**Table 1: Initial and final values of kinetic parameters estimated by the Particles Swarm parameter estimation algorithm in COPASI**

| Parameter Name | Reference Values (starting point for Manual Empirical-preparatory Tuning) | Initial Value for parameter estimation (after Manual Empirical-preparatory Tuning) | Margins | Estimated value (by global stochastic optimization) |
|---|---|---|---|---|
| $k_{WTasyn2merForm}$ | 5e-12 [1] | 6.89778e-10 | [6.89778e-12 , 6.89778e-08] | 1.46294e-09 |
| $k_{OligomerForm}$ | 5e-10 [1] | 8.1732e-09 | [8.1732e-11 , 8.1732e-07] | 3.3505e-08 |
| $k_{ProteasomeBind}$ | 1.7e-09 [1] | 1.7e-09 | [1.7e-11 , 1.7e-07] | 3.42469e-09 |
| $k_{OligAutophagUptake}$ | 4e-08 [1] | 2.38913e-06 | [2.38913e-08 , 2.38913e-04] | 2.39034e-08 |
| $k_{LampFreeWTasyn}$ | 0.001 [1] | 0.001 | [0.0001 , 0.01] | 0.000304457 |
| $k_{ProtOligDegr}$ | 1e-02 [1] | 3.70096e-05 | [3.70096e-06 , 3.70096e-04] | 0.000370096 |
| $k_{WTasyn1\_2merBindOnLamp}$ | 4e-08 [1] | 4e-08 | [4e-10 , 4e-06] | 6.86546e-07 |
| $k_{WTOligoBindOnLamp}$ | 4e-08 [1] | 4e-08 | [4e-10 , 4e-06] | 4e-06 |
| $k_{DisRate}$ | 5e-09 [1] | 5e-09 | [5e-11 , 5e-07 ] | 4.99953e-07 |
| $k_{DopModWTasynLampBind}$ | 4.8e-08 [1,2] | 8.268e-08 | [8.268e-10 , 8.268e-06] | 7.6716e-09 |
| $k_{WTasynSynth}$ | 2.8e-02 [1] | 0.011908 | [0.0011908 , 0.11908 ] | 0.0294219 |
| $k_{DopProd}$ | 2.0e-05 [1] | 0.01 | [0.001 , 0.1] | 0.0791823 |
| $k_{WTasynDopMod}$ | 5e-08 [1] | 5e-08 | [5e-10 , 5e-10] | 6.74768e-07 |
| $k_{DopDegr}$ | 0.001 [1] | 0.001 | [0.0001 , 0.01 ] | 0.00679501 |
| $k_{AggrGrowth}$ | 5e-09 [1] | 5e-09 | [5e-11 , 5e-07] | 4.90556e-07 |
| $k_{WTasynLysUptk}$ | 0.001 [1] | 0.001 | [0.0001 , 0.01 ] | 0.00999558 |
| $k_{WTasyn2LysUptk}$ | 0.001 [1] | 0.001 | [0.0001 , 0.01 ] | 0.00995312 |


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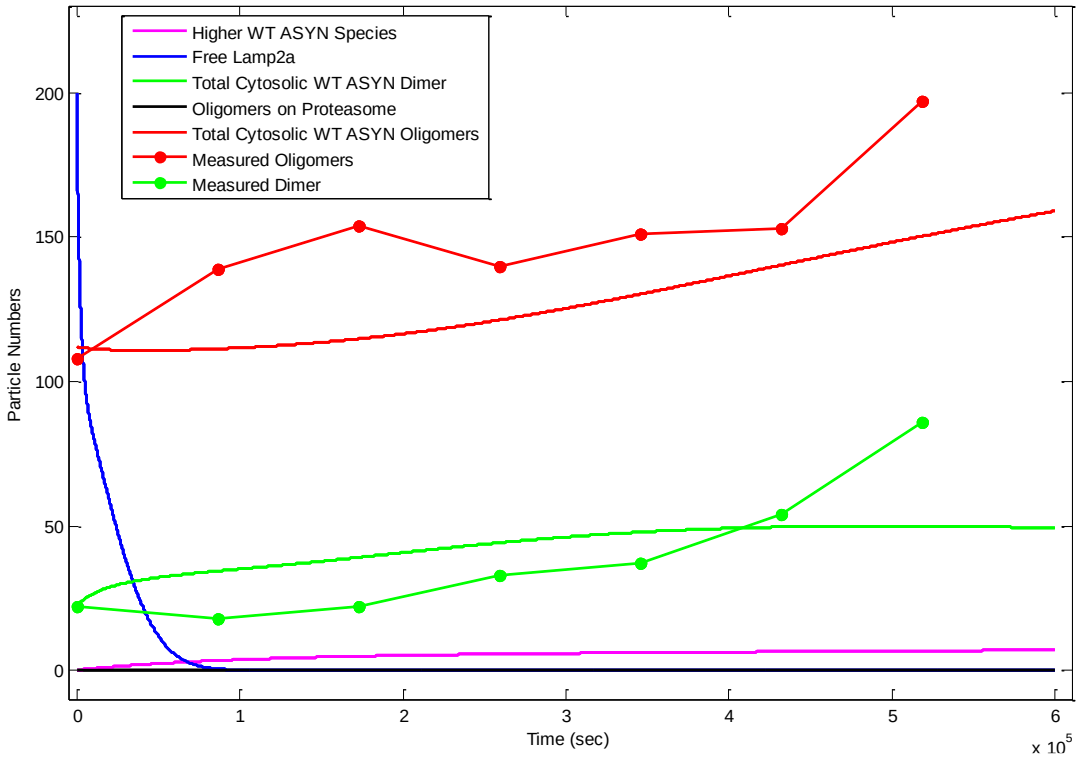


**Figure 1: Model simulation results using parameter values estimated by Genetic Algorithm.**

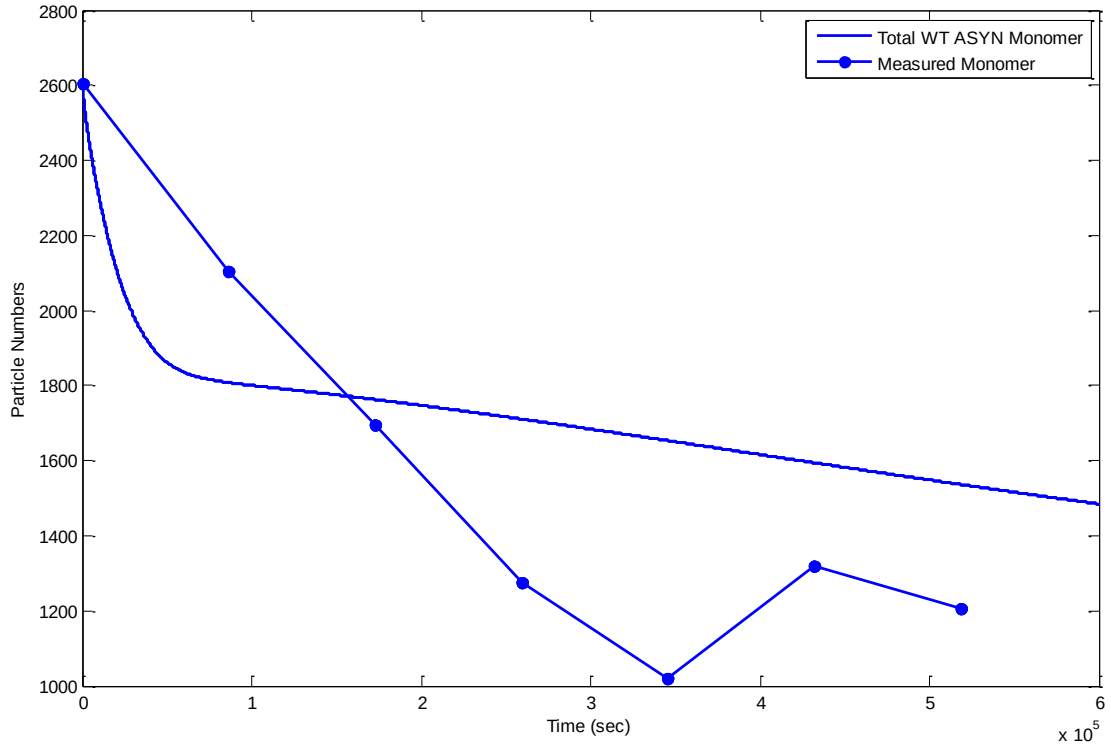


**Figure 2: Model simulation results for the monomeric ASYN using parameter values estimated by Genetic Algorithm.**

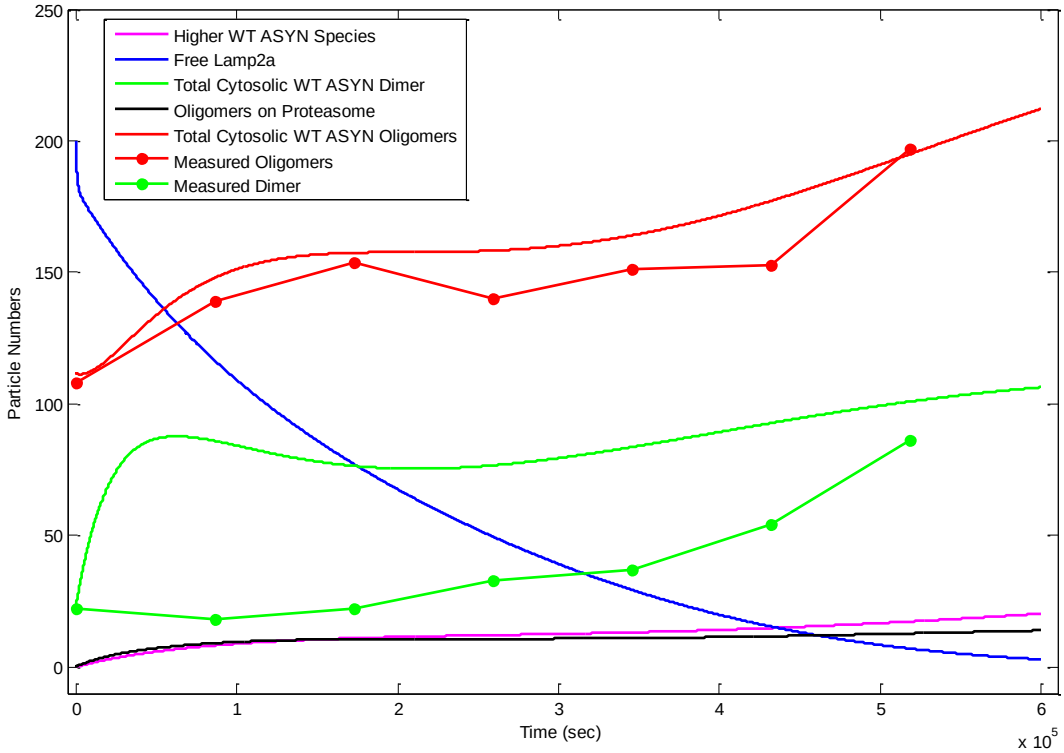


**Figure 3: Model simulation results using parameter values estimated by Genetic Algorithm with Stochastic Ranking.**

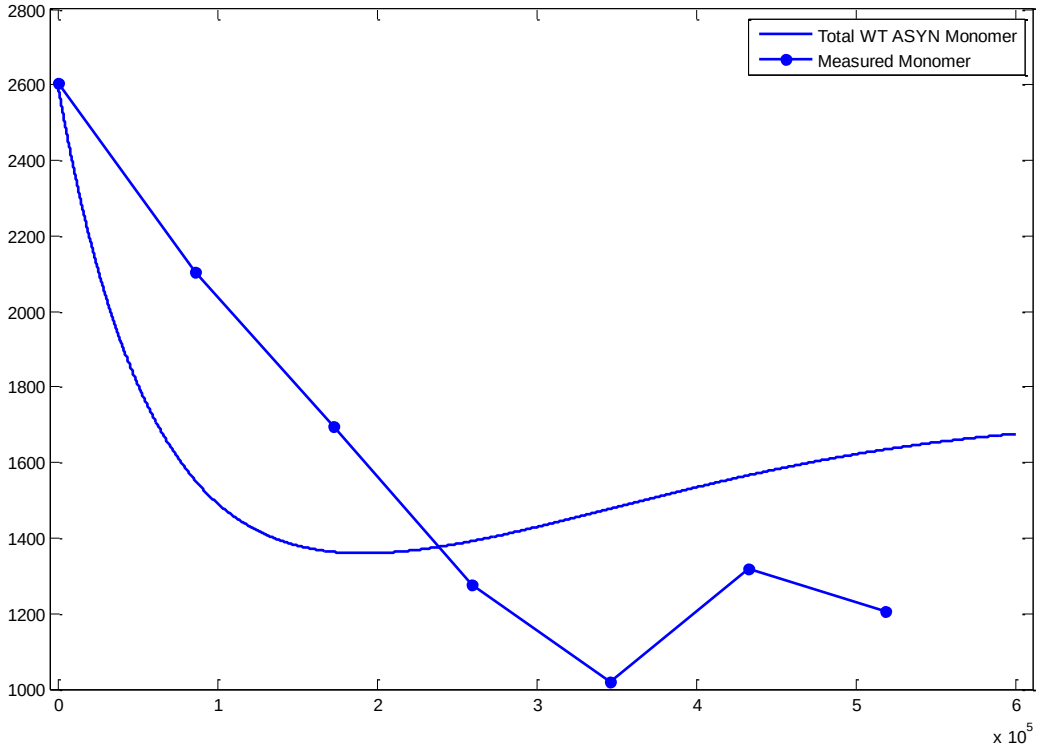


**Figure 4: Model simulation results for the monomeric ASYN using parameter values estimated by Genetic Algorithm with Stochastic Ranking.**

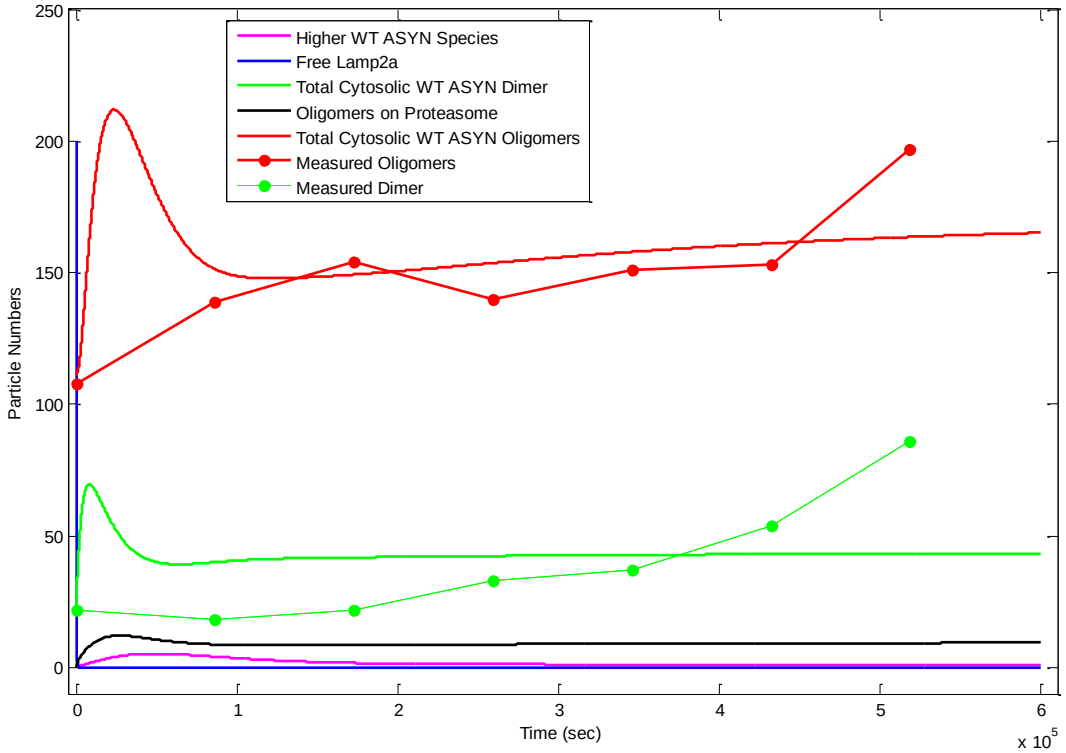


**Figure 5: Model simulation results using parameter values estimated by Evolution Strategy algorithm (SRES).**

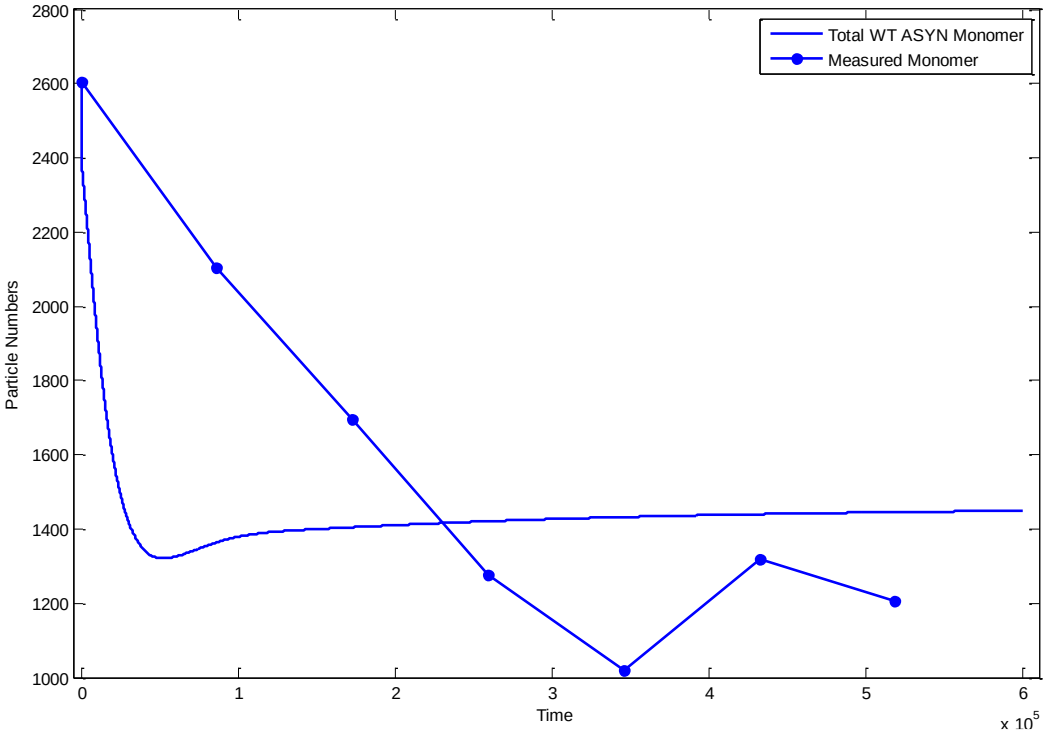


**Figure 6: Model simulation results for the monomeric ASYN using parameter values estimated by Evolution Strategy algorithm (SRES).**

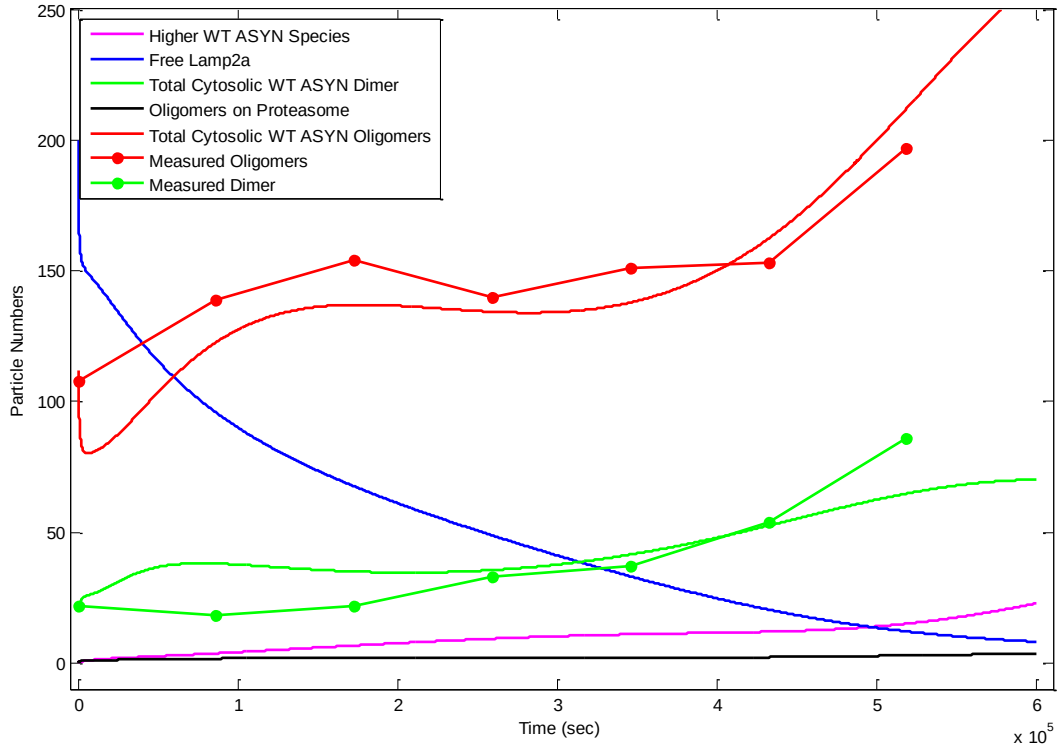


**Figure 7: Model simulation results using parameter values estimated by Particle Swarm algorithm.**

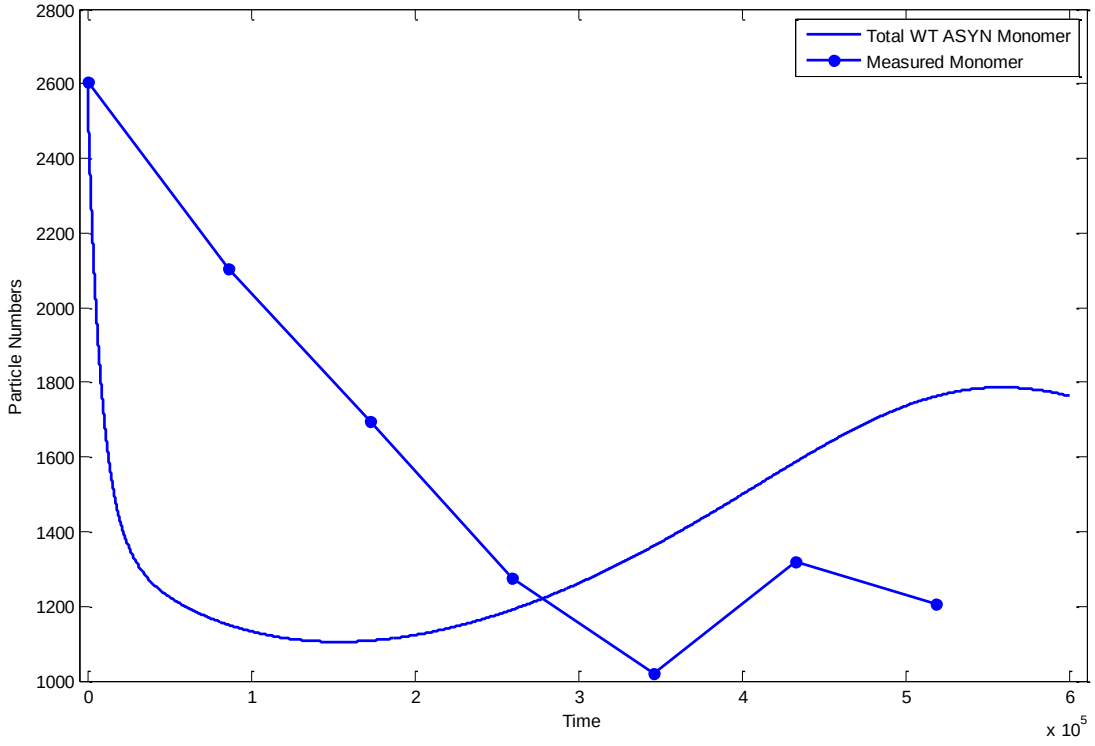


**Figure 8: Model simulation results for the monomeric ASYN using parameter values estimated by Particle Swarm algorithm.**