n_d^2 = n_c^2 - (n_0 \sin \xi)^2
\]  

(49)

where \( n_d \), \( n_c \) and \( n_0 \) are the refractive indices of the Delrin cladding, the fibre core and the ambient medium (air) respectively, and \( \xi \) the half-width of \( P(\theta) \) at \( P(\theta) = P_{\text{max}} e^{-2} \).

WANG AND JACQUES [85] have shown that the reduced scattering coefficient can be assessed in an oblique angle set-up, where a laser source is applied, incident on the sample with an angle oblique to the surface normal of the sample (Figure 9.10). Photons are injected into the turbid medium at an oblique angle and the photon distribution is assumed to be diffuse after one reduced mean free path. That is, the light transport is regarded as if there was a point source emitting light at a position located one \( mfp' \) inside the medium along the refracted laser beam direction. Hence, by assessing the separation between the diffuse profile and the entrance point (\( \Delta x \)), the reduced mean free path can be calculated from (50)–(51).
Monte Carlo simulation of surface curvature assessment

\[ \frac{mfp'}{\mu_a + \mu'_s} = \frac{1}{\mu_a + \mu_s (1 - g_{HG})} \]  

(50)

\[ \Delta x = mfp' \cos \theta_r \]  

(51)

where \( \theta_r \) is the refracted angle as decided by Snell's law from \( n_d, n_0 \) and the incident angle \( \theta \). For Delrin, \( \mu_a << \mu_s' \) and hence, the reduced scattering coefficient can be approximated as:

\[ \mu'_s \approx \frac{\cos \theta_r}{\Delta x} \]  

(52)

*Figure 9.10:* The oblique angle illumination method for determination of the reduced scattering coefficient of Delrin (left and middle, illustrating the use of samples 1 and 2 respectively). The recorded camera images (right) are analyzed to assess the distance, \( \Delta x \), from the entrance point of the beam, i.e., the hot spot, to the centre of mass of the diffuse scattering profile. The centre of the diffuse profile is located at the intersection of the symmetry line (dash dotted) and the hot spot is located at the intersection of the dashed line and the symmetry line in the x-direction.

The goniometric set-up in Figure 9.9 was also applied in the assessment of the scattering angle distribution for Delrin where the optical power of the light transmitted through the Delrin slab was measured as a function of transmission angle. In a set of transmission Monte Carlo simulations where the reduced scattering coefficient, as determined by means of the oblique angle method, was kept constant and the anisotropy factor, \( g_{HG} \), varied between 0.70 and 0.99 in steps of 0.01, \( g_{HG} \) for Delrin was decided from the best fit between the simulations and the goniometric measurement.

### 9.4.2 Monte Carlo implementation

The basic principles and flowchart of Monte Carlo modelling, described in section 5.3, apply to the simulations made in surface curvature assessment. However, as the surface curvature phantoms in the experiments cannot be
regarded as semi-infinite in the Monte Carlo model, adjustments to handle the spherical/cylindrical geometry of the solid optical phantoms were made.
10.1 Paper I

Title: Fibre optic array for curvature assessment – Application in otitis media

Nine polyacetal plastic objects (cylindrical rods made from Delrin) were utilised as surface shape phantoms. In the preparation of the phantoms, one end of each rod was reshaped in a turning lathe giving the surface the shape of a spherical cap, four with convex, four with concave curvature (with the curvature radii 20, 30, 40 and 50) and one left unchanged. The Delrin rod that was not reshaped, thus having plane surfaces on both ends, served as a reference. The end surfaces were polished with a rough polishing cloth, removing the traces from the lathe, giving the surfaces a smooth diffuse appearance. Details about the principle and methods used are to be found in sections 9.1-9.3.

The $SDIM$s for the convex Delrin rods, as measured with the dual array probe and simulated utilising the Lambertian model, are shown in Figure 10.1 where the surface curvature radii of the phantoms ranges from 20 to 50 from left to right. In Figure 10.2, the corresponding $SDIM$s for the concave phantoms are shown.
Figure 10.1: The source-detector intensity matrices (normalised with plane surface) from experiments (A) and simulations (B) when the surfaces of the sample objects are convex ($\Delta = 4.5$ mm). The surfaces of the sample objects are spherically symmetric, with a radius of 20, 30, 40 and 50 mm respectively (from left to right). Note different intensity scaling in A and B.

Figure 10.2: The source-detector intensity matrices (normalised with plane surface) from experiments (A) and simulations (B) when the surfaces of the sample objects are concave ($\Delta = 4.5$ mm). The surfaces of the sample objects are spherically symmetric, with a radius of 20, 30, 40 and 50 mm respectively (from left to right)
The discrepancies between measurements and simulations are most likely due to the simplifications made in the Lambertian model. The most obvious ones are found in the simulated concave series for large source-detector separations, where no intersection between the emitted light cone from the source, the cone of acceptance for the detector and the surface exists for the plane surface, even though it exists for the concave surface. When this occurs, normalization of simulations result in division by zero for certain elements of the SDIM.

An index that discriminated between convex and concave surfaces (Figure 10.3) was calculated from the SDIMs.

![Figure 10.3: The concave/convex discriminator index, D, for different distances between probe head and surface boundary, Δ. Note different positive and negative scaling.](image)

The relative dynamic range of D, defined as the difference of the maximum and the minimum divided by the mean of the index, was 1.37 for convex surfaces and 0.68 for concave surfaces, at a measuring distance of 4.5 mm. The index D was positive for convex surfaces and negative for concave surfaces, which shows that the system can distinguish between convex and concave surfaces (Figure 10.3).

In this paper, results from Monte Carlo simulations concerning the fraction of photons transmitting a tympanic membrane were presented. It was concluded that with tympanic membrane thickness ranging from 20-230 µm, the transmittance range from 94-60%. In the simulations, $10^6$ photons
were injected and the optical properties utilised were $\mu_a = 0.4 \text{ mm}^{-1}$, $\mu_s = 1.40 \text{ mm}^{-1}$ and $g_{HG} = 0.82$.

**10.2 Paper II**

*Title: Diffuse reflectance spectroscopy of the human tympanic membrane in otitis media*

In this study we incorporated two optical fibre bundles to a straight endoscope, one bundle feeding white light and the other serving as detector of diffusely reflected light. This modified endoscope served as the otoscope (Fig. 6.5).

![Fig. 10.4: a) shows the modified endoscope (otoscope) at the site of the measurement and b) the probe head. In the measurements, the otoscope was inserted in the external auditory canal to a position where the distance from the probe head to the tympanic membrane was approximately 5 mm. At this distance, the whole tympanic membrane was illuminated by the source fibres.](image)

We investigated if objective assessment of the colour of the tympanic membrane could aid the diagnosis of otitis in children. The endoscope was used in combination with a spectrophotometer to assess the colour of the tympanic membrane in 15 ears from children suffering from otitis media with effusion (OME) and in 15 ears from a group of healthy children. Diffuse reflectance spectra were acquired before and after myringotomy (perforation of the tympanic membrane; a simulation of AOM) in the 15 ears with OME. The OME ears were sub-divided into two groups, ears with mucous middle ear effusion and ears with serous or no middle ear effusion. In one subject, measurement of removed cerumen was performed. The results from the spectroscopic measurements are shown in Fig. 6.6. The spectra are shown as the logarithm (to base ten) of the inverse reflectance (LIR).
Figure 10.5: Reflectance spectra (LIR is the logarithm of the inverse reflectance, Eq. 2c) arranged in classes. A) before myringotomy from ears with mucous middle ear effusion; B) before myringotomy from ears with no or serous middle ear effusion; C) after myringotomy; D) the healthy reference group and E) cerumen.

In the analysis of the spectroscopic result we used two previously published erythema detection algorithms that yielded numerical quantities of haemoglobin content [82, 83]. Our hypothesis that the haemoglobin content in the tympanic membrane would increase after myringotomy was tested using the student’s t-test for independent groups and the paired t-test for dependent groups. With a combination of the algorithms, simulated AOM (after myringotomy) was distinguished from healthy ears (p < 0.01). Otitis media with mucous effusion was distinguished from 1) otitis media with serous effusion, 2) induced erythema and 3) healthy ears, (p < 0.05).
Chapter 10 - Surface curvature assessment

Table 1: The mean value, standard deviation and confidence intervals\(^1\) for the erythema indices that were applied to groups A-D in Paper II.

<table>
<thead>
<tr>
<th>Erythema index</th>
<th>Group A</th>
<th>Group B</th>
<th>Group C</th>
<th>Group D</th>
</tr>
</thead>
<tbody>
<tr>
<td>(E_D), (mean±sd, 95 % CI)</td>
<td>80±49, [39,121]</td>
<td>120±30, [88,152]</td>
<td>132±35, [112,151]</td>
<td>97±24, [84,110]</td>
</tr>
<tr>
<td>(100*E_F), (mean±sd, 95 % CI)</td>
<td>19±17, [5,34]</td>
<td>45±17, [27,63]</td>
<td>45±30, [28,62]</td>
<td>36±13, [29,43]</td>
</tr>
</tbody>
</table>

Group C was compared to groups A and B using paired t-test, whereas groups A, B and D were compared using unpaired t-test. The 95 % confidence interval of the erythema indices were calculated for groups A-D (Table 1). The \(E_D\) CI:s for groups C and D were disjunctive, suggesting that this erythema index has potential for distinguishing a hyperaemic TM from a healthy TM, on an individual level. Our results imply that reflectance spectroscopy is a promising technique to be used for the diagnosis of otitis media.

\(^{1}\) Re-analysis of the data from Paper II to include the confidence intervals, as they were not published in the original article.
10.3 Paper III

Title: Monte Carlo simulations of backscattered light intensity from convex and concave surfaces with an optical fiber array sensor

10.3.1 Optical properties

The refractive index and the anisotropy factor of scattering for Delrin were determined to 1.47 and 0.87, respectively, by means of goniometry (Figure 9.9). In the oblique angle set-up, the reduced scattering coefficient for Delrin was estimated to be 23.4 cm\(^{-1}\), yielding a scattering coefficient of 180 cm\(^{-1}\) (50). The calibration measurements of the refractive indices for water, human whole blood and the original cladding of the fibre, utilising the replaced cladding method, resulted in 1.34 (1.33), 1.36 (1.36-1.38) and 1.42 (1.42) respectively (expected results in parentheses).

The Delrin samples proved to be inhomogeneous, which can be seen in Figure 10.6 where the isopower lines in the contour plot for the backscattered light from the sample are shown. Small bumps on the contours, on the far side (left in the contour plot) of the cylinder symmetry line, are clearly visible. Measurements of the reduced scattering coefficient for Delrin were therefore performed on a piece of Delrin that was divided in half along its symmetry axis and the oblique laser beam incident on the peripheral parts of the piece (top and bottom right in Figure 10.6).

![Contour plots of Delrin samples](image)

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>refractive index, (n)</td>
<td>1.47</td>
<td>anisotropy, (g)</td>
<td>0.87</td>
</tr>
<tr>
<td>reduced scattering, (\mu_s')</td>
<td>23.4 cm(^{-1})</td>
<td>scattering coefficient, (\mu_s)</td>
<td>180 cm(^{-1})</td>
</tr>
</tbody>
</table>

Figure 10.6: Recordings using the oblique angle illumination technique on Delrin according to Fig. 3. Left: Image of the diffuse scattering profile (upper left) and its contour plot (lower left) obtained from sample 1. Right: Images for sample 2, hotspot (upper right) and the diffuse profile (lower right), \(\Delta x=0.375\) mm
10.3.2 Light source illumination profile

The best-fitted Gaussian profile was binned into 40 bins \((I_{gbf})\), at different radii, and compared to the corresponding binning of the measured profile \((I_m)\). The deviation was 3.8 % or less.

10.3.3 Measurements vs. simulations

Both the \(SDIMs\) and the \(SDIM_{MC}:s\) fulfilled the noise criteria, having a coefficient of variation below 0.5.

The \(SDIM_L:s\) generated from the Lambertian model (Paper I), the \(SDIM_{MC}:s\) and the measured \(SDIMs\) are shown in Figure 10.7. It is clear that the Monte Carlo model is in much better agreement with measurements than the Lambertian model. In Figure 10.8 the anti diagonals from the \(SDIMs\) and the \(SDIM_{MC}:s\) and their corresponding Gaussian fits are shown. The differences in the waist parameter \((\sigma)\), of the Gaussian fits, between simulations and measurements, were within 9.6 % in the convex case and 35 % in the concave case. The square of the Pearson’s coefficient of correlation \((r^2)\) was >0.94 for convex surfaces and >0.90 for concave surfaces \((p < 0.01)\).

**Figure 10.7:** The source-detector intensity matrix (\(SDIM\)) for simulations and measurements. Left three columns: The first column shows the previously published results from the simulations assuming backscattered light to be Lambertian sources in the surface for convex surfaces of radii 20, 30, 40 and 50 mm (from top to bottom). The second column shows the result from the Monte Carlo simulations for the same configuration; and the third column shows the \(SDIMs\) corresponding data from the measurements. Right three columns: Concave results, using the same layout as for the convex surfaces.
Figure 10.8: The anti diagonals, curve fitted (line) and observations (markers), for SDIMs (dotted fit and circles) and SDIMs (solid and squares) of convex phantoms with radius (r) 20–50 mm (from top to bottom). The table shows the $\sigma$ (convex, concave) of the best fit for simulations ($\sigma_{mc}$) and measurements ($\sigma_m$) along with the relative difference.

| R  | $\sigma_{mc}$ | $\sigma_m$ | $|\sigma_{mc} - \sigma_m| / \sigma_m$ | $r^2$ |
|----|---------------|-------------|--------------------------------------|-------|
| 20 | 0.81, 2.98    | 0.78, 2.23  | 0.040, 0.34                         | 0.99, 0.98 |
| 30 | 1.05, 2.26    | 1.00, 1.84  | 0.051, 0.23                         | 0.98, 0.97 |
| 40 | 1.19, 2.36    | 1.13, 1.75  | 0.049, 0.35                         | 0.94, 0.94 |
| 50 | 1.25, 1.69    | 1.14, 1.60  | 0.096, 0.060                        | 0.96, 0.90 |
10.4 Paper IV

**Title:** In vitro tympanic membrane position identification with a co-axial fiber optic otoscope

The technique for surface curvature assessment, described in Paper I, was miniaturized and incorporated in a Heine Beta 200 otoscope. Measurements were performed on vulcanized latex membranes in a model mimicking the human ear, where the membranes were positioned was varied. Moreover, measurements were performed on tympanic membranes in harvested human temporal bones where the position of the tympanic membrane was controlled by altering the middle ear pressure using a syringe pump coupled to the middle ear via the Eustachian tube.

External and internal normalization were performed on the SDIMs from both model and tympanic membranes, equations (53) and (54) respectively. A measuring distance compensating normalization was suggested for tympanic membrane SDIM data.

\[
SDIM_{ext}(i,j) = \frac{M(i,j)}{R(d,i,j)|_{d=15mm}} \tag{53}
\]

\[
SDIM_{int}(i,j) = \frac{M(i,j)}{M_{neutral}(i,j)} \tag{54}
\]

\[
SDIM_c(i,j) = \frac{M(i,j)}{R(d,i,j)|_{d=15mm}} \cdot \frac{R'(d,i,j)|_{d=15mm}}{R'(d,i,j)} \tag{55}
\]

In the external normalization (53), the SDIM from a polyacetal plastic reference was utilized in accordance with the normalization procedure described in Paper I. Internal normalization (54) was performed by relating the bulging or retracted membrane to the neutrally positioned membrane.

The normalized source detector intensity matrices were fitted to a two-dimensional Gaussian function, and the amplitude \(A\) and offset \(o\) of the Gaussian was used for surface shape representation. Typical SDIM\(_{ext}\) from the model measurements are shown in Figure 10.9 whereas typical SDIM\(_c\) from the tympanic membrane measurements are shown in Figure 10.10. Scatter-plots for the fitting parameters \(A\) and \(o\) are shown in Figure 10.11.
Figure 10.9: The series of SDIM_{ref} from a model ear measurement (top) with the corresponding Gaussian fit (middle) and the model fitting parameters for amplitude (squares) and offset (circles) (bottom). Each column represents a membrane volume displacement, ranging from -0.3 – 0.3 ml from left to right.

Figure 10.10: Typical SDIM, from a retracted, normally positioned and bulging tympanic membrane (left to right) as normalized by the polyacetal plastic reference phantom.
As can be seen in Figure 10.11, the amplitude and offset model fitting parameters can be utilised to separate between bulging and retracted tympanic membranes using the \( SDIM_{\text{int}} \) (upper right panel), \( SDIM_c \) (lower left panel) or \( SDIM_{\text{cr}} \) (lower right panel). Due to different measuring distances between measurements, the externally normalized \( SDIM_{\text{ext}} \) (upper left panel) did not discriminate bulging and retracted positions of the tympanic membrane.
Techniques for measuring the shape of the tympanic membrane shape are few. In vitro measurements of the shape have been carried out utilizing various techniques, including Moiré interferometry [4, 51-54, 56, 86-92], optical coherence tomography [93], ultrasound [50] and digital image processing [94] has also been utilised to assess the tympanic membrane shape, stiffness and mobility.

Moreover, Gaihede et al., [95], have reported on in vivo determination of the elasticity of the human tympanic membrane, even though not directly applicable to otitis diagnostics, an apparent resemblance is found in measuring the shape versus measuring the pressure-volume relationship of the tympanic membrane. Recently, digital imaging and telemedicine have been suggested as tools for the assessment of conditions related to the middle ear [96].

In this thesis, techniques for tympanic membrane characterisation for incorporation in a standard otoscope were developed and evaluated. Paper I, III and IV deal mainly with curvature assessment, whereas Paper II includes colour assessment for potential aiding in the diagnostic procedure. In Paper I, the conceptual idea was presented together with measurements and simulations utilizing a simplified mathematical model. The procedure for normalizing the SDIMs was outlined and demonstrated. However, the discrepancies between measurements and simulations were prominent, especially for the concave surfaces. It was concluded that the discrepancies were due to simplifications in the theoretical model used for simulations. Hence, a customised Monte Carlo model, statistically describing the photon transport in the polyacetal plastic blocks, was developed and presented in Paper III. With the Monte Carlo model, the agreement between mea-
measurements and simulations was substantially improved, and, as the Monte Carlo method is widely accepted as being correct, theoretical evidence for the surface shape assessment technique was established. Apart from proving that the system could separate convex solids from concave ones, the theoretical model facilitated means for probe design decisions, such as selecting the optimal optical fibres for a given fibre layout or vice versa, for example. In Paper IV, the technology for curvature assessment was implemented in a customized speculum for use with a standard otoscope. Retracted and bulging positions were separable both when measuring on a latex membrane model and on the tympanic membranes in harvested temporal bones. Using the compensation for measuring distance in the normalization procedure, a separation between bulging and retracted tympanic membranes was achieved from static measurements. Moreover, with internal normalization, potential for quantitative assessment of the tympanic membrane volume displacement upon dynamic pressure application, e.g., when implemented in a pneumatic otoscope, is implied by the results.

11.1 Tympanic membrane shape characterization

The SDIM represents the shape of a surface, e.g., a tympanic membrane. The matrix is composed of multiple backscattering profiles for spatially distributed optical fibres acting as transmitters and receivers of light. The surface shape is represented using the relative differences between such spatially resolved reflection profiles. Therefore; it is important that the sample is at rest during the measurement. In practice, the typical subject is a young child with earache who is likely to have trouble cooperating, which makes the acquisition of surface curvature data challenging if the acquisition time is in the order of seconds.

The discriminating index $D$ in Paper I was defined as a subtraction between the mean in the diagonal and the mean of the fifth off-diagonals of the SDIM. In general, indices based upon subtraction are sensitive to absolute energy, i.e., the amplitude of the signal, and they lack intuitive interpretations involving the laws of physics. In the diagonals (including off-diagonals) of the SDIM, the separation between the source and detector fibres is constant. In the main diagonal, that separation is minimal (0.75 mm in the sensor evaluated in Paper I) and in the fifth diagonal that distance is $0.75 \cdot \sqrt{26}$. In a contact measurement using optical fibres with such separations, the subtracted difference between the quantities would depend on $I_0$, i.e., the optical power output from the source fibre, whereas the relative difference between the quantities, i.e., the quotient between the two, would
depend on the difference in average photon path length for the two separations. In Paper I, the measuring distance was constant and deviations in output power from the sources taken care of in the calibrating normalisation procedure applied. However, when comparing measurements with varying measuring distances, a quotient index is preferred.

The theoretical model for generating simulations of $SDIM$s from the solid polyacetal plastic blocks was afflicted with other limitations as well. For instance, the representation of the fibre sources as obeying the cosine law between zero exit angle and the critical angle for total internal reflection yielded a discontinuity in the illumination power distribution on the sample. This was adjusted for in Paper III where the photon exit angle was based on probability expressions, and did allow photons to exit the optical fibre at an angle greater than the critical angle – a representation that is in agreement with the nature of light transport in waveguides. This simplification is not critical and does not falsify the theoretical model to the same extent as does the limitation that photons cannot exit the medium outside the cone of acceptance of the source fibre. The latter effect explains why the simulated $SDIM$s in Paper I approach infinity for large source-detector separations in the concave cases, when normalized with the $SDIM$ from the plane surface.

The Monte Carlo model for $SDIM$ simulations was developed in order to validate the experimental results with a theoretical model that is consistent with light transport theory in turbid media. The discrepancies between simulations and measurements in Paper I were assumed to be due to simplifications in the theoretical model; an assumption that was verified in Paper III where the results from the Monte Carlo simulations of the $SDIM$s from the solid phantoms were compared to the $SDIM$s acquired by the double array sensor. In addition, the Monte Carlo model can be a useful tool in the process of designing a sensor with a layout, size or other characteristic different from the sensor described in Paper I.

The Monte Carlo source code was validated by comparing the output from the code with the output from other Monte Carlo sources that had previously been validated using the scheme suggested in [73]. A semi-infinite geometry was defined and an infinitely narrow beam of photons impinged the surface under normal incidence. The detector was modelled as a ring detector at radius $r$ from the point of photon injection. The decay in photon density as a function of $r$ was analyzed for simulations using the Monte Carlo code in Paper I and the Monte Carlo code that had been validated
against the MCML validation scheme [73]. The Monte Carlo code utilised in Paper III was confirmed as valid in these tests.

For Monte Carlo simulations of the tympanic membrane, an approximation of the volume of interest can be made by separating a cylinder from a sphere with a membrane, thus interpreting the cylinder as the external auditory canal, the sphere as the middle ear cavity and the membrane as the tympanic membrane. Such geometry can be defined via analytical functions, which make the code implementation much easier. A more sophisticated approach is to make use of medical imaging and define a mesh from 3D data, e.g., from magnetic resonance tomography or computer tomography; an approach that has been applied by MARGALLO-BALBÁS and FRENCH, [97].

The source-detector intensity matrices of the human tympanic membrane, as reported in Paper IV, were able to separate retracted tympanic membranes from bulging ones, using a non-trivial signal normalisation. With internal normalisation (using the same membrane in a neutral position), pneumatic otoscopy is required; undermining the benefit and clinical relevance of the proposed technique as the tympanic membrane mobility is considerably impaired in aom and ome ears. Hence, it is probable that the volume displacement of the tympanic membrane upon applied pressure falls outside what is distinguishable with this type of sensor. On the other hand, by using the quasi-external normalisation (i.e., the $SDIM_c$ in Paper IV), means for measuring the distance from the probe to the tympanic membrane have to be added to the instrument, as data from the neutrally positioned eardrum are not accessible in the clinically relevant situation. The measuring distance is important, as it is an input parameter to the $SDIM_c$, which yield inter-measurement commensurability. The probe was miniaturized and incorporated in a standard otoscope to allow application through the external auditory canal of a subject or a harvested temporal bone. Initial trials were performed on voluntary adults during the Valsalva maneuver, i.e., pressurizing or depressurizing the middle ear by forcibly exhaling or inhaling against closed lips and nostrils. Unfortunately, the optical fibres selected for the otoscope prototype had too large numerical aperture, as a consequence of a prior underestimation of the measuring distance, i.e., the distance from the distal end of the ear speculum mounted on the otoscope head and the tympanic membrane. The measuring distance using the modified endoscope on the anaesthetized subjects in Paper II was measured to be 15 mm. When designing the otoscope speculum, a similar measuring distance was assumed. However, upon verification, the true
measuring distance was in the vicinity of 25 mm. Therefore, the data from the Valsalva maneuver showed large influences from the external auditory canal, an interference that could hardly be corrected for. Therefore, the present prototype was evaluated on tympanic membranes in harvested human temporal bones, in Paper IV, where a measuring distance of 15 mm was achievable. In addition to the temporal bone measurements, the otoscope prototype was evaluated in an ear model where the membrane mimicking the tympanic membrane was made from vulcanized latex. These results were also presented in Paper IV. It was shown that gradual convex and concave shapes of the ear model membrane were separable via a two-dimensional Gaussian fit, utilizing the amplitude and offset of the Gaussian function as the quantity discriminating between convex and concave surface shapes. For the temporal bone measurements, either internal normalization or a two-step normalization was required in order to separate bulging and retracted tympanic membranes.

11.2 Tympanic membrane colour assessment

The major tissue chromophores are haemoglobin, melanin, fat and water. The absorption of light by reduced haemoglobin peaks at 433 and 556 nm [81], whereas the absorption by oxygenated haemoglobin peaks at 418, 542 and 577 nm [69]. Melanin absorption decreases with wavelength, showing strong absorption in the ultraviolet and weak absorption in the infrared. These characteristics have been utilised in many studies in quantifying haemoglobin content by means of diffuse reflectance spectroscopy [75, 78, 98-105].

In Paper II, diffuse reflectance spectroscopy was applied to acquire diffuse reflectance spectra of the human tympanic membrane in vivo. The probe was designed for non-contact measurements in free-hand operation. Hence, the measuring distance was different from one measurement to another. This made comparisons of measurements to theoretical models demanding, and instead, relative indices reported by others were explored and employed. DAWSON et al., [82], developed an erythema index based on the influence of haemoglobin absorption in the reflectance spectra from human skin. They also managed to compensate the index from the influence of melanin absorption, yielding an index relatively insensitive to pigmenta-
tion variations. DIFFEY et al., [106], also developed an erythema index in the form of a quotient of the reflectance in the green and the red region of the electromagnetic spectrum. FEATHER et al., [83], showed that the index presented by DAWSON et al., [82], was sensitive to the relative mixture of
oxygenated and reduced haemoglobin of the tissue in the measurement site. They developed another erythema index based on the reflection at isobestic points (which are points in the spectrum where the absorption of oxygenated and reduced haemoglobin is equal). Their index was a difference of two gradients, making it rather insensitive to the influence of melanin absorption, as the melanin absorption is a descending function of irradiation wavelength with a nearly constant slope. The indices described by Dawson et al., [82], and Feather et al., [83], were applied to the diffuse reflectance spectra from the tympanic membranes as quantitative measures of tympanic membrane erythema. In the original Dawson erythema index, a term compensating for melanin content in the tissue is included [82]. The melanin compensation was omitted in Paper II, as the melanin concentration in the tympanic membrane was assumed to be zero [107]. Based on the results of the erythema detection algorithm study by Riordan et al., [108], the algorithms suggested by Dawson et al., [82], and Feather et al., [83], were chosen. This was, in part, done because melanin compensation was easily removed from the Dawson algorithm, whilst not included in the index by Feather et al., [83]. More important however, was that the Dawson and Feather indices showed reliability as well as reasonable sensitivity and specificity, as reported by Riordan et al., [108].

Significant group level differences in the applied erythema indices were seen between groups A-D (OME with mucous middle ear effusion, OME with serous or absent MEF, AOM as simulated by induced hyperaemia through myringotomy and the healthy reference group). The Feather index showed significant differences between groups A and B, and between A and D, whereas the Dawson index showed significant differences between groups A and C, and between C and D. As the statistical comparison was performed on a group level, a significant difference between the groups does not necessarily imply an individual diagnostic value of the index. For an index to be considered promising for clinical application, the confidence intervals, at some level of significance, for the groups to be separated by the indices should be non-overlapping. From the statistical data in Table 1 in section 10.2, it is clear that \( E_F \) does not meet the requirements for individual value to otitis diagnosis. The Dawson index however, shows disjunctive confidence intervals for groups C and D, implying that this index could be utilized to separate healthy and hyperaemic conditions of the tympanic membrane.
11.3 Implications for implementation in a clinical system

The incorporation of SDIM and erythema index acquisition in an otoscope is possible. The numerical aperture of the fibres used in the modified otoscope in Paper IV, did not allow for in vivo application. However, there are commercially available multi-mode fibres that fulfil the demand on the fibre NA associated with a measuring distance of ~25 mm. The time for acquiring both SDIM and DRS data can be made as short as 200 ms, making the proposed techniques compatible with the demands in a clinical application.

Results from tympanic membrane application of these techniques, Paper II and IV, support the idea that tympanic membrane shape and colour are quantitatively assessable and that the methods are incorporable in otoscope-like devices. However, clinical evaluations of the performance of these quantities in aiding the otitis diagnose are required. In an instrument for aiding otitis diagnosis, in my opinion, both the SDIM and the erythema index should be implemented, as a bulging and erythematic tympanic membrane is highly specific for acute otitis media, whereas a retracted tympanic membrane suggests otitis media with effusion. Future studies utilising the suggested curvature assessment technique could investigate the SDIM in dynamic registration, e.g., when applied in pneumatic otoscopy, acquiring SDIM variations to an applied pressure. There are indications in Paper IV that the tympanic membrane mobility could be quantitatively assessed from the SDIM using internal normalization.

11.4 Conclusions

In conclusion, diffuse reflectance spectroscopy has been utilised in a relevant setting, comparing the spectral signatures of healthy tympanic membranes, membranes from subjects with otitis media with effusion and tympanic membranes with increased blood content (induced erythema). Statistically significant differences between the groups were present. Moreover, one erythema index separated the hyperaemic tympanic membrane from the healthy on individual level (95 % CI). A fibre optic sensor capable of measuring surface curvature characteristics was incorporated in a standard otoscope and evaluated in an ear model and in a tympanic membrane in vitro set-up. A Monte Carlo model, describing the photon transport in the solid polyacetal plastic blocks was developed and utilized with comparisons made to actual measurements on said plastic blocks. In addition, methods for calibrating and normalising SDIM have been presented in Pa-
pers I, III and IV. Confirmation of the correctness of the calibration and normalisation schemes was implicitly shown by means of the Monte Carlo simulations presented in Paper III.
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Glossary of terms

Acute otitis media (a-KYOOT o-TI-tis MEE-dee-ah), A middle ear inflammation associated with infectious symptoms such as ache or fever., 24

AOM (acronym), Acute otitis media., 24, 30

Atelectasis (at·e·lec·TA·sis), Absence of gas in a normally gas spaced cavity, such as the middle ear. This is a severe retraction of the tympanic membrane where it, in a wall paper fashion coat the ossicles and the inner structures of the middle ear. Atelectasis may be resolved through surgery., 27

Cholesteatoma, a destructive and expanding tissue growth in the middle ear., 26

Chorda tympani, a nerve that branches from the facial nerve, running posteriory to anteriory through the middle ear cavity., 21

Cuboidal epithelium, epithelium made up of round or cube-shaped cells, as opposed to squamous or columnar, 20

Epidemiology (ep'-i-dē-mē-OL-ō-jē), The science that deals with why, when and where diseases occur and how they are transmitted in a human community., 25
Eustachian tube, The tube that anatomically connects the nasopharynx and the middle ear. It is through this the middle ear air pressure is kept at atmospheric pressure., 19, 21

Fibrosis, formation of scar tissue in response to injury, 27

Hypotympanum, the lower part of the middle ear cleft, 20

Lamina propria, thin layer of fibrous connective tissue immediately beneath the surface epithelium of mucous membranes, 20

Leukotriene, a mediator (signalling substance) that is partly responsible for histamine production., 30

Mastoid air cells, numerous small intercommunicating cavities in the mastoid process of the temporal bone that empty into the mastoid or tympanic antrum., 24

Mediator, Biological signalling substance., 30

Mesotympanum, the middle part of the middle ear, 21

Middle ear cleft, The cavity in the middle ear that houses the smallest bones of the body (malleus, incus and stapes) that constitutes the auditory conduction system from the tympanic membrane to the inner ear. The middle ear cleft is subdivided into four spaces - 1. The epitympanum, which is the superior to the tympanic membrane. In this space you find the body of the incus and the head of the malleus. 2. The mesotympanum, which is on a level with the tympanic membrane. 3. The protympanum, which lies in the anterior recess of the middle ear. This is where the eustachian tube connects to the middle ear. 4. The hypotympanum, which is the inferior part of the middle ear cavity., 24

Middle ear effusion (e-FYOO-zhun), An accumulation of fluid in the middle ear., 23, 24, 25, 26, 29, 30, 31, 32, 33, 34, 36, 80, 81

Mucus-producing goblet cells, unicellular mucus-secreting glands that are associated with columnar epithelia; also called mucous cells., 24

Myringoplasty, surgical closure of the tympanic membrane., 26

Nasopharynx, the upper part of the throat behind the nose. An opening on each side of the nasopharynx leads into the ear., 21, 30
Ossicles, the sound conductive bone structures in the middle ear, i.e., the malleus, the incus and the stapes., 19, 21

Otalgia, ear ache., 26

Otitis media with effusion, otitis media (see otitis media) without acute symptoms., 23

Otorrhoea, discharge from the external ear., 25

Pars flaccida, the triangularly shaped part of the tympanic membrane that lies superiorly. The size of the pars flaccida is approximately one ninth of the tympanic membrane., 20

Pars tensa, the eight ninths of the tympanic membrane that are not pars flaccida (see pars flaccida)., 20, 25

Squamous epithelium, consists of layers of flat, scaly cells., 20

Tympanic membrane (membrana tympani), the eardrum., 19

Tympanocentesis (similar to myringotomy), needle aspiration through the tympanic membrane., 29

Tympanosclerosis, a condition characterized by the presence of masses of hard, dense connective tissue around the auditory ossicles in the middle ear., 27

Tympanostomy tube, a tube that is placed through the tympanic membrane in order to aerate the middle ear. This process requires myringotomy and performed in cases where ome does not resolve by itself or in patient with recurrent otitis media., 35
References


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