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Halloysite Nanotubes as Active Modulators for Tunable Charge Transport in PEDOT:PSS

Luigi Fabiano¹  | Giuseppe Cinà²  | Rosalinda Sciacca¹  | Alessandra Armeli³  | Marina Massaro⁴  | Rita Sánchez-Espejo⁵  | Giovanna Calabrese³  | Grazia Maria Lucia Messina¹  | Giovanni Marletta¹ | Serena Riela² 

¹Laboratory for Molecular Surfaces and Nanotechnology (LAMSUN), Department of Chemical Sciences, University of Catania and CSGI, Catania, Italy |

²Department of Chemical Sciences, University of Catania, Catania, Italy | ³Department of Chemical, Biological, Pharmaceutical and Environmental Sciences (ChiBioFarAm), University of Messina, Messina, Italy | ⁴Department of Biological, Chemical and Pharmaceutical Sciences and Technologies (STEBICEF), University of Palermo, Palermo, Italy | ⁵Department of Pharmacy and Pharmaceutical Technology, Faculty of Pharmacy, University of Granada, Campus Universitario de Cartuja, Granada, Spain

Correspondence: Grazia Maria Lucia Messina (gml.messina@unict.it)

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ABSTRACT

Halloysite nanotubes (HNTs) are investigated as functionally active nanofillers for tuning PEDOT:PSS thin films. HNTs from Dragon Mine (DG, USA) and Matauri Bay (NZ, New Zealand), characterized by different aspect ratios and surface chemical characteristics, are incorporated at 1.0–7.5 wt.% without secondary dopants to highlight specific HNT-related interfacial effects. A non-monotonic dependence of local conductance on DG content is observed, with a maximum at low loading (2.5 wt.%). This trend reflects the balance between enhanced connectivity of PEDOT-rich domains at low concentrations and disruption of conductive pathways due to nanotube aggregation at higher loadings. It is suggested that DG acts as an active modulator, promoting polymer chain reorganization and enabling a denser hopping network, thereby enhancing local electrical response and mechanical stiffness. In contrast, NZ behaves as a passive filler, preserving the intrinsic ion-storage capability of PEDOT:PSS without improving charge transport, highlighting the dominant role of interfacial electrostatic interactions. Electrochemical analysis shows that DG favors electronic transport at the expense of ionic accumulation, whereas NZ maintains capacitive behavior. The nanocomposites exhibit good biocompatibility, with improved SH-SY5Y cell viability at low DG loading. These results provide design guidelines for independently tuning electrical, electrochemical, and mechanical properties in conductive polymer nanocomposites.

1 | Introduction

Conductive polymers have emerged as key materials in bioelectronics [1] owing to their unique ability to combine electronic conductivity with mechanical flexibility, chemical tunability, and biocompatibility, thereby enabling efficient signal transduction

at the interface with living cells and tissues [2, 3]. Within this context, conductive polymer nanocomposites represent complex multicomponent systems in which electrical [4], mechanical [5], and electrochemical properties [6] arise from the intricate interplay among molecular organization [7], interfacial electrostatic interactions [8, 9], and mesoscale morphology [10].

Luigi Fabiano and Giuseppe Cinà contributed equally to this work.

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In intrinsically conductive polymers, charge transport is strongly affected by structural heterogeneity [8], phase separation phenomena [11], and the degree of connectivity between ordered domains [12], all of which determine the formation of effective percolation pathways. In this broader framework, poly(3,4-ethylenedioxythiophene):poly(styrenesulfonate) (PEDOT:PSS) stands as a representative example, clearly illustrating how nanoscale organization governs macroscopic electrical behavior [13].

PEDOT:PSS is a prototypical biphasic system consisting of conductive PEDOT-rich domains dispersed within a PSS-rich matrix. Its electrical conductivity depends on the degree of phase separation, chain conformation, and interchain π - π stacking interactions. Subtle modifications in morphology or interfacial chemistry can induce significant variations in charge carrier mobility and electrochemical response [14, 15].

The incorporation of nanoscale, organic or inorganic, fillers into conductive polymers is a widely employed strategy to improve their physicochemical performance [6, 7]. Conductive nanofillers such as carbon nanotubes and metal nanoparticles have been extensively investigated due to their ability to enhance electrical properties through the formation of conductive pathways and interfacial interactions with the polymer matrix [16–18]. Such approaches have led to significant improvements in electrical performance and have enabled the development of advanced materials for applications requiring high conductivity and biocompatibility [13, 19, 20].

However, recent studies have highlighted that enhancements in PEDOT:PSS-based systems are not exclusively associated with intrinsically conductive fillers. At the nanoscale, electrically insulating nanostructures can also play an active role by inducing structural and interfacial rearrangements within the conductive polymer matrix. In these systems, the filler does not directly contribute to charge transport, but instead modulates polymer chain organization, phase separation, and the connectivity of conductive domains [21], which are known to govern charge transport in PEDOT:PSS [22, 23].

In this context, among various inorganic nanofillers used to tailor both mechanical and electrical properties, halloysite, a naturally occurring aluminosilicate clay mineral belonging to the Kaolin group, represents a particularly attractive class of materials due to its abundance, low cost, and versatile physicochemical properties [24]. Notably, halloysite predominantly occurs in the form of nanotubular structures, commonly referred to as halloysite nanotubes (HNTs), which exhibit a characteristic hollow tubular morphology [25]. HNTs are naturally sourced from different deposits (e.g., New Zealand, USA, China, Brazil, Turkey), and their dimensions are strongly dependent on both the extraction site and purification process; however, different studies have shown that HNTs coming from the same sites (available in tons) possess the same properties and chemical compositions [24]. In general, the distinct chemical composition of the inner and outer surfaces results in the tubes exhibiting opposite surface charges over a wide range of pH values [26]. Based on these findings, HNTs can interact with polymeric matrices through different mechanisms, including electrostatic attraction and hydrogen bonding, thereby enabling the development of nanocomposites

with enhanced and tunable properties. In addition, owing to their high biocompatible and intrinsic ability to cross cellular membranes, the use of HNTs as filler holds significant potential for a variety of biomedical applications [27, 28].

For example, Chen et al. reported the use of HNTs as a template for the chemical oxidative polymerization of EDOT on their external surface [29]. In this case, the authors find that the hydroxyl groups at the HNTs external surface can form hydrogen bonding interactions with the oxygen atoms of EDOT monomer, which polymerizes, after addition of ammonium persulphate, exclusively on the tube surface rather than in solution. The presence of HNTs as a template led to the synthesis of a composite with enhanced electrochemical performance than pure PEDOT. Conversely, Hu et al. studied the influence of the introduction of HNTs into a PEDOT:PSS dispersion to prepare PEDOT:PSS/HNTs composite films [30]. The authors reported that the aqueous PEDOT:PSS dispersion can be loaded into HNTs lumen for hydrophobic effects, forming composite films with higher conductivity than pristine polymer films, but these effects have generally been observed in presence of secondary dopants, which play a significant role in enhancing conductivity [31–33]. Another work reports the covalent grafting of PSS onto HNTs external surface of HNTs, and the filler so obtained was used as a template for the EDOT polymerization [34]. All the aforementioned examples demonstrate that the incorporation of HNTs influences the organization of polymer domains and the formation of charge transport pathways, thereby affecting the overall structural and functional properties of the composite systems, especially when conductivity is a key requirement. As previously noted, HNTs from different deposits may exhibit variations in size and chemical composition, therefore, it is of interest to investigate how these differences influence the organization of PEDOT:PSS. To date, to the best of our knowledge, the impact of nanotube-induced microstructural rearrangements on charge transport mechanisms and electrochemical stability has not been comprehensively explored.

In this study, we present a systematic analysis of PEDOT:PSS/HNTs nanocomposite thin films with HNTs content of 0.0, 1.0, 2.5, 5.0 and 7.5 wt.%, using nanotubes from two distinct sources: commercial HNTs Dragon Mine (USA), hereafter referred to as DG, and Matauri Bay (New Zealand), hereafter referred to as NZ, which differ in size distribution and surface chemical composition [35]. Importantly, no secondary dopants were added, ensuring that any observed variations in conductivity, mechanical performance, and electrochemical behavior arise solely from the nanotubes and their interfacial characteristics.

Our findings reveal that both the surface chemistry and dimensional properties of HNTs critically influence charge transport, mechanical response, and electrochemical stability. By correlating morphological features to electrical, mechanical, and electrochemical performance, we identify the structure-property relationships that govern the multifunctional behavior of these sustainable 2D-clay nanostructures, highlighting their potential for flexible electronic and electrochemical applications.

Finally, as a proof of concept for potential biomedical application, biological assays were conducted on the human neuroblastoma

cell line SH-SY5Y to assess biocompatibility. PEDOT:PSS-based polymers, due to their unique properties and inherent biocompatibility, have demonstrated promise for applications in the treatment of neuronal injuries [32].

2 | Results and Discussion

2.1 | Morphology and Nanomechanical Properties of PEDOT:PSS/DG Films

The PEDOT:PSS/HNTs composite films were prepared following the procedure described in the [Experimental Section](#) (see Section 4.3). Based on the physicochemical properties of both PEDOT:PSS and halloysite nanotubes (HNTs), [35] several interfacial interactions are expected to occur within the composite. In particular, electrostatic attractions can arise from the complementary charge distribution of the two components. The negatively charged PSS chains can interact with the positively charged inner lumen of the HNTs, whereas the positively charged PEDOT chains can establish favorable interactions with the negatively charged external siloxane surface of the nanotubes. These interactions are consistent with the charge distribution of halloysite at neutral pH, where the inner aluminol groups are protonated, and the outer siloxane surface remains negatively charged [26]. In addition to electrostatic interactions, PEDOT may also interact with the external surface of HNTs through hydrogen bonding, acting as a hydrogen bond acceptor, while the silanol groups present on the HNTs surface, particularly as structural defect sites, can serve as hydrogen bond donors.

Since the extent of these interfacial interactions may also depend on the morphological characteristics of the nanotubes, the influence of halloysite morphology, with particular emphasis on nanotube size, was further investigated. To this end, transmission electron microscopy (TEM) analyses were performed to determine the average length of the two halloysite nanotube samples, DG and NZ.

The measurements (Figure 1) revealed a clear difference between the two materials: DG exhibited an average length of 408 ± 142 nm and a diameter of 51 ± 7 nm, whereas NZ showed a significantly greater mean length of 1296 ± 470 nm while maintaining a comparable diameter of 51 ± 8 nm. These results highlight the distinct dimensional characteristics of the two halloysites, which are consistent with their differing aspect ratios, respectively 8 for DG and 25 for NZ.

First, the effect of HNTs on the morphological and mechanical properties of PEDOT:PSS composite films, was investigated at varying HNTs loading.

The surface morphology of the PEDOT:PSS-based thin films, was investigated by Atomic Force Microscopy (AFM). Figure 2 shows the topographical images of the polymer nanocomposite films containing different DG loadings: 0.0 (a), 1.0 (b), 2.5 (c), 5.0 (d) and 7.5 wt.% (e).

The bare PEDOT:PSS film (0.0 wt.% DG, Figure 2a) exhibits a smooth, homogeneous, and uniform surface, characterized by low roughness and the absence of surface defects. This

morphology is consistent with the good film-forming capability of PEDOT:PSS and indicates a continuous and uniform polymer matrix.

Upon incorporation of DG, the composite films maintain an overall uniform coverage of the surface; however, distinct nanostructured features become visible. At low DG contents (1.0 wt.%, Figure 2b and 2.5 wt.%, Figure 2c), the nanotubes appear sparsely and randomly distributed across the scanned area, with only limited aggregation, particularly at the lower loading. At 1.0 wt.%, the nanotube density appears insufficient to ensure effective connectivity. Nevertheless, the thin film remains relatively homogeneous, suggesting that the nanotubes are well embedded within the polymer matrix. As the DG concentration increases to 5.0 wt.% (Figure 2d) and 7.5 wt.% (Figure 2e), the surface density of the nanotubes progressively rises. At these higher loadings, the tendency of DG to aggregate becomes more pronounced, resulting in the formation of clustered domains and a more disordered morphology. This behavior is likely due to stronger nanotube-nanotube interactions at elevated concentrations, which partially overcome polymer-nanotube interfacial interactions.

A more detailed analysis is provided in Figure 2f, which displays a magnified topographic image of the PEDOT:PSS/DG 2.5 wt.% sample. The high-resolution image clearly reveals the characteristic tubular morphology of the halloysite nanotubes and their spatial distribution within the matrix. Furthermore, the phase image (Figure 2g) indicates that the PEDOT:PSS matrix uniformly coats and fully envelops the DG, confirming strong interfacial interaction and effective encapsulation of the clay by the polymer. This complete embedding suggests good compatibility between the two components and supports the formation of a structurally integrated composite system. At higher DG concentrations, the inter-nanotube aggregation becomes more pronounced, limiting the polymer's ability to effectively wrap around the nanotubes.

Overall, the AFM analysis demonstrates that DG incorporation modifies the surface morphology of the composite films in a concentration-dependent manner, reflecting the nanotube dispersion, aggregation behavior, and surface roughness, while preserving the structural continuity of the polymer matrix at low filler loadings.

To evaluate the suitability of the composite films for flexible electronics and wearable devices, where they are typically subjected to mechanical stresses such as bending and stretching, the local Young's modulus (E) and the related mechanical properties were measured with nanometer-scale spatial resolution [42].

The elastic modulus values were obtained using the Derjaguin–Muller–Toporov (DMT) mechanics model (see Section 4.4.2). Figure 3a shows the E values obtained for the different composite formulations, highlighting a clear and nearly linear increase in film stiffness with increasing DG content. This trend confirms the expected reinforcing effect of halloysite nanotubes within the PEDOT:PSS matrix, as the inorganic nanofiller is supposed to contribute to decrease polymer chain mobility. The progressive stiffening of the films is consistent with the morphological observations, where higher clay concentrations promote the formation of a more rigid interconnected polymer network.

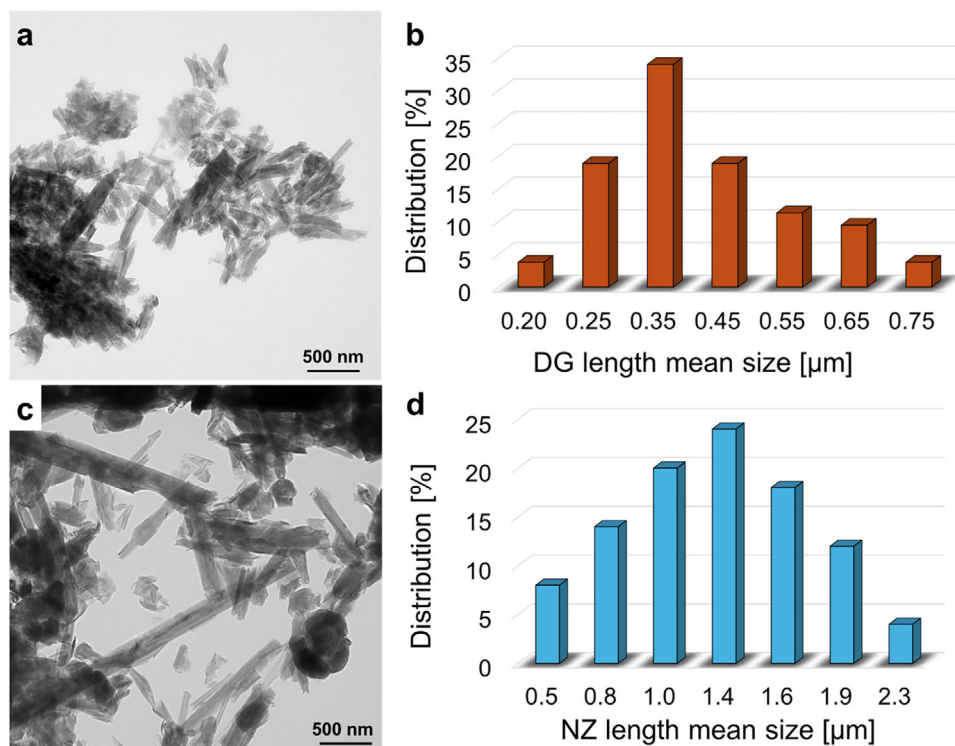


FIGURE 1 | (a,b) TEM images and (b,d) statistical length distribution ($n = 40$) for (a-b) DG and (c-d) NZ nanomaterials.

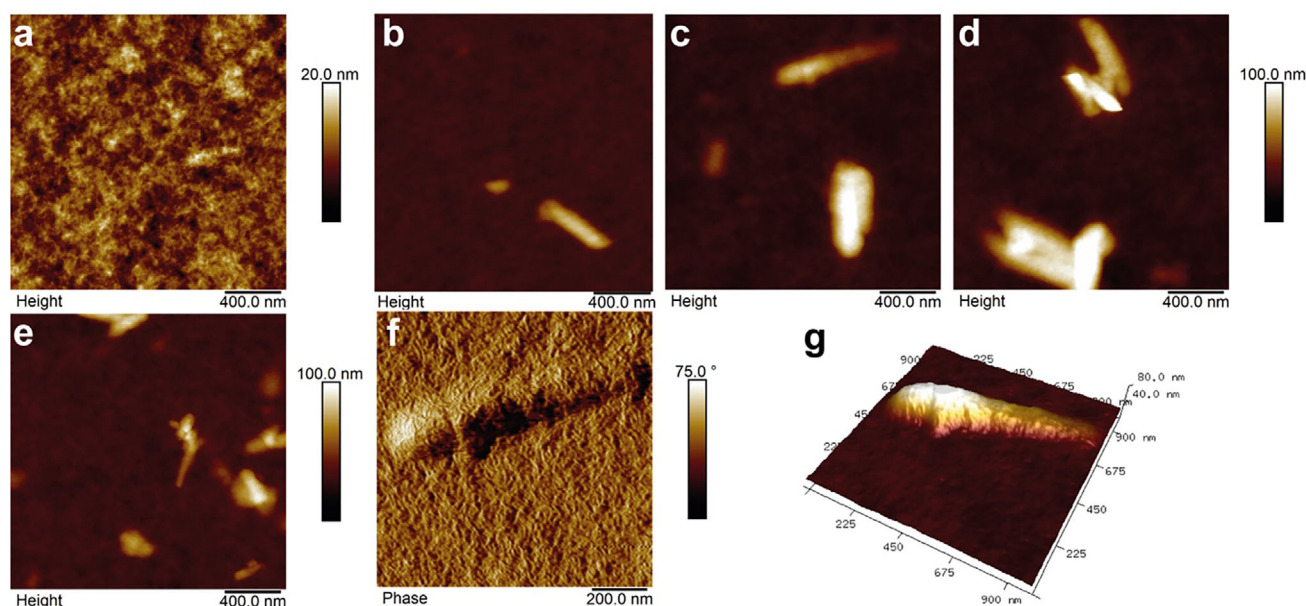


FIGURE 2 | Atomic force microscopy images of: bare PEDOT:PSS (a) PEDOT:PSS/DG 1.0 wt.% (b), PEDOT:PSS/DG 2.5 wt.% (c), PEDOT:PSS/DG 5.0 wt.% (d) PEDOT:PSS/DG 7.5 wt.% (e), scan size $2 \times 2 \mu\text{m}^2$. Magnification of PEDOT:PSS/DG 2.5 wt.% phase image (f); 3D height micrograph of PEDOT:PSS/DG 2.5 wt.% (g), scan size $1 \times 1 \mu\text{m}^2$.

A further relevant aspect concerns the statistical distribution of the Young's modulus values (Figure S2). Indeed, as the DG content increases, the distribution evolves from a lognormal profile, typical of heterogeneous polymeric systems, to a normal (Gaussian) distribution at the highest loading (7.5 wt.%), due to a more homogeneous mechanical response at elevated clay concen-

trations, possibly ascribable to a more uniform distribution and increased interfacial interactions between the polymer matrix and the nanotubes.

The average Young's modulus values for all samples are summarized in Table 1. Overall, the FS-AFM results demonstrate that

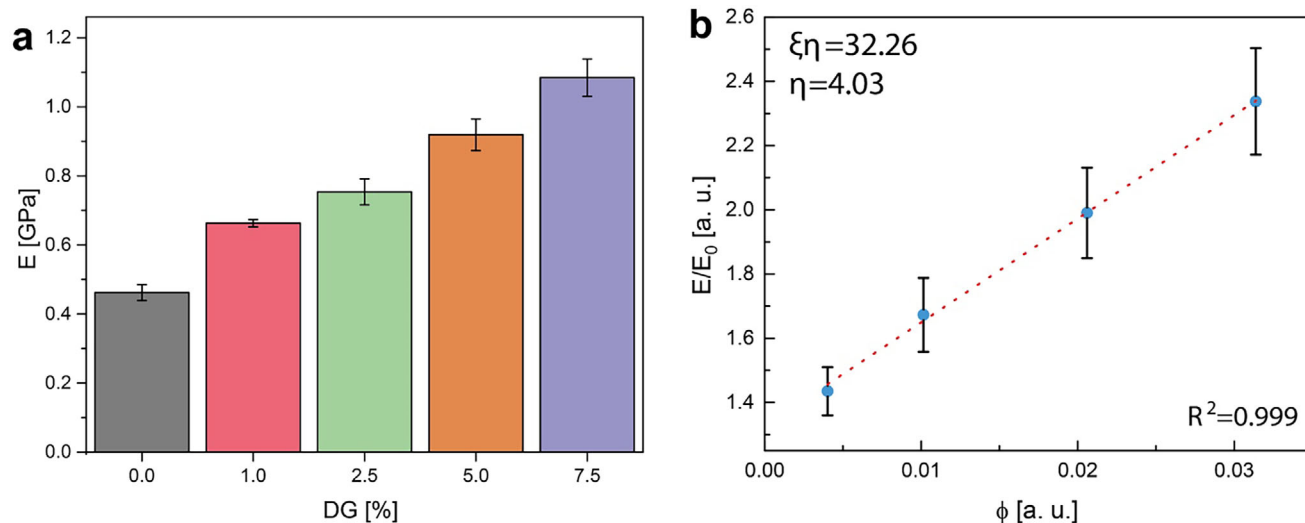


FIGURE 3 | Young Modulus (mean value $\pm$ st. dev., $n = 3$) values of thin films deposited on Si (a). Halpin-Tsai fitting of such films E normalized to PEDOT:PSS (DG 0.0 wt.%) (b).

TABLE 1 | Young Modulus (E) and Conductance (G) values for pristine PEDOT:PSS and composited with DG.

Sample	E [MPa]	E/E_0	G [nS]	G/G_0
PEDOT:PSS	462.02 ± 23.10	/	238.68 ± 1.19	/
1.0 wt.% DG	663.13 ± 10.39	1.44 ± 0.08	272.78 ± 1.38	1.14 ± 0.01
2.5 wt.% DG	753.78 ± 37.69	1.67 ± 0.12	296.75 ± 2.19	1.24 ± 0.01
5.0 wt.% DG	919.29 ± 45.96	1.99 ± 0.14	259.01 ± 9.99	1.09 ± 0.04
7.5 wt.% DG	1084.41 ± 54.20	2.34 ± 0.17	143.14 ± 6.57	0.6 ± 0.03

DG incorporation enhances the stiffness of the composite films and influences the mechanical uniformity of the material in a concentration-dependent manner.

The mechanical reinforcement of PEDOT:PSS nanocomposite films incorporating halloysite nanotubes was analyzed using the Halpin-Tsai model [36, 37] (Figure 3b), which is widely applied to predict the elastic modulus of polymer composites containing anisotropic fillers. According to this model (Equation 1):

$$\frac{E}{E_0} = \frac{1 + \xi\eta\phi}{1 - \eta\phi} \approx 1 + \xi\eta\phi \quad (1)$$

where E is the Young modulus of the nanocomposite, E_0 is the modulus of pristine PEDOT:PSS, ξ is the shape factor related to the filler aspect ratio, η is the geometry efficiency parameter, and ϕ is the filler volume fraction.

For the fitting procedure, the shape factor (ξ) was fixed at 8, a suitable value derived from the standard aspect ratio of halloysite nanotubes (average length $\approx 408 \pm 142$ nm and diameter $\approx 51 \pm 7$ nm). The densities of the polymer matrix and the filler (ρ_m , ρ_f) were set to 1.01 and 2.53 g/mL, respectively, according to supplier specifications. The fitting process yielded a combined parameter $\xi\eta$ value of 32.26, corresponding to an apparent reinforcement efficiency factor (η) of 4.03. This result confirms that HNTs play a significant role in reinforcing the compos-

ite. In particular, the relatively high η value suggests efficient stress transfer between the polymer matrix and the nanotube, confirming that their elongated tubular morphology strongly enhances the stiffening effect. In other words, the aspect ratio of the DG is a key parameter governing their reinforcing capability. The model shows excellent agreement with the experimental data ($R^2 = 0.9997$). This strong correlation is likely due to the relatively low filler concentrations investigated, where the main assumptions of Halpin-Tsai model, good dispersion of the filler, minimal filler-filler interactions, and effective load transfer at the interface, are more likely to be satisfied. Overall, the fitted η value supports the hypothesis that, within this concentration range, the halloysite nanotubes are well embedded in the polymer matrix and actively contribute to load bearing. Moreover, the tubular geometry of HNTs appears to amplify their reinforcing effect compared to fillers with lower aspect ratio, such as spherical or irregular particles. These findings highlight the critical role of filler geometry and orientation in optimizing stress transfer and mechanical performance in polymer nanocomposites [36–39].

2.2 | Local Electrical Characterization by Conductive AFM

The electrical conductivity can be characterized by several established macroscopic techniques, such as the collinear four-point probe and the van der Pauw configuration, which provide

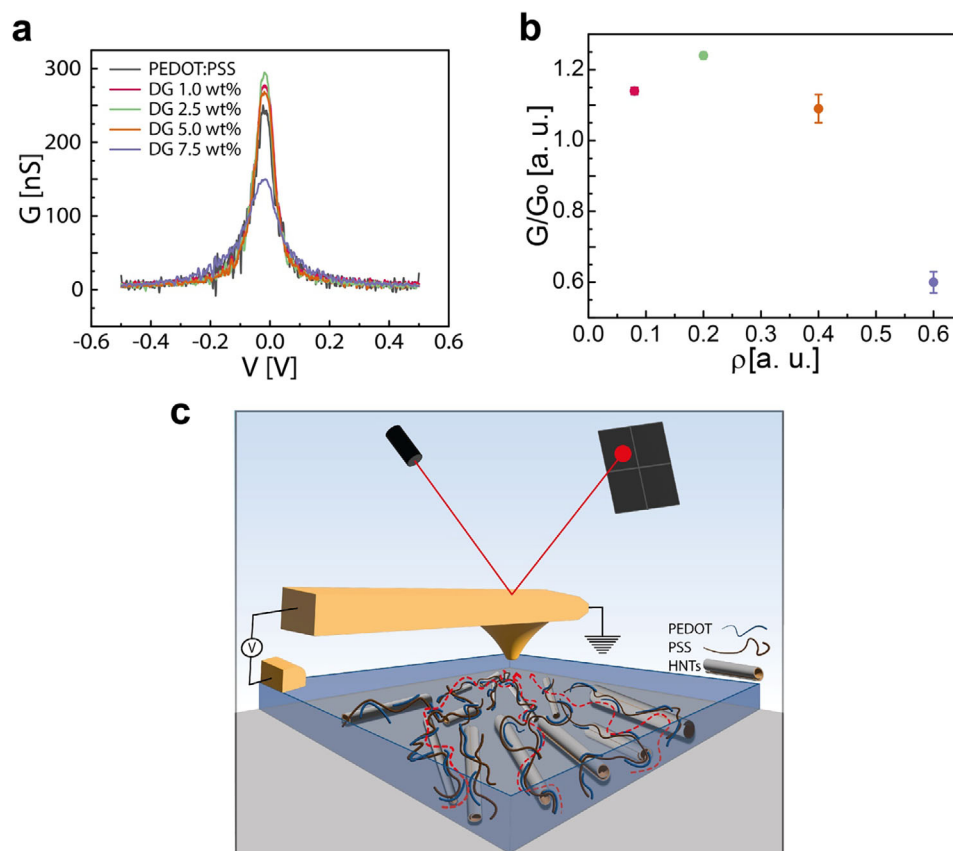


FIGURE 4 | G-V characteristics (a) of PEDOT:PSS/HNTs thin films on Si; (b) $G_{rel} = G/G_0$ plotted as a function of the parameter $\rho = w \cdot AR$, where w is the filler mass fraction and $AR = L/d$ is the aspect ratio of the nanotubes. (c) Schematic representation showing the mechanism on which improvement of local conductivity is based. Figure S3 reports I - V characteristics in linear and semi-log scales.

reliable macroscopic measurements of sheet resistance and bulk conductivity.

In this work, however, current-voltage (I - V) measurements were performed using conductive Atomic Force Microscopy (C-AFM) in a two-electrode lateral (horizontal) configuration. This approach enables localized electrical characterization at the nanometer scale, prompting the evaluation of nanometric spatial variations in local conductance closely associated with the incorporation of nanotubes. By probing the nanocomposite thin films point by point, it is possible to correlate local electrical behavior with morphological features and to assess how the presence and the concentration-dependent distribution of DG affect charge transport within the composite matrix.

Unlike the gradual increase of stiffness with rising HNT content, the local conductance does not follow a monotonic trend; as shown in Figure 4a, it exhibits distinct changes at different HNT concentrations.

Indeed, PEDOT:PSS/DG films containing 1.0 wt.% HNTs exhibited a slight increase in local conductance compared to pristine PEDOT:PSS. Increasing the HNT content to 2.5 wt.% further enhanced the local conductance, reaching its maximum value. In contrast, a further increase in DG loading to 5.0 wt.% resulted in conductance values comparable to those of the unmodified film,

whereas at 7.5 wt.%, the local conductance decreased markedly (Table 1).

Overall, these results indicate that low DG loadings promote the electrical performance of PEDOT:PSS without disrupting its conductive network. Indeed, films containing 2.5 wt.% HNTs exhibit the highest normalized local conductance ($G_{rel} > 1$), whereas a progressive decrease is observed as the filler content increases from 2.5 to 7.5 wt.% (Figure 4a). At the highest loading, the local conductance falls below that of pristine PEDOT:PSS, indicating that the beneficial effect of the nanotubes is gradually outweighed by their insulating character.

Since DG nanotubes are electrically insulating, the parameter ρ (Figure 4b) does not describe an electrical percolation process. Rather, it represents the geometrical perturbation introduced by a quasi-one-dimensional insulating filler within the conductive PEDOT:PSS matrix. Similar geometrical descriptors have been widely used to describe transport in polymer nanocomposites containing high-aspect-ratio insulating fillers, where excluded-volume effects and increased tortuosity dominate over charge transport through the filler itself [40, 41]. Accordingly, the dependence of the normalized conductance on ρ highlights the key role of filler morphology in governing the local electrical response.

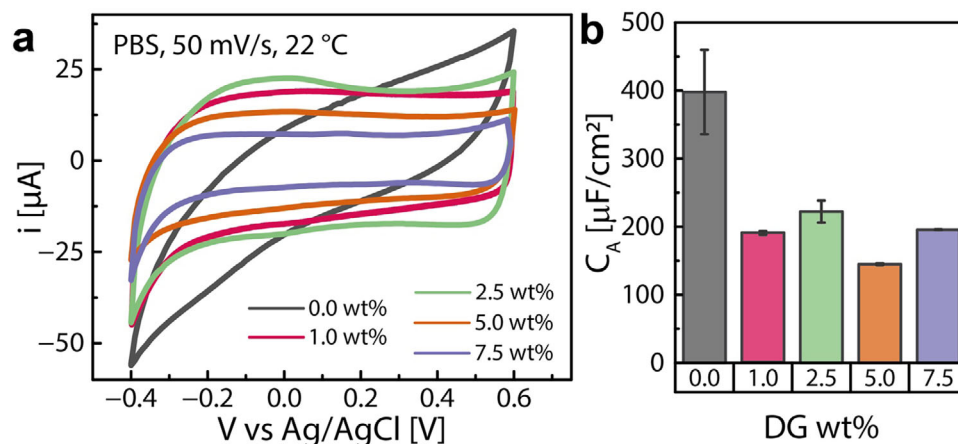


FIGURE 5 | PEDOT:PSS and its nanocomposites voltammograms (a) and capacitance values in PBS (b) with different percentages of DG; capacitance results reported as mean value $\pm$ st. deviation ($n \geq 3$).

The observed behavior can be rationalized considering the morphology of the PEDOT:PSS conductive network. The electrical conductivity of PEDOT is known to depend strongly on the nanoscale organization of PEDOT-rich domains, their connectivity, and the degree of phase separation from the insulating PSS matrix [42, 43]. Interfacial interactions and confinement effects can promote reorganization of these domains, producing significant variations in both local and macroscopic conductivity [44, 45].

At low DG concentrations, the nanotubes are well dispersed and remain below the effective percolation threshold of the insulating phase. Under these conditions, they do not interrupt the conductive pathways but instead promote a favorable reorganization of the polymer nanostructure. As the HNTs loading increases, the system gradually approaches and eventually exceeds a critical concentration at which the insulating filler begins to interfere with the percolative network of PEDOT-rich domains. At higher concentrations, the increased tendency of HNTs to aggregate further amplifies this effect by introducing physical barriers to charge transport and increasing carrier scattering. As a result, the conductive pathways become partially disrupted, leading to a reduction in the local conductance. In addition to this morphological effect, the distinct surface charges of HNTs are also expected to play an important role in determining the local electrical properties of PEDOT:PSS/HNTs composite film. The negatively charged polystyrene sulfonate (PSS^-) chains can preferentially interact with the positively charged inner lumen of nanotubes through electrostatic attraction. This interaction may weaken the Coulombic attraction between the positively charged PEDOT chains and the PSS counterions, thereby increasing the conformational freedom of the PEDOT-rich domains. At the same time, PEDOT chains may establish hydrogen bonding and electrostatic attraction interaction with the negatively charged external surface of the nanotubes. Together, these interactions can promote a transition of PEDOT chains from a compact coil conformation toward a more extended or quasi-linear structure. Such conformational rearrangement is widely recognized to enhance charge transport by promoting π - π stacking, improving interchain coupling, and facilitating charge-carrier delocalization along and between polymer chains. When combined with a homogeneous nanotube dispersion and the preservation of the

PEDOT percolation network, these effects provide a plausible explanation for the local conductance enhancement observed at moderate HNT loadings. However, as the nanotube concentration increases further, the insulating nature of HNTs and their increased aggregation progressively dominate the electrical response, disrupting the conductive network and ultimately leading to a decrease in conductivity, as previously reported in the literature [30].

2.3 | Electrochemical Capacitance

Finally, in view of their potential applications as active substrates in bioelectronics, cyclic voltammetry (CV) measurements were employed to provide deeper insight into the electrochemical response of the polymeric thin films.

By analyzing the shape of the voltammograms and the enclosed current–potential area, it is possible to estimate the capacitance and gain insight into the charge transfer and ion diffusion processes occurring within the film.

Figure 5 reports the histograms of the surface capacitance for PEDOT:PSS films containing different DG loadings, measured in phosphate-buffered saline (PBS), a physiologically relevant electrolyte commonly employed in biological applications. For all nanocomposite thin films, the capacitance values remain approximately about 200 $\mu\text{F}/\text{cm}^2$.

PEDOT:PSS is a mixed ionic–electronic conducting polymer composed of electronically conductive PEDOT-rich domains embedded within a PSS-rich phase that facilitates ionic transport. Unlike conventional capacitive materials, its electrochemical response is dominated by volumetric charging: electrolyte ions penetrate the polymer bulk and compensate the electronic charges along the PEDOT backbone. Consequently, charge storage arises from coupled ion–electron transport throughout the film rather than solely from double-layer formation at the electrode surface. The large number of internal interfaces between PEDOT-rich and PSS-rich domains provides an extensive area for ionic–electronic coupling, giving rise to the high capacitance of the material [15, 46].

TABLE 2 | Capacitance values of PEDOT:PSS and HNTs at different percentages in PBS, reported as mean value $\pm$ st. dev. (at least $n = 3$).

DG	C_A [$\mu\text{F cm}^{-2}$]
0.0 wt. %	397.73 ± 61.92
1.0 wt. %	194.64 ± 2.62
2.5 wt. %	222.21 ± 16.17
5.0 wt. %	144.88 ± 1.40
7.5 wt. %	195.58 ± 0.42

The incorporation of DG progressively decreases the surface capacitance compared with pristine PEDOT:PSS (Table 2). Although all cyclic voltammograms recorded in PBS exhibit similar features, increasing the nanotube content produces a gradual transition from a more resistive and asymmetric profile to a more rectangular and symmetric shape, characteristic of an ideal capacitive response. Despite this apparent improvement in the voltametric shape, the measured capacitance decreases, indicating that the presence of HNTs modifies the internal charge storage mechanism. As discussed in the local electrical characterization, the incorporation of HNTs induces morphological and conformational changes in the polymer matrix. These structural rearrangements may reduce the degree of phase segregation between PEDOT-rich and PSS-rich regions, resulting in fewer or less distinct internal interfaces. Because these interfaces serve as the primary sites for ion accumulation and charge compensation, their reduction decreases the effective area available for volumetric charge storage, ultimately leading to the observed decrease in capacitance.

This interpretation is consistent with the scan-rate analysis. The $\log(i) - \log(v)$ plots (Figure S4) yield b values close to 0.5 for all samples, indicating that charge storage remains predominantly diffusion-controlled and governed by ion transport within the polymer bulk rather than by surface-limited processes [47–49]. Therefore, the addition of DG does not alter the fundamental volumetric charging mechanism of PEDOT:PSS but instead modifies its nanostructure, reducing the effective ionic–electronic interfacial area responsible for charge storage.

2.4 | Effect of HNT on the Charge Transport in PEDOT:PSS System

To further verify the mechanism proposed to explain the improved electrical performance of the PEDOT:PSS/DG 2.5 wt. % nanocomposite, a comparative study was conducted using a different type of halloysite nanotube, namely the NZ variant. Unlike the commercial DG nanotubes, NZ exhibits a greater average length (i.e., higher aspect ratio) and a lower density of silanol groups at the interface.

A PEDOT:PSS/NZ 2.5 wt. % dispersion was prepared following the same procedure adopted for the DG-based composites and deposited by spin-coating to obtain films with comparable thickness and surface uniformity. Identical morphological, mechanical, and electrical characterizations were performed to

ensure a reliable and direct comparison between the two systems. The corresponding results are reported in Figure 6.

Morphological analysis clearly confirms the structural differences between the two halloysites samples, highlighting the significantly greater length of the NZ nanotubes. This morphological feature directly influences the mechanical properties of the composites. In particular, PEDOT:PSS/NZ nanocomposite exhibits a significantly higher Young's modulus than the corresponding DG-based composites, indicating that nanotubes with a higher aspect ratio provide more effective mechanical reinforcement within the polymer matrix.

The larger dimensions of the NZ nanotubes, however, are also expected to affect the organization of the conductive PEDOT network. At a fixed filler loading (2.5 wt. %), the higher aspect ratio of NZ results in a lower number density of dispersed nanotubes than in DG composites. Consequently, fewer but larger insulating objects are distributed throughout the polymer matrix, generating more extended geometrical constraints that locally interrupt the continuity of PEDOT-rich pathways and force charge carriers to follow more tortuous transport routes. Since electrical conduction in PEDOT relies on the connectivity of PEDOT-rich domains embedded within the insulating PSS matrix, these morphological perturbations can negatively affect charge transport [50].

Overall, these observations indicate that the electrical behavior of PEDOT:PSS/HNT composites is governed not by the intrinsic electrical properties of the filler, which is insulating in both cases, but by the way in which the nanotubes modify the morphology and organization of the conductive polymer network. The parameter $\rho = w \cdot AR$, which combines filler loading and nanotube aspect ratio, provides a useful descriptor of the geometrical perturbation introduced by the nanotubes. Nevertheless, the similar ρ values obtained for DG and NZ (Figure 5) cannot fully account for the markedly different relative conductance (G_{rel}) of the two systems, indicating that geometrical factors alone are insufficient to explain the experimental results.

These findings point to an important contribution from interfacial interactions. As discussed in the previous section, the local conductance enhancement observed in PEDOT:PSS/DG composites was attributed to electrostatic interactions between the negatively charged PSS chains and the positively charged lumen of the nanotubes, together with interactions between PEDOT and the external HNT surface.

The comparison between DG and NZ provides an opportunity to distinguish the effects of nanotube geometry from those of surface chemistry. Although NZ nanotubes possess the same overall surface charge distribution, they are ca. 3 times longer than DG and result in a lower density of structural defects and, consequently, fewer surface silanol (Si–OH) groups than DG. This reduction in available interaction sites could weaken hydrogen-bonding interactions with PEDOT and limit the nanotube-induced conformational rearrangement of the polymer chains. Therefore, despite providing superior mechanical reinforcement, NZ nanotubes appear less effective than DG in promoting the structural organization of PEDOT required for efficient charge transport, resulting in a lower local electrical performance.

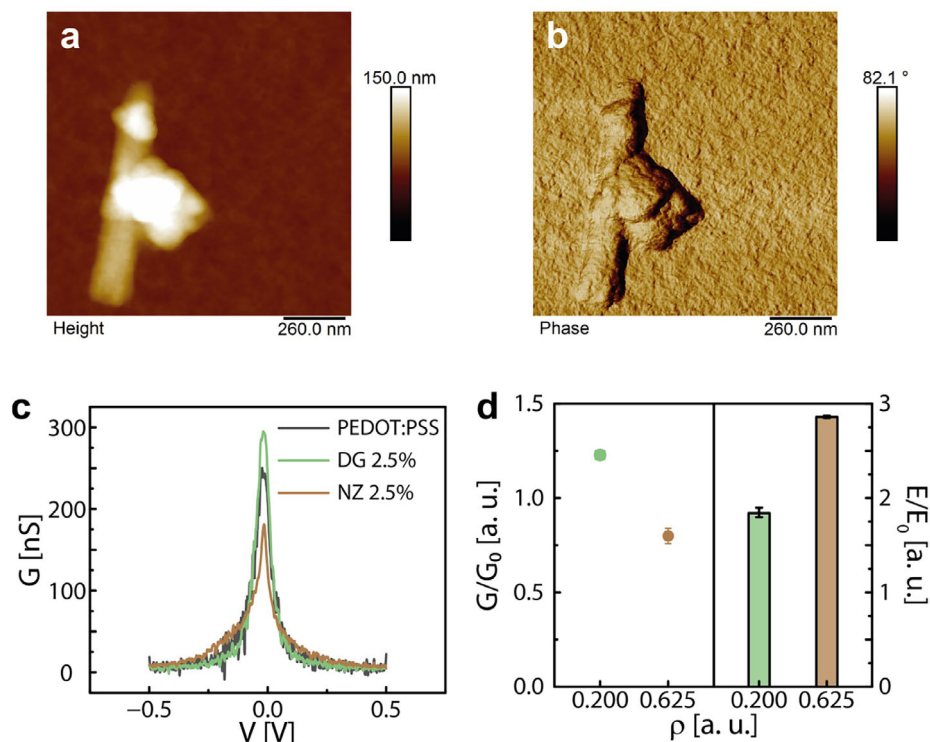


FIGURE 6 | PEDOT:PSS/NZ 2.5% height (a) and phase (b) micrographs, G-V curves (c), relative Conductance (left axis), and Young Modulus (right axis) (E/E_0) (d); G and E results are reported as mean value $\pm$ st. deviation ($n = 3$).

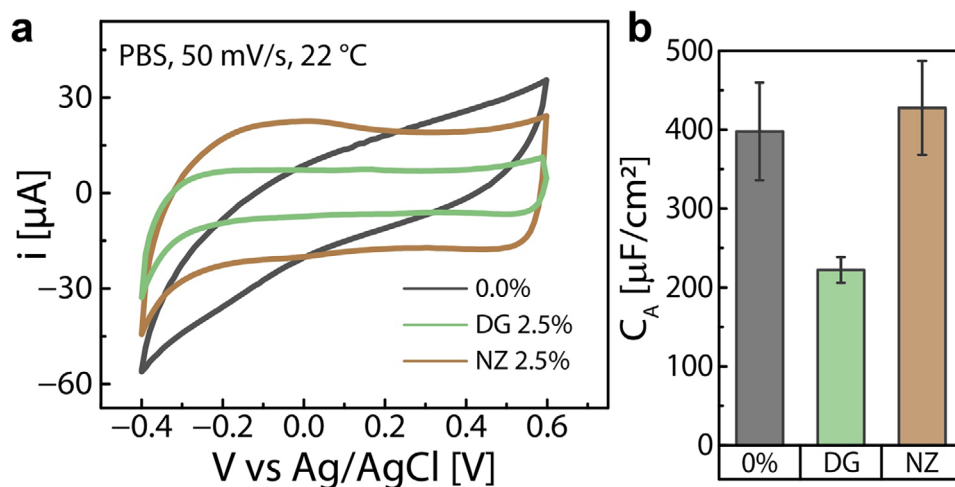


FIGURE 7 | PEDOT:PSS voltammograms (a) and capacitance values in PBS (b) of NZ and DG HNTs at 2.5%, compared to pristine PEDOT:PSS film. Capacitance results are reported as mean value $\pm$ st. dev. ($n \geq 3$).

To further investigate the effect of the different nanotube types on the polymer nanostructure and its electrochemical behavior, comparative measurements were performed to evaluate the film capacitance.

Consistent with the mechanism proposed for the DG composites, the electrochemical response of the PEDOT:PSS/NZ films provides further evidence of the relationship between nanotube-induced polymer reorganization and charge storage. Unlike the DG-based composites, the capacitance of the NZ films remains

comparable to that of pristine PEDOT:PSS (Figure 7), indicating that the incorporation of NZ does not significantly alter the ion-storage capability of the polymer. This behavior could be rationalized by considering both nanotube geometry and surface chemistry. At the same filler loading (2.5 wt.%), the larger dimensions of the NZ nanotubes result in a lower number density, reducing their overall influence of the PEDOT:PSS nanostructure.

Moreover, as discussed above, the lower density of surface defect sites on NZ is expected to weaken its interactions with the

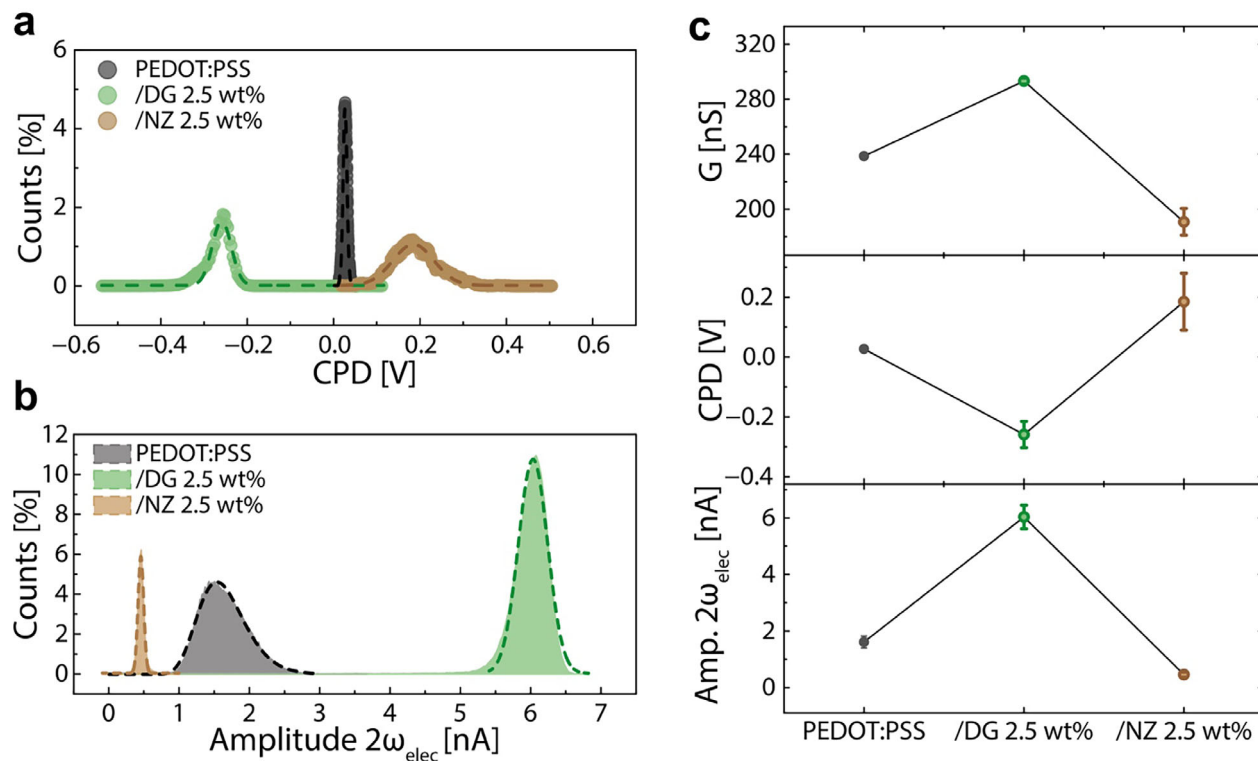


FIGURE 8 | (a) CPD distributions obtained by PM-SKM for PEDOT:PSS, DG 2.5 wt.%, and NZ 2.5 wt.%, referenced to PEDOT:PSS (-0.26 ± 0.04 eV for DG; $+0.16 \pm 0.09$ eV for NZ). (b) Corresponding $2\omega_{elec}$ amplitude distributions acquired in PM-SKM-SCM mode. (c) Resume of the electrical properties from IV spectroscopy, SKM and SCM. Gaussian fitting μ and σ are reported in Table S1.

polymer chains, limiting the conformational rearrangement of PEDOT. Consequently, the native organization of PEDOT-rich and PSS-rich domains, which governs volumetric charge storage in PEDOT, is largely preserved, and the capacitance remains essentially unchanged.

Taken together, these results reinforce the interpretation proposed for the DG composites: the local electrical response and electrochemical properties of PEDOT:PSS/HNT films are governed by the combined effects of nanotube geometry and interfacial interactions. While DG promotes a stronger reorganization of the polymer nanostructure, enhancing electronic transport at the expense of a slight reduction in capacitance, NZ induces a much smaller structural perturbation, thereby largely preserving the intrinsic charge-storage capability of PEDOT:PSS.

To gain deeper insight into the mechanisms governing the electrical response induced by filler variation, Kelvin Probe Microscopy (KPM) measurements were carried out to systematically probe the electronic properties of the film surface. This technique enables mapping of the local contact potential difference (CPD), providing access to the effective work function and surface potential distribution, and thereby revealing how the incorporation of DG and NZ modifies the energetic landscape of the PEDOT:PSS system.

Phase-modulated SKM measurements show well-separated surface potential distributions for pristine PEDOT:PSS and the nanocomposites containing DG 2.5 wt.% or NZ 2.5 wt.% (Figure 8a). Taking pristine PEDOT:PSS as the reference, DG

composite exhibits a negative CPD shift of -0.23 ± 0.04 eV, whereas NZ shows a positive shift of $+0.16 \pm 0.09$ eV. The narrow potential distributions indicate a high degree of electronic homogeneity, while the opposite CPD shifts demonstrate that the two halloysite samples modify the local electronic environment in different ways. Consistent with the structural and electrical results discussed above, these variations are more plausibly attributed to nanotube-induced reorganization of the PEDOT:PSS nanostructure than to changes in the intrinsic doping level of the polymer. In particular, the stronger interfacial interactions established by DG are expected to promote a more favorable arrangement of PEDOT-rich domains, whereas the weaker interactions associated with the smoother, less defective NZ surface produce a much smaller structural perturbation.

This interpretation is further supported by phase-modulated SKM-SCM measurements. The electrostatic force-gradient amplitude ($2\omega_{elec}$ channel) follows the same trend, being highest for DG 2.5 wt.%, intermediate for pristine PEDOT:PSS, and lowest for NZ 2.5 wt.%. Because this signal depends on carrier density, carrier mobility, and local RC relaxation dynamics, it is particularly sensitive to nanoscale charge transport. Its larger variation compared with the DC conductance therefore indicates that the HNT-induced structural rearrangements influence not only electronic conductivity but also the dynamic ionic-electronic response of the polymer.

Conductive AFM measurements are fully consistent with this picture, showing an increase of approximately 25% in local conductance for DG 2.5 wt.% and, conversely, a decrease of about

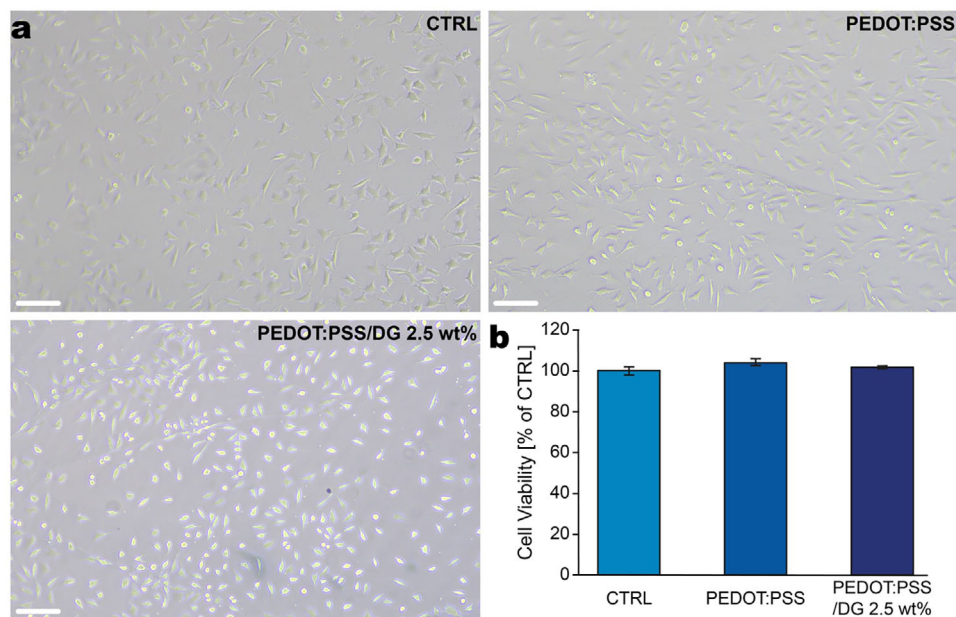


FIGURE 9 | Biocompatibility of PEDOT:PSS-based substrates. (A) Representative images of SH-SY5Y cells cultured for 24 h under different treatment conditions: CTRL, PEDOT:PSS, PEDOT:PSS/DG 2.5 wt.%. Scale bar: 50 μm . (B) Cell viability was assessed by MTT assay after 24 h of exposure to the same conditions. Data are presented as mean percentage of CTRL $\pm$ SD. Statistical analysis was performed using one-way ANOVA followed by Tukey's post hoc test. ** $p < 0.01$; ns = not significant.

25% for NZ 2.5 wt.% relative to pristine PEDOT:PSS. The excellent agreement between contact potential difference, dynamic electrostatic response, and local conductance demonstrates that the electrical behavior of the composites is governed by the combined effects of nanotube geometry and interfacial interactions, which modulate the nanoscale organization of PEDOT:PSS and, consequently, charge transport.

Among the investigated systems, PEDOT:PSS/DG 2.5 wt.% provides the most favorable combination of enhanced local electrical performance. These characteristics make this composition particularly attractive for neural biointerfaces, where efficient electronic communication with electrically excitable cells is essential. On this basis, its biocompatibility was evaluated using SH-SY5Y cells, a widely employed human neuroblastoma-derived model for neuronal differentiation, network formation, and electrical responsiveness. To the best of our knowledge, the cytotoxicity of halloysite nanotubes toward this cell line has not yet been systematically investigated.

2.5 | PEDOT:PSS and PEDOT:PSS/DG 2.5 Wt.% as Biocompatible Substrates for SH-SY5Y Cells

The results presented in Figure 9 show that SH-SY5Y cells maintain high viability when cultured for 24 h on PEDOT:PSS-based substrates, confirming the excellent biocompatibility of this conductive polymer coating. Cells grown on PEDOT:PSS exhibit morphology and viability values comparable to the untreated control, consistent with previous evidence demonstrating that PEDOT:PSS supports neural adhesion, neurite extension, and stable bioelectronic interfacing [20, 51]. Incorporation of DG 2.5 wt.% into polymer matrix does not compromise cell viability;

instead, viability remains slightly above control levels, although without reaching statistical significance.

Overall, these findings confirm that both PEDOT:PSS and PEDOT:PSS/DG 2.5 wt.% substrates are well tolerated by SH-SY5Y cells, supporting their suitability for neurobiological and bioelectronic applications. The absence of cytotoxic effects highlights the potential of these materials as stable, neuron-compatible platforms for future neurogenerative and neuroelectronic device development.

3 | Conclusions

In this work, PEDOT:PSS/halloysite nanotube (HNT) nanocomposite thin films were successfully fabricated using halloysite samples of different geographical origin and morphology over a range of filler loadings. The results demonstrate that HNTs act as active modulators of the structural, mechanical, electrical, electrochemical, and biological properties of PEDOT:PSS rather than as inert reinforcing fillers. Among the investigated compositions, the incorporation of 2.5 wt.% DG provides the best overall performance, simultaneously improving film stiffness, local conductance, and biocompatibility while preserving a homogeneous morphology.

The combined structural, electrical, electrochemical, and surface-potential analyses reveal that the properties of PEDOT:PSS/HNT composites are governed by the interplay between nanotube geometry and interfacial interactions. At moderate DG loading, favorable electrostatic and hydrogen-bonding interactions between the nanotubes and the polymer promote a reorganization of the PEDOT:PSS nanostructure, leading to enhanced connectivity between PEDOT-rich domains and improved charge

transport. At higher filler contents, however, the insulating nature of the nanotubes and their tendency to aggregate progressively disrupt the conductive network, resulting in reduced local electrical performance. The comparison with the NZ nanotubes further demonstrates that morphology alone cannot account for the observed behavior. Despite their higher aspect ratio and superior mechanical reinforcement, NZ nanotubes do not reproduce the local electrical response enhancement achieved with DG, indicating that the density of interfacial interaction sites plays a decisive role in regulating polymer organization and charge transport.

Electrochemical measurements further support this interpretation. While DG-induced polymer reorganization enhances electronic transport, it is accompanied by a slight reduction in capacitance, consistent with a modification of the internal ionic–electronic architecture of PEDOT:PSS. In contrast, NZ preserves the intrinsic capacitance of the polymer, indicating a much smaller perturbation of its nanostructure. Kelvin probe and phase-modulated surface potential measurements corroborate these findings, showing that the changes in local electronic properties closely follow the trends observed in conductivity and arise from filler-induced modifications of the polymer electronic environment.

Finally, the enhanced viability of SH-SY5Y cells on PEDOT:PSS/DG (2.5 wt.%) demonstrates that the simultaneous optimization of mechanical compliance, electrical performance, and surface properties translates into improved biological response. These findings identify DG-based PEDOT:PSS composites as promising materials for neural and bioelectronic interfaces.

Overall, this work establishes a clear structure–property–function relationship in PEDOT:PSS/HNT nanocomposites and demonstrates that the performance of these materials can be rationally tailored by controlling not only nanotube morphology but, more importantly, their interfacial interactions with the polymer matrix. This strategy provides a practical framework for designing multifunctional mixed ionic–electronic conductors with independently tunable mechanical, electrical, and electrochemical properties for next-generation flexible bioelectronic devices.

4 | Experimental Section

4.1 | Materials

All chemicals were used without any further purification. PBS and $K_3Fe(CN)_6$ reagent grade were purchased from Merck.

DG are a Dragonite halloysite from the Dragon Mine (Utah, USA), and were purchased from Merck and used as received, while NZ are the Matauri Bay halloysite from Northland, New Zealand, supplied by Imerys Tableware, New Zealand [35].

4.2 | Substrates Preparation

Nanocomposite thin films were deposited on different substrates: indium tin oxide (ITO) for electrochemical analysis, and silicon

wafer (Si) to investigate morphology, mechanical, and electrical properties. Each substrate was initially washed with water and ethanol and subsequently treated with UV- O_3 to enhance surface cleanliness and wettability.

4.3 | Thin Films Deposition

Thin films of PEDOT:PSS/HNTs were prepared using an aqueous dispersion of commercial PEDOT:PSS (1.1 wt.%, Sigma–Aldrich) combined with different weight percentages of halloysite nanotubes (1.0, 2.5, 5.0, and 7.5 wt.%).

The dispersions were magnetically stirred for 18 h to ensure homogeneous mixing. Subsequently, (3-glycidyloxypropyl)trimethoxysilane (GOPS, Sigma–Aldrich) was added as a crosslinking agent to improve the stability of PEDOT:PSS films at the solid/water interface [52]. The PEDOT:PSS-GOPS/HNTs dispersions were sonicated with a FALC instruments ultrasound bath at a power of 180 W for 5 min before deposition. Thin nanocomposite films were obtained by spin-coating (3500 rpm) onto ITO-coated glass and Si wafers, followed by thermal treatment at 140°C for 30 min.

For comparison, films containing NZ nanotubes were also prepared using the same protocol described above. In this case, only the 2.5 wt.% concentration was investigated in order to directly compare the results with those of the corresponding DG films.

4.4 | TEM and SPM Techniques for Morphology and Nanomechanical Properties Assessment

4.4.1 | Transmission Electron Microscopy (TEM)

HNTs morphologies were imaged by means of a FEI Titan G2 60–300 ultra-high resolution transmission electron microscope (FEI, Lausanne, Switzerland) coupled with analytical electron microscopy (AEM) performed with an energy dispersive x-ray spectroscopy (XEDS) detector. AEM spectra were saved in scanning transmission electron microscopy (STEM) mode with a high angle annular dark field (HAADF) detector. Elemental maps were also collected using x-rays.

4.4.2 | Scanning Probe Microscopy

Nanocomposite film morphology was investigated by means of Atomic Force Microscopy (AFM). The measurements were performed in tapping mode using a Nanoscope IIIA-MultiMode AFM. The interaction force was minimized by continuously adjusting the set point during the imaging process. Images were collected using phosphorus (n)-doped silicon tips (0.5–2 $\Omega\cdot\text{cm}$) mounted on cantilevers with a nominal spring constant of 40 N/m and a resonance frequency of 300 kHz (Tap 300-G, BudgetSensors). Acquisition was performed at a scan rate of 1 Hz with a resolution of 512×512 pixels. The resulting datasets were processed with first-order flattening in Nanoscope Analysis 2.0 (Bruker), with no additional modifications applied.

Mechanical properties and nanoscale electrical characterization were performed using a NTEGRA II Atomic Force Microscope (NT-MDT) operated with Nova_Px control electronics. All measurements were conducted under ambient conditions at 25 °C and relative humidity of approximately 40%.

The Young's modulus was determined from Force Spectroscopy. The force-distance curves were collected using stiff single-crystal silicon cantilevers with a symmetric tip shape (nominal frequency 300 kHz, nominal spring constant 40 N m⁻¹, tip radius < 10 nm). The AFM measurements were carried out in triplicate, and the cantilever spring constant was measured using the Sader method [53]. Each probe was calibrated by performing a force-curve on a hard-cleaned substrate ((100) silicon wafer), where no indentation occurred. Probe calibration was needed to calculate their optical sensitivity and the spring constant. The Young's modulus was calculated from the experimental force-distance curves using the Derjaguin-Müller-Toporov (DMT) model [54, 55] (Equation 2):

$$F + F_{ad} = \frac{4 \cdot E}{3(1 - \nu^2)} \sqrt{R} \cdot \delta^{\frac{3}{2}} \quad (2)$$

where F is the applied force, F_{ad} the adhesion force, E the sample's Young modulus, ν the Poisson's ratio of the sample (0.3), R the probe radius, and δ the indentation depth.

Each surface was indented in different areas, and approximately three hundred force-distance curves were collected, with a tip-sample approaching rate of 0.3 $\mu\text{m s}^{-1}$ for all measurements. The experimental curves were fitted in the elastic region using the DMT model to determine the Young's modulus. The distribution of the elastic modulus was analyzed using OriginPro 2024 software.

Spreading Resistance atomic force microscopy (C-AFM) measurements were performed in contact mode using Pt/Ir-coated silicon probes (FMG01/Pt, NT-MDT; curvature radius ≤ 35 nm, nominal spring constant 3 N/m, resonance frequency 60 kHz). Current-voltage (I - V) characteristics were acquired by Electric Current Spectroscopy by sweeping the bias voltage from -0.5 to $+0.5$ V at 0.66 V/s, corresponding to a total acquisition time of 6 s. The applied force was set to the default contact-mode setpoint to ensure stable electrical contact without inducing mechanical damage.

Because the effective tip-sample contact area and the exact current-path geometry cannot be independently determined, the dI/dV values are reported as local conductance rather than absolute conductivity. The measurements were therefore used to compare the relative nanoscale electrical response of the different film formulations. For each sample, I - V curves were acquired from three independent surface areas, collecting at least 300 curves per area. The maximum dI/dV value in the vicinity of 0 V was used as the representative local conductance for comparison among the samples. Data acquisition was carried out using Nova_Px software, while data analysis and post-processing were performed with OriginPro 2024.

Surface potential and capacitance gradient measurements were carried out in single-pass Phase-Modulated Scanning Kelvin

Microscopy combined with Scanning Capacitance Microscopy (PM-SKM-SCM) mode. Imaging was performed in semi-contact regime using Pt/Ir-coated silicon probes (NSG01/Pt, NT-MDT) with nominal resonance frequency of 160 kHz and spring constant of 5.1 N/m (curvature radius ≤ 10 nm). Measurements were acquired under low-force conditions to minimize tip-sample interaction and avoid unintended ohmic contact during single-pass operation.

In the PM-SKM-SCM configuration, the topography was acquired at the cantilever's mechanical resonance frequency (ω_{mech}), while the electrostatic excitation was applied at a modulation frequency (ω_{elec}) set well below ω_{mech} . This frequency separation ensures effective decoupling of the mechanical and electrostatic responses and minimizes crosstalk between the two signals. The electrostatic response was detected using heterodyne phase modulation, allowing simultaneous acquisition of both the contact potential difference (CPD) and the amplitude of the electrostatic force-gradient at $2\omega_{elec}$ within a single scan. All measurements were carried out using the same conductive probe at the same experimental conditions. To account for possible instrumental drifts or tip-induced variation in surface potential, repeated calibrations were performed on freshly exfoliated HOPG during the measurement session. Films were deposited on Si substrates to enable a horizontal measurement geometry. For each sample, three independent regions were scanned (512×256 pixels per images). Histograms of CPD and the $2\omega_{elec}$ amplitude were generated from the full pixel distributions of each scanned area. Statistical analysis and Gaussian fitting were carried out using OriginPro 2024, yielding the most probable value (μ) and distribution width (σ).

4.5 | Electrochemical Measurements

Electrochemical measurements were fulfilled using a Palm-Sens3 Potentiostat in a standard three-electrode electrochemical glass cell (25 mL). Cyclic Voltammetry (CV) measurements were performed using a Pt wire serving as the counter electrode, an Ag/AgCl electrode as the reference, and the film deposited on ITO as the working electrode. CV experiments were conducted in phosphate-buffered saline solution (PBS, pH 7.4) as support electrolyte, within a potential window ranging from -0.4 to $+0.6$ V. Capacitance values for all films were normalized to the electroactive area. All measurements were performed in air at room temperature, using ultrapure Millipore water.

4.6 | Evaluation of SH-SY5Y Cell Response to PEDOT:PSS-HNTs Based Substrates

The cell line used in this study was the human neuroblastoma SH-SY5Y, obtained from the American Type Culture Collection (ATCC, USA). Cells were cultured in DMEM/F12 medium (1:1 mixture; Merck Life Science S.r.l., Milan, Italy) supplemented with 10% fetal bovine serum (FBS; Merck Life Science S.r.l.), 2.5 mM L-glutamine (Merck Life Science S.r.l.), and 1% penicillin/streptomycin/amphotericin B (PSA; Merck Life Science S.r.l.). Cultures were maintained under standard conditions at 37 °C in a humidified incubator with 5% CO₂. The medium was

replaced two to three times per week, and cells were kept at 70–80% confluence throughout the culture period.

To evaluate the biological response of SH-SY5Y cells, cultured on PEDOT:PSS-based substrates incorporating DG 2.5 wt.%, 5×10^5 cells were resuspended in 200 μ L of complete growth medium and seeded onto slides coated with PEDOT:PSS or PEDOT:PSS/DG 2.5 wt.%, while uncoated slides served as controls. The slides were placed in 24-well plates and incubated under standard conditions for 24 h.

Cell viability was then assessed using the MTT assay [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide] (Merck Life Science S.r.l., Milan, Italy) following the procedure previously described [56]. Briefly, cells seeded onto slides coated with PEDOT:PSS, PEDOT:PSS/DG 2.5 wt.% or left uncoated were transferred to a new 24-well plate. Subsequently, 200 μ L of MTT solution (1 mg/mL in FBS-free medium) was added, and the plate was incubated at 37°C for 2 h. After incubation, the MTT solution was removed, formazan crystals were solubilized, and absorbance was measured at 540 nm (OD540) using a microplate reader (AMR-100 Biosigma, Verona, Italy). Each experimental condition was analyzed in 12 replicates to ensure reproducibility, and cell viability was expressed as a percentage relative to the control group (uncoated substrates).

Author Contributions

Luigi Fabiano: methodology, investigation, formal analysis, data curation, writing – original draft, visualization, validation. **Giuseppe Cinà:** methodology, investigation, formal analysis, data curation, writing – original draft, visualization, validation. **Rosalinda Sciacca:** investigation, methodology, writing – original draft, data curation, validation. **Alessandra Armeli:** investigation, data curation, formal analysis. **Marina Massaro:** conceptualization, writing – review and editing. **Rita Sánchez-espejo:** investigation. **Giovanna Calabrese:** conceptualization, funding acquisition, writing – review and editing, formal analysis, supervision. **Grazia Maria Lucia Messina:** conceptualization, funding acquisition, writing – review and editing, visualization, formal analysis, supervision, resources, project administration, validation. **Giovanni Marletta:** conceptualization, writing – review and editing. **Serena Riela:** conceptualization, funding acquisition, writing – review and editing, formal analysis, supervision, resources, project administration, validation.

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Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.

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