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A S-Parameters-Based Detection Method for a Multilayer SPR Biosensor

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Abstract— **In this paper, S-parameters investigation of a variable incidence angle multilayer SPR biosensor is presented. Both magnitude and phase of the S-parameters are taken into account in the investigation. The work presented in this paper is the first attempt to apply S-parameters analysis to a multilayer SPR biosensor. The goal is to improve sensitivity through involving S-parameters including their phase values. In addition, further investigation is carried out to understand the relationship between the S-parameters and thickness of biomolecular layer and also the design parameters including the number of graphene layers.**

I. Introduction

Surface plasmon resonance (SPR) is an excitation phenomenon of collective free electrons oscillation at the metal/dielectric interface. The SPR occurs at a certain incidence angle when momentum matching between the incident photon and the surface plasmon is achieved. At the resonance incidence angle, the reflected wave is completely attenuated producing a sharp dip on the optical spectrum whose location is dependent on the refractive index of the sensing medium [1]. Since the SPR condition is modified based on the refractive index change, the method becomes an important tool for studying biomolecular interactions in pharmaceutical and biomedical research. SPR biosensors rely on surface plasmons on nanostructured metal surfaces to detect antigen-antibody bindings by measuring either the shift of resonance angle [2] or the change of intensity [3]. SPR biosensors are well-suited for a range of biomedical applications because of their advantages including label-free detection, rapid analysis, and spectral tunability [4].

The angular interrogation is the most widely used scheme where the optical parameters are measured as a function of the incidence angle. Compared to reflectivity variation measurements, which are widely used in traditional SPR devices, phase based detection is another method which has recently attracted the attention of researchers because of its rapid change in response to the binding events [5]. In this method, the phase of the detected optical signal is changed abruptly comparing with the change of the intensity of the signal. This is due to the change of the refractive index or the thickness of the binding layer on the surface. This results in higher detection sensitivity. Among some existing schemes including polarization state [6], and Mach–Zehnder interferometry [7], Wu et al. [8] presented the measurement of phase variation based on the heterodyne interferometric system. Their attempt was related to the conventional gold thin film SPR sensing where the introduction of the heterodyne interferometric system in phase variation measurement was new. In another study, Xinglong et al. [9] developed a numerical study on a phase based SPR biosensor focusing on the understanding of different design parameters on the sensitivity. Although several articles have been reported on the phase change detection, the phase variation detection of multilayer SPR biosensor involving graphene is not reported.

Our idea of involving of S-parameters in SPR biosensors facilitates a new detection method. The S-parameters are complex-valued wavelength dependent matrices, and therefore contain both magnitude and phase information. In our work, the proposed SPR biosensor is modeled using a two-port network (Fig. 1). The S-parameters change whenever any resonance condition (e.g., refractive index of the analyte, concentration of target molecules and incidence angle) is modified. Thus, the change of the magnitude or phase of the S-parameters gives an indication of the detected target biomolecules.

Although the sensitivity characteristics of conventional thin-film phase based SPR biosensors have been investigated in recent studies, further improvement of the sensitivity by employing a multilayer configuration involving a graphene layer has not yet been fully explored in phase variation and S-parameters measurement. The incorporation of the graphene layer on the conventional SPR biosensor has enhanced the sensitivity. This improved sensitivity is due to the stronger adsorption of biomolecules on graphene and the optical property of graphene [10]. In addition, the graphene-on-gold can offer faster electric conduction property for the identification of single biomolecules improving the signal-to-noise ratio [11]. In this paper, the S-parameters are considered as an indication of the biomolecular reactions of DNA hybridization. The high-frequency complex valued S-parameters are dependent on the refractive index of the sample analyte resulting from biomolecular reactions between single-stranded DNA (ssDNA) and complementary DNA (cDNA) to from a double stranded DNA (dsDNA). The aim is to improve the sensitivity through measurement of different S-parameters. In addition, we have investigated the effect of biomolecules and the number of graphene layers on the measurement parameters. The advantage is that some of the S-parameters have rapid response in some specific design parameters. For example, $|S_{11}|$ provides larger change compared to $|S_{21}|$ and $|S_{22}|$ in response to the target analyte. Both $|S_{11}|$ and $|S_{22}|$ have an upward slope for variation of the thickness of the target biomolecules, while $|S_{21}|$ and $|S_{12}|$ have a downward slope. In our simulations, we have used the finite-difference time-domain (FDTD) method using CST MICROWAVE STUDIO [12].

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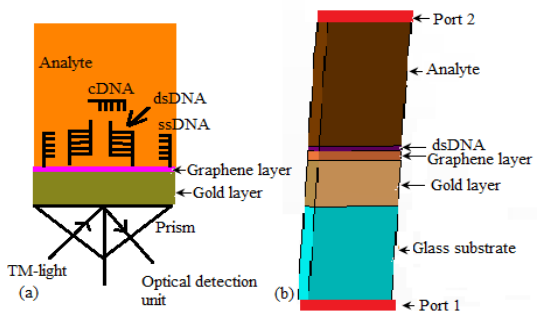

Figure 1. Schematic representation of SPR biosensing: (a) Kretschmann configuration of prism coupling, and (b) a unit cell of a two port model of the proposed SPR biosensor.

II. Multilayer Model System

A modeling and simulation exercise is carried out for the proposed multilayer SPR biosensor on biomolecular reaction of DNA hybridization. A schematic of the proposed SPR biosensor in a Kretschmann configuration is shown in Fig. 1. To excite the surface plasmon to match the evanescent wave, the laser beam is coupled with a prism (flint glass prism). The base of the prism is covered by a thin gold film with a graphene layer on top of the gold layer. The thicknesses of the gold and graphene layers are fixed at 50 nm and 2 nm, respectively. The complex refractive index of graphene in the visible range is obtained by the calculation of Fresnel coefficients as follows [10]: $n_G(\lambda_0) = 3 + i(1.82\,\lambda_0)$, where λ_0 is the vacuum wavelength in μm.

To determine the optical response of DNA hybridization, the sensor surface is functionalized with specific receptors (e.g., ssDNA for cDNA) that recognize and bind to the target biomolecules. Biomolecules which are introduced into the liquid solution are diffused and captured by the receptor molecules. A TM-polarized plane wave light of fixed wavelength 632.8 nm with various incidence angles is launched into the prism to find out the optimum coupling condition. The reflected beam was directed to an optical detection system producing a SPR curve.

The principles underlying the DNA hybridization in this SPR biosensor stems from the refractive index change caused by biomolecular reactions between ssDNA and cDNA to form a dsDNA. With the attachment of the ssDNA, the initial refractive index of the immobilized ssDNA is assumed to be 1.462 for a density of 0.028 g/cm^3 obtained from the ellipsometry measurements [13]. However, this value of refractive index is gradually increases during the course of DNA hybridization reaction. After the formation of dsDNA of density 0.061 g/cm^3, the refractive index reported to be 1.52 [14]. And, the refractive index of the dsDNA is assumed to be linear with the increase in concentration of the bound DNA. To measure the S-parameters and their phase, the proposed device is modeled in a two-port network (Fig. 1 (b)) where the input terminal is termed as port 1 and the output terminal as port 2. The biomolecular interactions between ssDNA and cDNA results in the modulation of the sensor characteristics. Measuring the shift of the optical characteristics (e.g., S-parameters), the presence of the target biomolecules is identified.

III. Theory

In order to get the plasmon resonance with photons, the energy and momentum should be preserved which is obtained by the following equation:

$$K_{sp} = K_{ev} = \frac{\omega}{c}\sqrt{\frac{\varepsilon_M\,\varepsilon_D}{\varepsilon_D + \varepsilon_M}} = \frac{\omega}{c}\sqrt{\varepsilon_p}\,\sin\theta_{res} \quad (1)$$

where K_{sp} and K_{ev} are the wave vectors of the propagation constant of the surface plasmon and the evanescent wave, respectively, and c is the speed of light. ε_M and ε_D are the dielectric constant of metal and dielectric layer, respectively. The S-parameters are complex-valued wavelength dependent matrices expressing device characteristics (e.g., transmission and reflection of electromagnetic energy) using the amount of absorption or transmission. For a two-port device (Fig.1), the S-parameters are defined as:

$$S = \begin{bmatrix} S_{11} & S_{12} \\ S_{21} & S_{22} \end{bmatrix} \quad (2)$$

where S_{11} is the S-parameter for the reflected wave and S_{21} is the S-parameter for the transmitted wave. Furthermore, $S_{11} = \sqrt{\frac{\text{Power reflected from 1}}{\text{Power incident on 1}}}$ and $S_{21} = \sqrt{\frac{\text{Power delivered to 2}}{\text{Power incident on 1}}}$. The magnitudes of S_{11} ($|S_{11}|$) gives the normalized reflectance. And, the normalized reflectance for this multilayer SPR is calculated as follows [13]:

$$S_{11} = \left|\frac{M_{11}}{M_{12}}\right|^2 \exp(i\varphi_{11}) \quad (3)$$

where φ_{11} contains the phase information of S_{11} and

$$M = \begin{bmatrix} M_{11} & M_{12} \\ M_{21} & M_{22} \end{bmatrix} = I_{01}L_1I_{12}L_2I_{23}L_3I_{34}L_{41}\ldots I_{jk}L_k \quad (4)$$

$$I_{jk} = \begin{bmatrix} 1 & r_{jk} \\ r_{jk} & 1 \end{bmatrix} \text{ and } L_j = \begin{bmatrix} e^{id_z k_{zj}} & 0 \\ 0 & e^{-id_z k_{zj}} \end{bmatrix} \quad (5)$$

$$r_{jk} = \frac{\left(\frac{k_{zj}}{\varepsilon_j} - \frac{k_{zk}}{\varepsilon_k}\right)}{\frac{k_{zj}}{\varepsilon_j} + \frac{k_{zk}}{\varepsilon_k}}, k_{zj} = \sqrt{\left(\frac{\omega}{c}\right)^2\left[\varepsilon_j - \varepsilon_0\sin^2\theta\right]} \quad (6)$$

where ε_j and d_j are the dielectric constant and thickness of the j-th layer.

IV. Results and Discussions

As a quantitative measure of the sensor performance, we have considered the change of the S-parameters along with their phase variation for detection. While most of the published articles employ the shift of the plasmon dip as the detection platform, we employ sensitivity enhancement representing change of optical parameters including the phase and magnitudes values of the S-parameters. It is outlined that introducing a graphene layer on to the thin gold film improving change of the detection parameters. In our proposed design, the resonance occurs at incidence angle of 50.069^o before binding, and 50.69^o after binding, therefore the shift of resonance angle is only 0.62^0. It is noticed that before the resonance (48^0), the intensity plasmon wave is reflected back (total internal reflection) whereas at resonance angle (50.69^0) the oscillation of plasmon wave is maximum (Fig. 2).

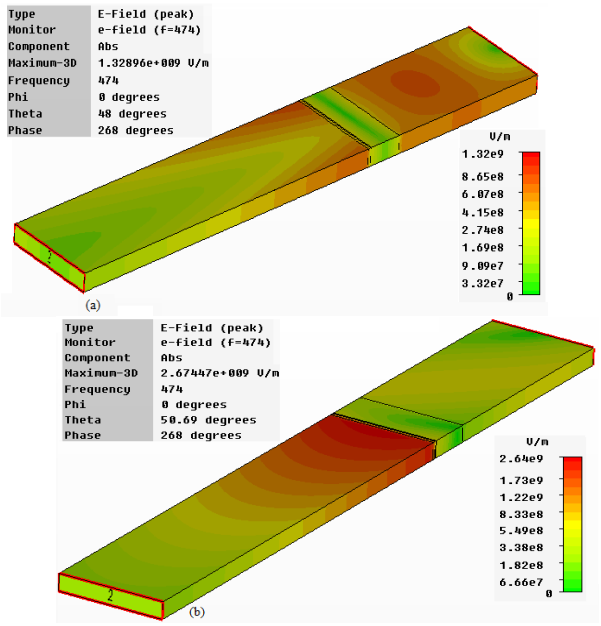

Figure 2. Contour plot of electric field before and at the resonance condition: (a) before and (b) at resonance.

Fig. 3 shows the change of S-parameters versus the incidence angle for the proposed and a conventional SPR biosensor. The changes of S-parameters, $\Delta|S_{11}|$, $\Delta|S_{12}|$, $|\Delta S_{22}|$ and $\Delta|S_{21}|$, attain their maximum value at their resonance angle. However, the change is highest for S_{11} (Fig. 3 (c)).

In Fig. 4, the phase plot of S_{11} is shown. It is observed that there is a rapid transition of the phase of S_{11} at the resonance angle of 50.07^0 (before binding). And the maximum phase shift of 329.8^0 is achieved at this transition period (Fig. 4 (b)).

The effect of the thickness of dsDNA, and hence, the refractive index resulted from the DNA hybridization reaction is shown in Fig. 5. The plasmon dip is shifted with the thickness of dsDNA, however, the minimum value at their dip is almost the same ensuring that the change of $|S_{11}|$ at the resonance for different thickness of dsDNA will remain constant. On the other hand, the phase of $|S_{11}|$ produces significant change once the resonance happens (Fig. 5 (b)).

Since the sensitivity is increased with the inclusion of geaphene, we have further investigated the number of graphene layers. Fig. 6 shows that both the magnitudes and the phase of S_{22} start to decrease by increasing the number of layers of graphene.

V. Conclusion

This paper presented the design and analysis of a multilayer SPR biosensor through a theoretical framework using the FDTD method. The ssDNA is used as a receptor molecule which is immobilized on the sensor surface to specifically adsorb its complementary counterpart (cDNA) immersed in a phosphate buffer solution. The change of magnitudes and phases of S-parameters are considered as a detection indicator instead of measuring the shift of resonance peak reported in most of SPR biosensor literature. The S-parameters-based detection for a multilayer SPR biosensor is a new concept presented in this paper. Additionally, an investigation of the electric filed distribution of the proposed design was presented for resonance and no resonance conditions agreeing with the theoretical concepts.

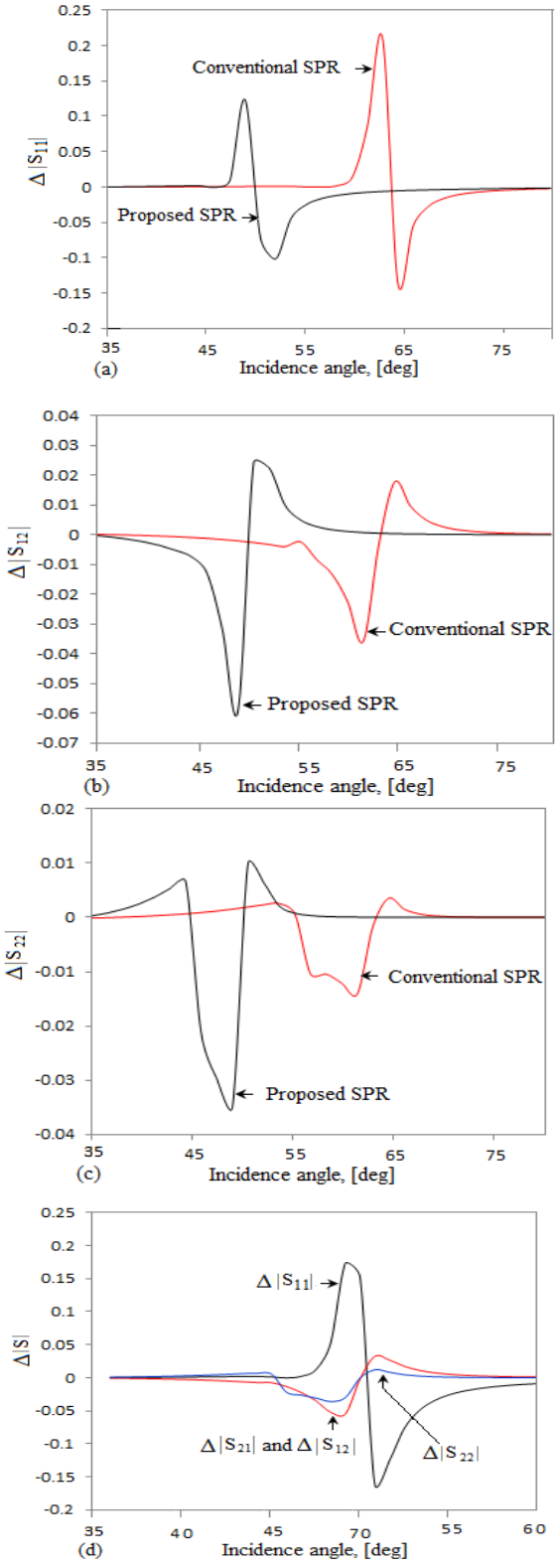

Figure 3. FDTD simulation results to show the change of different S-parameters: (a) $\Delta|S_{11}|$ (b) $\Delta|S_{12}|$ (c) $\Delta S_{22}|$ (d) $\Delta|S|$.

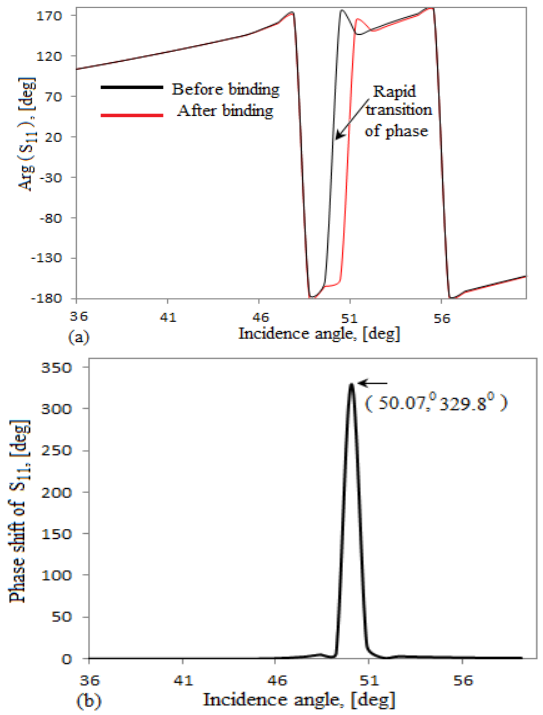

Figure 4. Illustration of the phase change detection using S_{11}: (a) pattern of phase before and after binding of cDNA, and (b) Phase shift.

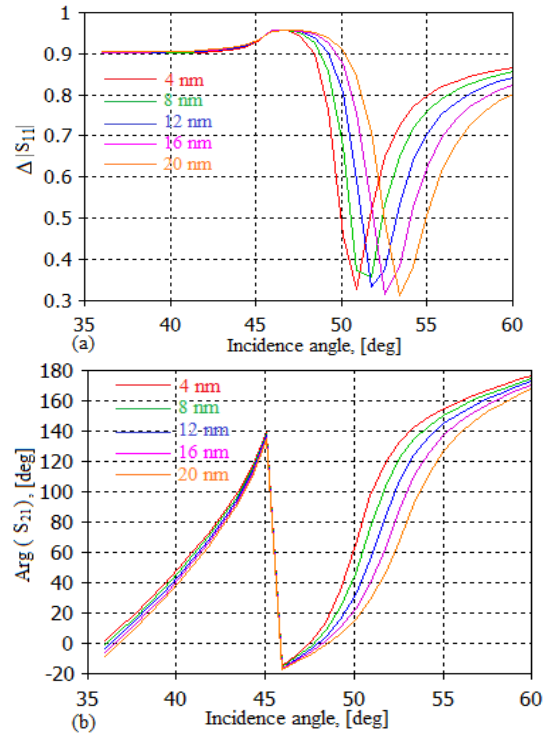

Figure 5. Graph demonstrating the dependence of the S-parameter and phase on the thickness of target biomolecules: (a) $|S_{11}|$ and (b) arg (S_{21}).

REFERENCES

[1] J. Homola, S. S. Yee, and G. Gauglitz, "Surface plasmon resonance sensors: review," *Sensors and Actuators B: Chemical,* vol. 54, pp. 3-15, 1999.

[2] M. S. Islam, A. Z. Kouzani, X. J. Dai, W. P. Michalski, and H. Gholamhosseini, "Design and Analysis of a Multilayer Localized Surface Plasmon Resonance Graphene Biosensor," *Journal of Biomedical Nanotechnology,* 2011 (Accepted on 22 September 2011).

[3] P. Guedon, T. Livache, F. Martin, F. Lesbre, A. Roget, G. Bidan, and Y. Levy, "Characterization and optimization of a real-time, parallel, label-free, polypyrrole-based DNA sensor by surface plasmon resonance imaging," *Anal Chem,* vol. 72, pp. 6003-9, Dec 15 2000.

[4] A. V. Kabashin, P. Evans, S. Pastkovsky, W. Hendren, G. A. Wurtz, R. Atkinson, R. Pollard, V. A. Podolskiy, and A. V. Zayats, "Plasmonic nanorod metamaterials for biosensing," *Nat Mater,* vol. 8, pp. 867-871, 2009.

[5] V. E. Kochergin, A. A. Beloglazov, M. V. Valeiko, and P. I. Nikitin, "Phase properties of a surface-plasmon resonance from the viewpoint of sensor applications," *Quantum Electronics,* vol. 28, p. 444, 1998.

[6] A. Kruchinin and Y. G. Vlasov, "Surface plasmon resonance monitoring by means of polarization state measurement in reflected light as the basis of a DNA-probe biosensor," *Sensors and Actuators B: Chemical,* vol. 30, pp. 77-80, 1996.

[7] A. V. Kabashin and P. I. Nikitin, "Interferometer based on a surface-plasmon resonance for sensor applications," *Quantum Electronics,* vol. 27, p. 653, 1997.

[8] C. M. Wu, Z. C. Jian, S. F. Joe, and L. B. Chang, "High-sensitivity sensor based on surface plasmon resonance and heterodyne interferometry," *Sensors and Actuators B: Chemical,* vol. 92, pp. 133-136, 2003.

[9] Y. Xinglong, W. Dingxin, and Y. Zibo, "Simulation and analysis of surface plasmon resonance biosensor based on phase detection," *Sensors and Actuators B: Chemical,* vol. 91, pp. 285-290, 2003.

[10] L. Wu, H. S. Chu, W. S. Koh, and E. P. Li, "Highly sensitive graphene biosensors based on surface plasmon resonance," *Opt. Express,* vol. 18, pp. 14395-14400, 2010.

[11] S. H. Choi, Y. L. Kim, and K. M. Byun, "Graphene-on-silver substrates for sensitive surface plasmon resonance imaging biosensors," *Optics Express,* vol. 19, pp. 458-466, 2011.

[12] Available: www.cst.com

[13] S. H. Choi, Y. L. Kim, and K. M. Byun, "Graphene-on-silver substrates for sensitive surface plasmon resonance imaging biosensors," *Opt. Express,* vol. 19, pp. 458-466, 2011.

[14] D. Gray, S. Case-Green, T. Fell, P. Dobson, and E. Southern, "Ellipsometric and interferometric characterization of DNA probes immobilized on a combinatorial array," *Langmuir,* vol. 13, pp. 2833-2842, 1997.

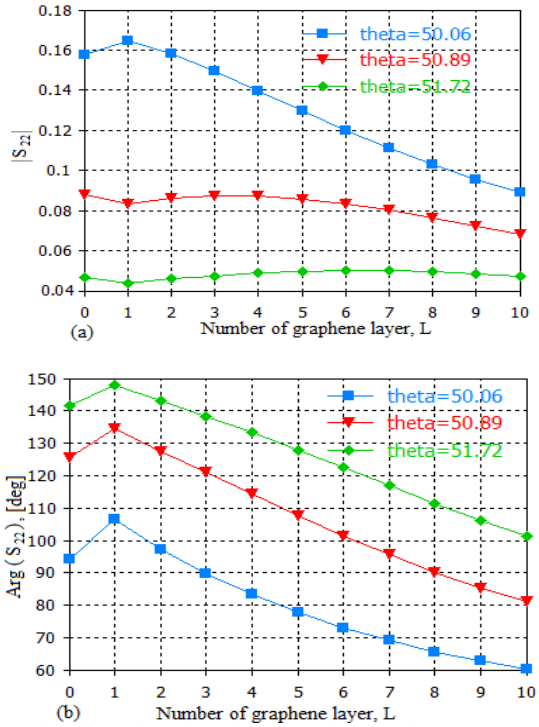

Figure 6. The effect of number of graphene layer on the S-parameters with different incidence angle: (a) $|S_{22}|$, and (b) arg (S_{22}).