Electrodynamic Investigations of Conduction Processes in Humid Microcrystalline Cellulose Tablets

Martin Nilsson and Maria Strømme*

Department of Engineering Sciences, The Ångström Laboratory, Uppsala University, Box 534, SE 751 21 Uppsala, Sweden

The conduction mechanism in microcrystalline cellulose (MCC) tablets at varying relative humidity (RH) has been investigated by using the techniques of low frequency dielectric spectroscopy and transient current analysis at room temperature. The dependence on RH on the measured conductivity and charge carrier density indicates that a high-power-law-exponent percolation process of cations being conducted on water molecules occupying available 6-OH units on the cellulose chains is the dominating dc conduction mechanism at RH below 3 wt % of moisture content. The experimentally observed decrease in charge carrier mobility with increasing moisture content shows that protons and H_3O^+ ions that are being blocked at empty 6-OH sites also contribute to the charge transport process in cellulose at low moisture contents.

1. Introduction

Microcrystalline cellulose is one of the most frequently used filler/binder materials for direct compaction tablets.[1] Upon contact with water in the gastro intestinal channel the tabletted cellulose absorbs water then swells and the tablet finally disintegrates. Simultaneously the drug, being incorporated inside the cellulose matrix, dissolves and is released. Geometrically, the drug may be located inside granules of the cellulose or situated between particles or agglomerates of the cellulose. Especially in the first case, the ability of the cellulose to transport charges in a humid environment is important for the drug release process. In earlier work of ours[2,3] we have, in fact, shown that the average diffusion coefficient for the release process of Na^+ and Cl^- ions from the interior of compacted cellulose granules is of the same order of magnitude as the diffusion coefficient of the current carrying species in a humid (22% relative humidity) cellulose matrix where no ions have been intentionally introduced.

The charge transport mechanism in humid cellulose has previously been studied in a few publications (see e.g. refs 4−7 and references therein) after Murphy[8] first presented a power-law model to explain the observed increase in the dc conductivity σ_{dc} in cellulose with increasing water content according to

$$\sigma_{dc} = \sigma_s\left(\frac{M}{M_s}\right)^9 \tag{1}$$

Murphy[8] found that the saturation conductivity σ_s was varying with the impurity content in the cellulose, but that the exponent remained invariant and always close to 9. In the above equation M_s is the water content of the cellulose at saturation, expressed as a percentage of the dry weight, and (M/M_s) is the fraction of saturation prevailing when the cellulose is in equilibrium with a relative humidity such that its water content is M. Although Murphy assumed the conduction current in humid cellulose to be carried solely by impurity cations such as Na^+ and K^+, the nature of the charge carriers and the distribution of the sites from which they are released are still not clear. In addition to the alkali ions naturally present in the cellulose as a result of the extraction procedure of cellulose from land plants, there is also the possibility of protons, introduced in the ion exchange process carried through to remove the alkali ion impurities,[8] and dissociated water molecules contributing to the current. The common conclusion, however, of all experiments we are aware of is that the strong increase in cellulose conductivity with increasing water content is connected to the fact that adsorbed water molecules create a phase in which the charge carrying molecules, whatever their nature, can move.

To our knowledge, the only dc charge transport parameter that has been studied as a function of cellulose humidity is the conductivity. Since the conductivity,

$$\sigma_{dc} = nq\mu \tag{2}$$

in addition to the single carrier charge q, depends on both the charge carrier concentration n and the carrier mobility μ, it is essential to acquire knowledge about the dependence of both these quantities on the moisture content in order to gain deeper insight into the conduction process in cellulose, and thus being able to create a base for analyzing the importance of water interactions with cellulose for processes such as, e.g., the drug release from cellulose containing systems.

The aim of the present article is to analyze the charge transport mechanisms in cellulose by extracting the dependence of conductivity, mobility, and carrier concentration on humidity in order to obtain a more fundamental understanding than what has been presented hitherto of this widely used material's ability to host and transport ions. As analysis tools the electrodynamic methods Low-Frequency Dielectric Spectroscopy (LFDS) and Transient Current (TC) measurements are employed. While the former is an excellent technique to extract information about both ac and close-to dc behavior of the conductivity, the latter is needed in order to split up the conductivity into its constituent components n and μ, as will become clear below. Since one of our long-term goals is to create a knowledge-bank consisting of fundamental materials science and physical properties that may affect the performance of drug-delivery systems, we will use cellulose of pharmaceutical quality in this study. The

Humid Microcrystalline Cellulose Tablets

J. Phys. Chem. B, Vol. 109, No. 12, 2005 **5451**

cellulose has a crystallinity of about 75%[9,10] and is denoted microcrystalline cellulose (MCC).

2. Materials and Methods

2.1. Materials. The as-delivered MCC powder (Avicel PH 101, FMC, Ireland) has a particle size of about 50 μm.[11] The powder was compacted to tablets with a single punch tablet machine (Korch, EK 0, Germany) equipped with punches having a diameter of 11.3 mm, producing tablets at 206.5 $\pm$ 2.6 MPa, with weight 300.6 $\pm$ 0.27 mg and height 2.31 $\pm$ 0.05 mm (mean values $\pm$ standard deviation). After compaction the tablets were divided into four groups and, to ensure equilibrium in their moisture content, they were stored for approximately one month over saturated salt solutions producing a relative humidity (RH) of 11% (LiCl), 37% (NaI), 75% (NaCl), and 96% (KNO$_3$), respectively.

According to unpublished measurements comparing the conductivities in water baths containing tablets consisting of pure MCC and MCC tablets containing known concentrations of NaCl, the MCC grade used in the present study contains impurity ions giving rise to a conductivity corresponding to 0.7 wt % of NaCl being incorporated in the MCC. Transformed into numbers of Na$^+$ or H$^+$ ions, which are possible charge carriers in cellulose, this conductivity corresponds to 1 impurity ion per 41 or 284 cellulose monomer units, respectively (the weight of a unit being 162 g/mol). In the above estimation of impurity concentration, the density of H$^+$ comes out lower because of its higher mobility in water as compared to Na$^+$.

2.2. Methods. *2.2.1. Setup.* The setup used for both electrodynamic methods employed in this work has been described previously.[3,12] In brief, for the LFDS measurements a cylindrical, electrically screened sample cell was connected to a Novocontrol broadband dielectric converter (Novocontrol GMBH, Hundsangen, Germany) and a Solartron 1260 frequency response analyzer (Solartron Instruments, Hampshire, UK), while for the TC measurements the same cell was connected to a HP 4156A Precision Semiconductor Parameter Analyzer (PSPA). The electrodes of the sample cell were cylindrical and made of copper. Copper is an excellent electron conductor but it is unable to act as a transport medium for alkali ions and water constituent ions such as H$_3$O$^+$ and will, thus, act as a blocking electrode to the ions considered in the present study. The bottom of the sample cell was filled with the same salt solution over which the tablet to be measured had been stored to ensure equilibrium conditions in the moisture content during the measurements.

In all LFDS measurements the amplitude of the voltage applied across the electrodes was 1.0 V and the frequency was scanned from $\sim$10^7 to $\sim$10^{-3} Hz. For the TC measurements the current was stepped from a voltage value of 0 V to a value between 1.0 and 40 V and the resulting current was measured. The purpose of using a higher voltage in the TC measurements than in the LFDS measurements is to enhance the current to give a large enough signal-to-noise ratio for reliable results with the PSPA. The voltages used all belong to the linear ohmic-response regions of our samples.[3] The measurements took place at room temperature.

The upper electrode was rather heavy (907 g) and, thus, induces a pressure on the tablets of $\sim$90 kPa. This value, which is only 0.04% of the pressure used in the compaction process, should be low enough to not alter the tablet structure. However, it has proven high enough to suppress the contact resistivity since the conductivity data obtained with the above-described setup agrees well with literature data on MCC.[3,5] Josefowicz et

al.[13] and Bauer-Brandl et al.[14] have discussed in detail how to handle contact resistivity in electrodynamic measurements on cellulose.

2.2.2. dc Conductivity Extraction from LFDS. In this work we prefer to work with the real part σ' of the frequency dependent conductivity σ from the LFDS measurements. The real part of the conductivity is related to the imaginary part ϵ'' of the permittivity as

$$\sigma' = \omega\epsilon_0\epsilon'' \tag{3}$$

where ω is the angular frequency and ϵ_0 is the permittivity of free space (8.854 $\times$ 10^{-12} F/m).

There are several ways to extract a value of σ_{dc} from frequency dependent conductivity data. A method that is built on the amply documented power-law response[15] at frequencies above the dc regime is used here. If we assume that σ' has an approximate power-law behavior within some frequency range, it can be expressed as

$$\sigma' = \sigma_{dc} + B\omega^m \tag{4}$$

where B and m are constants. By rewriting the derivative of σ', we obtain

$$\sigma_{dc} = \sigma' - \frac{1}{m}\frac{d\sigma'}{d \ln \omega} \tag{5}$$

and σ_{dc} can be extracted by plotting σ' vs dσ'/d ln ω. To determine for which frequency region this plot should be made, one may first plot σ' and dσ'/d ln ω vs frequency separately, as is done in Figure 1a for a measurement on a MCC tablet at 37% RH. The region for which eq 5 should be applied is the one where dσ'/d ln ω has a good power-law behavior (is proportional to ω^m) and where σ' starts to level off toward low frequencies as a consequence of σ_{dc} becoming the dominant contribution.[16] The appropriate frequency region is the one located between the arrows in Figure 1a. When the correct frequency interval for the use of eq 5 is identified, the σ' values in this interval are plotted against dσ'/d ln ω on a lin$-$lin scale, as in Figure 1b. A linear fit to these data then gives the dc conductivity. For the measurement in Figure 1, σ_{dc} is 6.15 $\times$ 10^{-12} S/cm.

At frequencies lower than $\sim$10 mHz a decrease toward lower frequencies of *both* σ' and dσ'/d ln ω can be observed. This behavior can be related to blocking of the ions responsible for the above extracted σ_{dc} at the electrodes.[17] It should be noted that in the ideal case, i.e., when the interfaces between the studied material and the electrodes are very smooth, nonfractal, and nonporous, both σ' and dσ'/d ln ω are expected to fall off by a power-law exponent of 2.[17] Figure 1a clearly shows that for the MCC tablets under present study the corresponding slopes of σ' and dσ'/d ln ω are smaller. This deviation from ideal behavior has in fact been seen for most experimental systems, and can be attributed to various surface topographies and fractal dimensions of the electrode contact interface regions.[17,18]

2.2.3. dc Conductivity, Mobility, and Charge Carrier Concentration Extraction from TC Measurements. When the potential across the sample is changed from zero to a specified value taking the sample from a uniform charge distribution to a polarized state, the equation describing the transient current can be expressed as[16,19]

$$I(t) = \frac{A\sigma_{dc}U}{d}\exp\left(-\frac{\mu U}{d^2}t\right) \tag{6}$$

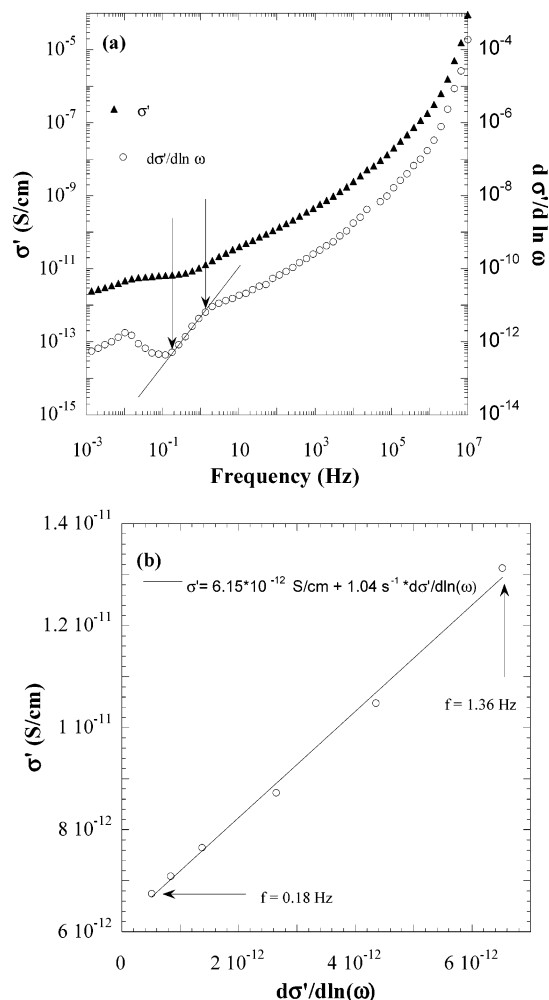**Figure 1.** (a) The real part, σ', of the conductivity in MCC tablets at 37% RH is displayed together with the derivative of σ' with respect to the logarithm of the angular frequency. The derivative, $d\sigma'/d \ln \omega$, is fitted to a power-law (full line) in order to recognize the region, situated between two arrows, to be used for the extraction of the dc conductivity, σ_{dc}. (b) The σ' values within the frequency region boarded by the two arrows in (a) are shown vs $d\sigma'/d \ln \omega$ on a lin−lin scale. Also included in the panel is a linear fit to the data (full line) whose equation reveals that σ_{dc} for the setup is 6.15×10^{-12} S/cm.

Here A denotes electrode area, d the sample thickness, and U the applied voltage. This equation neglects space-charge effects and is, thus, only valid for the initial current decay dominated by migration of ions toward the ion-blocking electrode. By fitting the TC response to an exponential function of time, the charge carrier mobility can be extracted from the exponent and the dc conductivity from the pre-factor. The carrier concentration is, then, readily obtained from the dc conductivity by using eq 2.

The above equation holds when there are only identical ions carrying the current. The equation is, however, easily adapted to the case when more than one type of ion reside in the sample simultaneously by just adding one additional term—identical with the one already at the right-hand side of the equation—per ion type.

In our previous work[3] we found two exponentially decaying regions in the TC response of MCC tablets at 22% RH. These two regions were then attributed to the movement of two different ionic species having similar conductivities within the humid cellulose. We speculated on the possibility that these two ion types were stemming from the dissociation of water molecules into protons and OH$^-$ ions. Also in the TC measure-
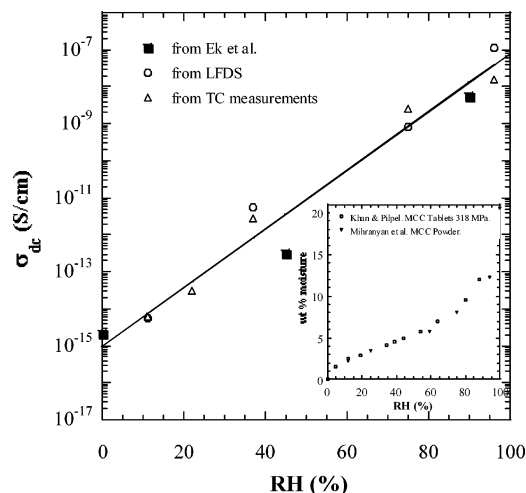

Figure 2. Conductivity versus relative humidity in MCC tablets extracted from LFDS and TC measurements. The data are median values of ∼3 measurements. The variation in the measurements was between 10% and 20%. Data calculated from the MCC powder dielectric spectroscopy response presented in Ek et al.[5] are also included. An exponential curve fit with the equation $\sigma_{dc}= 9.7 \times 10^{-16}$ S/cm $*$ exp[0.18*RH] is displayed as a solid line. The inset in the figure shows water adsorption isotherms in MCC powders and tablets as extracted from refs 20 and 21, respectively.

ments performed in the present work, at four other RH values, two more or less pronounced exponentially decaying regions are visible. Since the current response described by eq 6, strictly, only is valid in the time interval when space-charge contributions are negligible—i.e., before a significant number of ions have had time to pile up at the electrodes to create an electric field counteracting the applied field—we will only analyze the conduction parameters connected to the first process using eq 6. In the discussion following the result section we will, however, consider the conduction mechanism that may govern the second exponentially decaying region.

3. Results

Figure 2 shows the dc conductivity values obtained from the LFDS and TC measurements using eqs 5 and 6, respectively, as a function of relative humidity. Also included in this figure is the conductivity obtained from the first exponential decay of the TC measurement carried out at 22% RH[3] as well as conductivity values that have been extracted from the MCC powder dielectric spectroscopy response presented in Ek et al.[5] As observed earlier[3,4] the conductivity seems to increase exponentially with RH (an exponential fit to the data points is included in the figure).

To be able to relate the measured conductivities not only to the relative humidity, but also to the weight % of moisture in the tablets we use previously published information on the moisture adsorption process in MCC. The inset in Figure 2 integrates the room-temperature moisture adsorption isotherms taken on MCC powder[20] and on MCC tablets[21] compacted at a pressure of 318 MPa. From the inset it is obvious that the adsorption isotherms are almost identical. Thus, since the tablets used in the present study are compacted at a pressure below 318 MPa, these isotherms should work well as estimates of the relation between RH and weight % moisture in our tablets.

Figure 3 shows the conductivity data from Figure 2 vs weight % moisture in the tablets (as obtained from the Figure 2 inset). In addition to the apparently exponential increase in conductivity with increasing moisture content, observed in Figure 2, it is
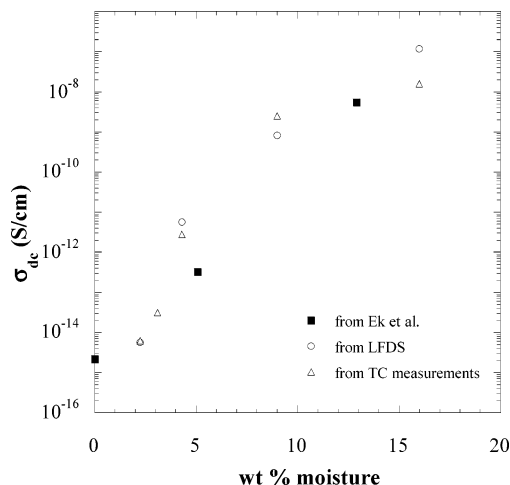
Humid Microcrystalline Cellulose Tablets

J. Phys. Chem. B, Vol. 109, No. 12, 2005 **5453**

Figure 3. Conductivity data from Figure 2 shown vs weight % moisture. The relative humidity has been transformed to weight % interpolating between data points in the inset of Figure 2.
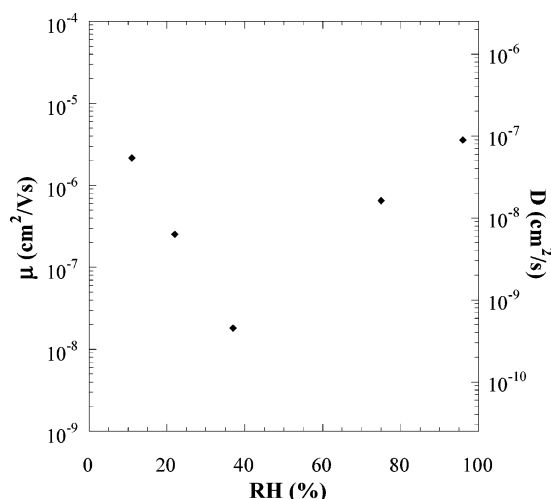

Figure 4. The mobility and diffusion coefficient of the carrier ions in tabletted MCC vs relative humidity. The data were obtained by extracting the initial TC response to eq 6 and are presented as the median value of ∼3 measurements. The variation in each data point is less than 20%.

evident in this figure that the increase eventually levels off, as earlier indicated in conductivity data taken on paper at relatively low moisture contents.[6]

From the TC measurements, the mobility of the carrier ions was extracted by fitting the initial current response to eq 6. The variation in carrier ion mobility with relative humidity is displayed in Figure 4. The corresponding diffusion coefficient values, D, as obtained from the Einstein equation

$$\mu kT = qD \qquad (7)$$

are shown on the right-hand side vertical axis of this figure. In the above equation, k is the Boltzmann constant. The figure shows that the mobility initially decreases with increasing RH, reaches a minimum at ∼37% RH, and thereafter increases to a value of ∼3.6 × 10⁻⁶ cm²/Vs at 96% RH.

When both σ_{dc} and μ are known, the charge carrier density is readily extracted from eq 2. Figure 5 shows n as a function of RH as obtained from the TC measurements using eqs 6 and 2. Included in the figure is also the water adsorption isotherm, expressed as the number of water molecules present at the various RH values. From this figures we observe that the initial rapid increase in number of charge carriers seems to level off
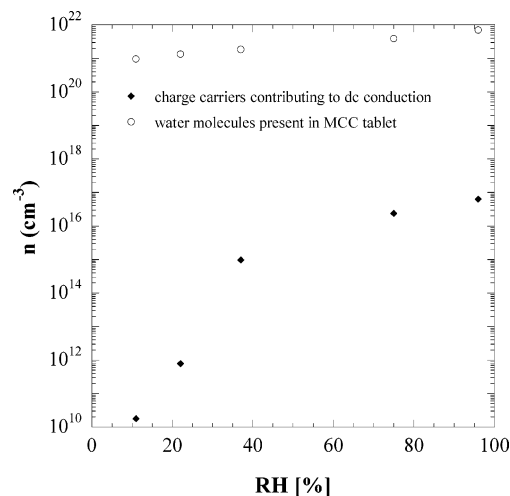

Figure 5. The number of charge carriers and total amount of water molecules present in the tablet vs relative humidity.

at high moisture contents. We also observe that the number of charge carriers is between 10^{11} and 10^5 orders of magnitude lower than the number of water molecules present in the tablet, the difference decreasing with increasing RH.

4. Discussion

Water vapor adsorption on microcrystalline cellulose has been shown to occur in different steps, and various binding strengths (tightly bound, less tightly bound, and bulk water) of the water molecules to the cellulose structure have been identified.[22] In the first step, each water molecule attaches to two carbon-6 hydroxyl (6-OH) groups on neighboring cellulose chains, i.e., to 6-OH groups located in the amorphous chain-surface regions. The crystallinity index of MCC being ∼75%[9,10] implies that only ∼25% of these are available for water molecules to bind to. A moisture content of ∼1.5 wt % in MCC, thus, represents a ratio of one water molecule to two monomer units in the cellulose[21] (the molecular mass of a cellulose monomer and of water is 162 and 18 g/mol, respectively and 162 g/mol × (0.015/18 g/mol) ≈ 1/8 = 1/2 × 25%). The water adsorbed in this step is tightly bound.[21] At moisture contents exceeding ∼1.5 wt %, it is still energetically favorable for the water molecules to bind to the 6-OH groups. Hence, during the adsorption process above ∼1.5 wt % moisture content, the tightly bond water molecules present in the structure have to let go of one of the hydrogen bonds to leave room for the incoming water molecules to attach to a 6-OH group. At ∼3 wt % moisture, each water molecule is attached to the cellulose chain by only one hydrogen bond, and is thus less tightly bond than in the initial step. On adding further moisture to the MCC structure, polymer−polymer hydrogen bonds in the cellulose may be broken to make more primary binding sites available. Water may also attach to the water molecules already bound to the cellulose by dipole attraction or by weak hydrogen bonds.[21] At humidities higher than ∼60% RH (∼6 wt % moisture) water can also bind to other water molecules, including those not bound to primary sites,[22] and, thus, form a weakly bound bulk liquid phase.

Interpreting the results in Figures 2 and 3 with an exponential model may seem logical because of the straight lines the conductivity curve seems to produce when plotted vs moisture content on a log−lin scale. Simula et al.[4] made an attempt to explain this presumed exponential increase in conductivity by a model where the number of water molecules per hydroxyl group on the cellulose fibers was Poisson distributed and where

the conductivity was linearly increasing with the number of occupied hydroxyl groups. Just like Murphy,[8] they also assumed that the water molecules create a transport path on which charged impurities, such as Na^+ and K^+, present in the cellulose can travel. This model does not, however, explain the leveling off in the log–lin plot of the conductivity vs moisture content, as observed in our Figure 3 for MCC and in earlier measurements on cotton cellulose paper.[6] Sapieha et al.,[6] who also presented an exponential model for the increase in cellulose conductivity, explained the deviation from a pure exponential behavior above moisture contents of ~3 wt % by the fact that structural changes in cellulose may take place at moisture contents higher than those at which structural bonding of water to the cellulose takes place (i.e. when water is relatively tightly bond to the cellulose).

Below we will argue against the exponential model, which seems difficult to find backing for on a microscopic charge transport basis, and instead give some support to the power-law model initially introduced by Murphy.[8] However, we will show that Murphy's quite unrealistic[4] explanation to the power-law model—involving a distribution of impurity-cation-generating sites at every ninth cellulose monomer (assumed to explain the form of eq 1[8])—is not essential for the validity of the power-law model, and that, instead, a percolation behavior[23] in the transport mechanism of protons and/or impurity cations may explain the observed increase in conductivity with moisture content.

From the above referred work of Khan and Pilpel[21] it is clear that, at cellulose moisture contents of ~3 wt %, every available 6-OH group in the MCC is occupied by one water molecule. Thus, 3 wt % of moisture can be interpreted as the amount required for monolayer coverage of the cellulose fiber surfaces in accordance with the classical BET theory.[24] The recently published[20] value of 117 m² water molecules/g of MCC needed for monolayer coverage in MCC, in fact, almost exactly corresponds to 3 wt % of moisture in the MCC structure. From Figure 4, it is evident that the average charge carrier mobility initially decreases by 2–3 orders in magnitude with increasing humidity and reaches a minimum around 37% RH. This RH value corresponds to a moisture content slightly larger than 3 wt % according to the inset in Figure 2. A decrease in ion mobility is to be expected as sites available for ion transport are progressively being more occupied and, thus, blocked for carrier ions to jump to. Hence, it lies near at hand to draw the conclusion that the observed decrease in mobility stems from the fact that hydronium ions (H_3O^+), at least to some extent, contribute to the measured conductivity.

Analyzing the number of charge carriers participating in the conduction process as a function of moisture content in further detail in Figure 6, it is obvious that n initially increases 5–6 orders in magnitude according to a power-law (solid line) with an exponent as high as 16.7, while at monolayer coverage a transition to a linear increase (dashed line in inset) takes place. According to percolation theory[23] this behavior can be interpreted as follows: For values of n lower than the ~3 wt % of moisture, signifying monolayer coverage, the power-law rise in the number of charge carriers participating in the conduction process can be explained by the fact that an increasing moisture content increases the number of connected conduction paths on which the charge carriers can move through the entire sample. Above monolayer coverage, all the conduction paths are connected and a transition from the power-law increase to a linear effective medium theory increase is to be expected.[25] According to the standard theory of transport in isotropic
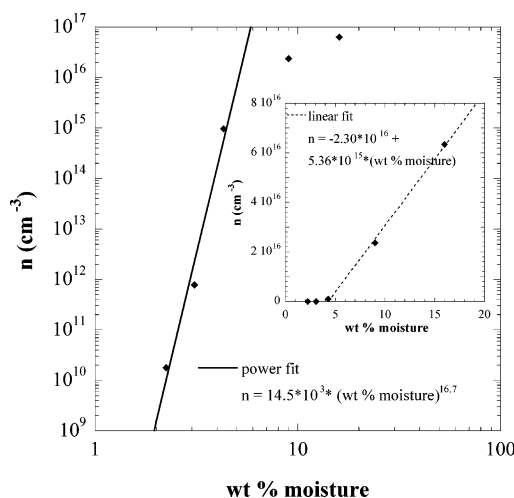

Figure 6. The number of charge carriers in Figure 5 fitted to a power-law (full line) with an exponent of 16.7 for low moisture contents (log–log scale). The inset shows a linear fit (dashed line) to the data for higher moisture contents (lin–lin scale).

percolating materials, the power-law exponent takes on values around 2.0 for three-dimensional systems.[23,26] However, exponents of the order of 10 have been observed earlier for conduction processes in polymer systems.[27] The reasons for this lack of universality in the power-law exponents are probably many. Tunneling conductivity between nonstructural spherical particles or sites separated by a distance much larger than their radius[28] may be one explanation. Another is anisotropy in the inter grain conductance.[29] Taking that the transport process in MCC occurs by ion jumping between neighboring 6-OH sites, the relatively large distance between the 6-OH sites on the cellulose chain may support the first explanation while the anisotropic nature of the long cellulose fibers may support the second. For completeness it is appropriate to mention that, while the observed power-law increase in n has an exponent of ~16, the conductivity in our Figure 3 initially increases with a power-law exponent of ~9 as previously observed by Murphy.[8] Hence, the Murphy exponent is a result of an extremely rapid increase in number of charge carriers and a more moderate decrease in their average mobility as a function of MCC moisture content.

Impurity cations, such as Na^+ and K^+, present in the MCC, show rather strong electrostatic interactions with water molecules.[7,30] Thus, when a water molecule is adsorbed on cellulose in the vicinity of an impurity, this impurity may trigger the water molecule to dissociate into an OH^- ion, which is strongly attracted to the impurity cation, and a proton, which is left free to move to the closest adsorbed water molecule in order to form a hydronium ion (H_3O^+). On a strict chemical basis, water dissociates into OH^- and H_3O^+ (not into OH^- ions and protons). However, the ion conduction in a water phase can be viewed as protons jumping from H_2O to H_2O instead of the large H_3O^+ ion moving.[7] For the conduction process in a water phase to proceed like this, a connected path of H_2O molecules is needed. Thus, to be able to measure a dc conductivity below monolayer coverage, as was done in our TC measurements, some movement of H_3O^+ between adjacent 6-OH groups must probably take place. Under the action of an applied field a proton will, hence, be able to jump between neighboring adsorbed water molecules provided they create a continuous conduction path, i.e., when all the 6-OH groups on its way between the electrodes are occupied. In addition to this, the impurity ion itself may also participate in the conduction process—as suggested in earlier work[4,6,8]—in a manner similar to that of the proton if it can

Humid Microcrystalline Cellulose Tablets

J. Phys. Chem. B, Vol. 109, No. 12, 2005 **5455**

dissociate from the OH^-. If this is the case, the nature of the suggested transport process is such that the number of impurity ions and protons participating in the conduction is very similar. The explanation to our observation of two exponentially decaying regions in the TC measurements[3] may, thus, not necessarily be explained by protons and OH^- carrying the current, but maybe preferably by the movement of similar numbers of protons and impurity cations.

5. Summary and Conclusion

Summarizing, the behavior of the charge carrier concentration n indicates that the conduction process, by protons and/or impurity cations, takes place on a percolating network of water molecules adsorbed to 6-OH units on the cellulose chain. The extent of these sites and the distance between them are such that a tunneling transport mechanism[28] may be needed in order to explain the large power-law exponent describing the conduction process at low moisture contents. The large exponent could alternatively, or additionally, be described by the strong anisotropy of the cellulose fibers.[29]

The variation in the average carrier mobility with relative humidity, Figure 4, indicated that the sites available for transport of at least some of the charge carrying ions are progressively being blocked as the moisture content increases up to the value signifying monolayer coverage. This shows that the above-presented model—in which an increasing moisture content causes more and more percolation paths to be created for the transport of protons and/or impurity ions—cannot alone explain the conduction mechanism in humid cellulose. Below monolayer coverage, when a water molecule is sitting at the end of a conduction path that is not spanning through the whole sample, a H_3O^+ ion is created when a proton ends it journey at that water molecule. The most favorable way to continue the conduction process from this point on may be for the H_3O^+ ion to move to the adjacent available 6-OH group. The more water molecules that are adsorbed, the less probable is this process because of the increasing occupancy of the 6-OH sites, something that leads to the observed decrease in the average carrier mobility. Above monolayer coverage, all available 6-OH groups are occupied and connected paths of H_2O molecules span through the entire sample. The observed increase in average mobility with increasing moisture content probably has its explanation in the structural changes that take place at high humidities.

To conclude, this paper demonstrates the importance of analyzing not only the conductivity but also its constituent parameters in order to obtain in-depth information about charge transport phenomena. The results presented in this paper may be used for understanding transport processes of other types of ions in celluloses than the ones investigated here, like e.g. various kinds of charged drug molecules. We also believe that the combined LFDS and TC analysis performed in this paper may prove useful for characterizing electrical properties of a wide range of polymers in addition to cellulose.

References and Notes

(1) Alderborn, G.; *Tablets and Compaction*; Churchill Livingstone: New York, 2002.

(2) Brohede, U.; Frenning, G.; Strømme, M. *J. Pharm. Sci.* **2004**, *93*, 1796−1803.

(3) Nilsson, M.; Alderborn, G.; Strømme, M. *Chem. Phys.* **2003**, *295*, 159−165.

(4) Simula, S.; Niskanen, K. *Nord. Pulp Pap. Res. J.* **1999**, *14*, 243−246.

(5) Ek, R.; Hill, R. M.; Newton, J. M. *J. Mater. Sci.* **1997**, *32,* 4807−4814.

(6) Sapieha, S.; Inoue, M.; Lepoutre, P. *J. Appl. Polym. Sci.* **1985**, *30*, 1257−1266.

(7) Pethig, R. *Dielectric and Electronic Properties of Biological Materials*; Wiley: Chichester, UK, 1979.

(8) Murphy, E. J. *J. Phys. Chem. Solids* **1960**, *16*, 115−122.

(9) Kothari, S. H.; Kumar, V.; Banker, G. S. *Int. J. Pharm.* **2002**, *232*, 69−80.

(10) Kumar, V.; de la Luz Reus-Medina, M.; Yang, D. *Int. J. Pharm.* **2002**, *235*, 129−140.

(11) Ek, R.; Alderborn G.; Nyström, C. *Int. J. Pharm.* **1994**, *111*, 43−50.

(12) Hägerström, H.; Edsman, K.; Strømme, M. *J. Pharm. Sci.* **2003**, *92*, 1869−1881.

(13) Josefowicz, J. Y.; Anczurowski, E.; Jones, A. Y.; Deslandes, Y. *Rev. Sci. Instrum.* **1981**, *52* (6), 926−932.

(14) Bauer-Brandl, A. D.; Craig, D. Q. M.; Newton, J. M. *Powder Technol.* **1992**, *73*, 91−92.

(15) Jonscher, A. K. *Dielectric relaxations in solids*; Chelsea Dielectric Press: London, 1983.

(16) Strømme Mattsson, M.; Niklasson, G. A. *J. Appl. Phys.* **1999**, *85*, 8199−8204.

(17) Schütt, H. J.; Gerdes, E. *J. Non-Cryst. Solids* **1992**, *144*, 1−13.

(18) Bates, J. B.; Chu, Y. T.; Stribling, W. T. *Phys. Rev. Lett.* **1988**, *60*, 627−630.

(19) Watanabe, M.; Rikukawa, M.; Sanui, K.; Ogata, N. *J. Appl. Phys.* **1985**, *58*, 736−740.

(20) Mihranyan, A.; Llagostera, A. P.; Karmhag, R.; Strømme, M.; Ek, R. *Int. J. Pharm.* **2004**, *269*, 433−442.

(21) Khan, F.; Pilpel, N. *Powder Technol.* **1987**, *50*, 237−241.

(22) Zografi, G.; Kontny, M. *J. Pharm. Res.* **1986**, *3*, 187−194.

(23) Stauffer, D.; Aharony, A. *Introduction to Percolation Theory*, 2nd ed.; Taylor & Francis: London, UK, 1992.

(24) Brunauer, S.; Emmet, P. H.; Teller, E. *J. Am. Chem. Soc.* **1938**, *60*, 309−319.

(25) Kirkpatrick, S. *Rev. Mod. Phys.* **1973**, *45*, 574−588.

(26) Sahimi, M.; *Heterogeneous Materials I*: *Linear Transport and Optical Properties*; Springer: New York, 2003.

(27) Soares, B. G.; Gamboa, K. M. N.; Ferreira, A. J. B.; Ueti, E.; Camargo, S. S., Jr. *J. Appl. Polym. Sci.* **1998**, *69*, 825−833.

(28) Balberg, I. *Phys. Rev. Lett.* **1987**, *59*, 1305−1308.

(29) Wu, J.; McLachlan, D. S. *Phys. Rev. B* **1997**, *56*, 1236−1248.

(30) Gurney, R. W. *Ionic Processes in Solution*; McGraw-Hill: New York, 1953.