二、重要研究成就（至多 5 頁）：請敘述重要研究成就及對學術研究發展之具體貢獻

我的研究以電腦輔助藥物設計(Computer-aided drug design)及結構生物資訊(Structural bioinformatics)為主軸。**在電腦輔助藥物設計方面**，目前我們是分子對接(Molecular docking)軟體(GEMDOCK)提供者之一，我們也與國內外超過十個實驗室合作，經由生物實驗證實我們的方法確實可找到藥物標的(如 Envelop protein、Skimate kinase、 influenza virus neuraminidase)前導藥物(Lead compound)、功能催化部位(如 ß-lactoglobulin)、及蛋白質功能設計(如 endo-chitosanase to exo-chitosanase)等，這些成果已發表多篇論文在這些領域最好的期刊上。這些論文從 2004 年起被引用次數已超過 70 次 (根據 ISI)；另外 GEMDOCK 被國內外數十個實驗室使用，除研究的應用外，此軟體也使用在教學上。這些成果讓我們獲得 2007 年國家新創獎(由國家生技醫療產業策進會主辦)，是唯一以電腦軟體獲獎的團體。

在結構生物資訊方面，我們在蛋白質結構預測(PS2)、高速蛋白質結構的搜尋與應用(3D-BLAST)、及結構為基的蛋白質網路(3D-partner)已有相當成果，這些研究已發表在相關領域最好的期刊上(如 *Nucleic Acids Research* 、*Genome Biology*) 。最值得一提的研究成果是 3D-BLAST，3D-BLAST 搜尋蛋白質結構的速度與 BLAST 搜尋胺基酸序列一樣快，同時具備 BLAST 的優點與操作介面，也就是能提供可信的統計基礎(e-value)及高效率的搜尋能力。因此 3D-BLAST 可能成為蛋白質結構搜尋的標準，對於結構搜尋有巨大影響，此研究成果已引起相關學者的重視與討論。2007 年起這些論文被引用次數已超過 13 次，目前已有 44 個國家，超過 5,100 人次使用我們提供的服務。**這些成果全都是在台灣完成**。五篇代表作(我皆為通信作者)之具體貢獻簡述如下:

高速蛋白質結構搜尋與分類 (代表作 1~3)

代表作 1: **J.-M. Yang*** and C.-H. Tung, "Protein structure database search and evolutionary classification," *Nucleic Acids Research*, vol. 34, pp. 3646-3659, 2006. **(IF:6.954**; Times Cited: 8; Ranking 29/263 in BIOCHEMISTRY & MOLECULAR BIOLOGY**)**

代表作 2: C.-H. Tung, J.-W. Huang and **J.-M. Yang*,** "Kappa-alpha plot derived structural alphabet and BLOSUM-like substitution matrix for fast protein structure database search," *Genome Biology*, vol. 8, pp. R31.1-R31.16, 2007. **(IF: 6.589;** Times Cited: 2; Ranking 7/138 in BIOTECHNOLOGY & APPLIED MICROBIOLOGY**)**

代表作 3: C.-H. Tung and **J.-M. Yang*,** "fastSCOP: a fast web server for recognizing protein structural domains and SCOP superfamilies," *Nucleic Acids Research*, pp. W438-W443, 2007. **(IF: 6.954;** Times Cited: 3; Ranking 29/263 in BIOCHEMISTRY & MOLECULAR BIOLOGY**)**

大規模基因定序之後隨之而來的問題就是如何確定這些基因序列的生物功能，BLAST 是以序列比對，提供功能註解最常用的工具。另一方面，由於結構基因體學(structural genomics)及解蛋白質立體結構的技術愈臻成熟，在 2007 年增加的新結構就有 7, 273 個，目前(2008/9)蛋白質結構資料(PDB)有 53,000 結構。這時結構－功能之間就產生了愈來愈大的鴻溝，因此如何在結構比對上發展類似 BLAST 的工具，是結構生物資訊學上最重要的議題。**代表作 1 及代表作 2** 即針對上述議題所進行的研究。我們發展高速蛋白質結構搜尋與分類的軟體 3D-BLAST，這是第一個結構搜尋軟體的速度，可與 BLAST 在搜尋蛋白質胺基酸序列一樣快，同時具備 BLAST 的優點與操作介面，也就是能提供可信的統計基礎(e-value)及高效率的搜尋能力，使用者極易使用此軟體。3D-BLAST 可在 3 秒內，搜尋三萬個以上的蛋白質三級

結構，比一般的蛋白質結構比對軟體約快 20,000 倍(如 CE、DALI)。3D-BLAST 的服務網址是在 http://3d-blast.life.nctu.edu.tw/。這一系列的研究成果發表在 *Genome Biology* (IF:6.589)與 *Nucleic Acids Research* (IF:6.954)。*Genome Biology* 的影響係數是 6.589，在 BIOTECHNOLOGY & APPLIED MICROBIOLOGY 的 138 種期刊中，排行第七。*Nucleic Acids Research* 的影響係數是 6.954，在 BIOCHEMISTRY & MOLECULAR BIOLOGY 的 263 種期刊中，排行第 29 名。此篇論文被 *Nucleic Acids Research* 期刊從當期 33 篇論文中，選為熱門下載論文(hot papers)，也被交通大學選為刊登在“Science jobs and vacancies from Nature jobs” 上。

另外蛋白質結構分類資料庫，對於瞭解蛋白質功能及演化關係有重大價值，最常用的 SCOP and CATH 就是這類資料庫，目前這二個資料庫採用專家分類或半自動分類，更改的週期常常超過半年，對於新蛋白質結構的快速累積，無法即時提供服務。因此如何自動且準確的分類是結構生物資訊學急需解決的問題。**代表作 3** 即針對此問題，發展高速蛋白質結構分類的工具 fastSCOP，此工具以 3D-BLAST 為基礎，並整合結構比對軟體。fastSCOP 可在 9 小時內，自動辨識約 7300 蛋白質結構的結構功能單元及分類，準確度超過 95%。

3D-BLAST 是第一個在蛋白質結構搜尋上，同時具備 BLAST 優點與操作介面的工具，自 2006 年 7 月發表後，從世界 44 幾個國家超過 5,100 人次使用此服務。這些論文自 2007 年起，被引用次數已超過 13 次。部分引用本研究的期刊論文列舉如下：

1. Alves, R., E. Vilaprinyo, and A. Sorribas. 2008. *Current Bioinformatics* **3:** 98-129.
2. Aung, Z. and K.L. Tan. 2007. *Drug Discovery Today* **12:** 732-739.
3. Dong, Q.W., X.L. Wang, and L. Lin. 2008. *Proteins-Structure Function and Bioinformatics* **72:** 353-366.
4. Giuseppe, P.O., F.O. Neves, A.L.T.O. Nascimento, and B.G. Guimaraes. 2008. *Journal of Structural Biology* **163:** 53-60.
5. Hetenyi, C., U. Maran, A.T. Garcia-Sosa, and M. Karelson. 2007. *Bioinformatics* **23:** 2678-2685.
6. Offmann, B., M. Tyagi, and A.G. de Brevern. 2007. *Current Bioinformatics* **2:** 165-202.
7. Tyagi, M., A.G. De Brevern, N. Srinivasan, and B. Offmann. 2008. *Proteins-Structure Function and Bioinformatics* **71:** 920-937.
8. Wu, F.M., J.H. Zhang, J.P. Sun, H. H.D., P. Ji, W.S. Chu, M.J. Yu, F.F. Yang, Z.Y. Wu, J.H. Wu, and Y.Y. Shi. 2008. *Proteins-Structure Function and Bioinformatics* **71:** 514-518

電腦輔助藥物設計 (代表作 4 and 5)

代表作 4: **J.-M. Yang*** and C.-C. Chen, "GEMDOCK: A generic evolutionary method for molecular docking," *Proteins: Structure, Function, and Bioinformatics*, vol. 55, pp. 288-304, 2004. (**IF: 3.354**, **Times Cited: 28;** Ranking 18/69 in BIOPHYSICS)

代表作 5: **J.-M. Yang*** Y.-F. Chen, T.-W. Shen, B. S. Kristal, and D. F. Hsu*, "Consensus scoring criteria for improving enrichment in virtual screening," *Journal of Chemical Information and Modeling*, vol. 45, pp. 1134-1146, 2005. (**IF: 2.986; Times Cited: 25**; **Ranking 6/92** in COMPUTER SCIENCE, INFORMATION SYSTEMS)

實際應用論文:

1. **J.-M. Yang*** and T.-W. Shen, "A pharmacophore-based evolutionary approach for screening selective estrogen receptor modulators," *Proteins: Structure, Function, and Bioinformatics*, vol. 59, pp. 205-220, 2005. (**IF: 3.354, Times Cited: 13;** Ranking 18/69 in BIOPHYSICS)
2. **J.-M. Yang*** "Development and evaluation of a generic evolutionary method for protein-ligand docking," *Journal of Computational Chemistry*, vol. 25, pp. 843-857, 2004. (IF: 4.297; Ranking 17/127 in CHEMISTRY, MULTIDISCIPLINARY)

3. [flaviviruses envelop protein] **J.-M. Yang**, Y.-F. Chen, Y.-Y. Tu, K.-R. Yen, and Y.-L. Yang*****, "Combinatorial computation approaches identifying tetracycline derivates as flaviviruses inhibitors," *PLoS ONE*, pp. e428.1- e428.12, 2007.
4. [ß-lactoglobulin] M.-C. Yang, H.-H. Guan, M.-Y. Liu, Y.-H. Lin, **J.-M. Yang**, W.-L. Chen, C.-J. Chen, and Simon J. T. Mao*, "Crystal structure of a secondary vitamin D_3 binding site of milk ß-lactoglobulin," *Proteins: Structure, Function, and Bioinformatics*, vol. 71, pp. 1197-1210, 2008. (**IF: 3.354;** Ranking 18/69 in BIOPHYSICS)
5. [endo-chitosanase to an exo-chitosanase] Y.Y. Yao, K.L. Shrestha, Y.J. Wu, H.J. Tasi, C.C. Chen, **J.-M. Yang**, A. Ando, C.Y. Cheng, Y.K. Li*, "Structural simulation and protein engineering to convert an endo-chitosanase to an exo-chitosanase," *Protein Engineering Design & Selection*, 2008, vol. 21, pp. 561-566. (**IF: 2.662;** Ranking 43/138 in BIOTECHNOLOGY & APPLIED MICROBIOLOGY)
6. [influenza virus neuraminidase] H.-C. Hung, C.-P. Tseng, **J.-M Yang**, Y.-W. Ju, S.-N. Tseng, Y.-S. Chao, H.-P. Hsieh, S.-R. Shih, J.T.-A. Hsu*, "Aurintricarboxylic acid inhibits influenza virus neuraminidase," *Antiviral Research*, 2008, in revision (**IF: 3.358;** Ranking 50/208 in PHARMACOLOGY & PHARMACY)
7. [ß-lactoglobulin] M.-C. Yang, H.-H. Guan, **J.-M. Yang**, C.-N. Ko, M.-Y. Liu, Y.-H. Lin, C.-J. Chen*, and Simon J. T. Mao*, " Rational design for crystallization of ß-Lactoglobulin and vitamin D3 complex: Reveal of a secondary binding site," *Crystal Growth & Design*, in revision (**IF: 4.046;** Ranking 1/25 in CRYSTALLOGRAPHY)

電腦輔助藥物設計的核心包含分子對接(molecular docking)、pharmacophore model、post-analysis、及 QSAR，我們在這四核心步驟皆有相關的成果發表。**代表作 4** 是根據我們家族競爭演化方法，發展分子對接的軟體 GEMDOCK，此軟體的服務網址是在 http://gemdock.life.nctu.edu.tw/dock/，其準確度超過目前世界上常用的工具(如 DOCK, GOLD, FlexX 等)。自此軟體發表後，從世界各地已有超過千人次下載 GEMDOCK。在實際應用上，我們與國內外超過十個實驗室合作，成功應用我們的軟體在不同的藥物標的蛋白上：如 influenza virus neuraminidase (國家衛生院：許祖安教授)、flaviviruses envelop protein (交通大學：楊昀良教授)、幽門桿菌之 shikimate kinase(清華大學：王雯靜教授)、bovine beta-lactoglobulin(交通大學：毛仁淡教授)、sulfotransferase、imidase(交通大學：楊裕雄教授)、geranylgeranyl pyrophosphate synthase(中央研究院：梁博煌教授)等，部分應用成果已經發表在該領域的好期刊上(如 *PLoS ONE*; *Proteins: Structure, Function, and Bioinformatics*; *Protein Engineering Design & Selection*)。從 2004 年起此論文被引用次數已超過 28 次。

計分系統(scoring system)的不完善及無法反應 binding affinity，被視為是電腦輔助藥物設計困難的 open problem。我們以演化式 pharmacophore model 提升藥物篩選的準確度。此方法利用蛋白質的演化、藥物小分子的官能基(functional group)、蛋白質-小分子交互作用，提升辨識藥物標 pharmacophore model 的可信度。此 pharmacophore model 具創見，並能提升藥虛擬物篩選的解釋能力及準確度。另外前人相關研究證實 Consensus scoring 可提昇虛擬藥物篩選的準確度，但這些研究多著重在實証的結果上。如何以理論分析證明何時(when)及如何(how)作計分系統的組合，是目前重大的研究議題。在**代表作 5** 中我們證明計分系統的組合需具備二個條件才能有效提昇藥物篩選的準確度：第一是每個組合的計分系統需要有好的預測能力；第二是組合的計分系統間要具備大的差異度。這篇論文是此領域中，第一個證明計分系統的組合條件，已引起相關學者的重視與討論，從 2005 年起此論文被引用次數已超過 25 次。

我們在電腦輔助藥物設計領域上，發表多篇論文在相關領域好的期刊上。我們合作的實驗室，從 2007 起相關的成果(如 flaviviruses envelop protein、bovine beta-lactoglobulin、influenza virus neuraminidase neuraminidase)也陸續發表或準備投稿中。另外我們也開發此軟體之圖形介面，此圖形軟體獲得 2007 年國家新創獎，對於大幅縮短分子對接模擬的學習時間，有決定性

的提升。一些研究人員也已使用我們的軟體完成其論文。自 2004 年起，我們相關的論文被引用次數已超過 70 次。部分引用本研究的期刊論文列舉如下:

1. Celik, L., S. Sinning, K. Severinsen, C.G. Hansen, M.S. Moller, M. Bols, O. Wiborg, and B. Schiott. 2008. ***Journal of the American Chemical Society*** **130:** 3853-3865.
2. Coupez, B. and R.A. Lewis. 2006. ***Current Medicinal Chemistry*** **13:** 2995-3003.
3. Feher, M. 2006. ***Drug Discovery Today*** **11:** 421-428.
4. Joseph-McCarthy, D., J.C. Baber, E. Feyfant, D.C. Thompson, and C. Humblet. 2007. ***Current Opinion in Drug Discovery & Development*** **10:** 264-274.
5. Knox, A.J.S., M.J. Meegan, V. Sobolev, D. Frost, D.M. Zisterer, D.C. Williams, and D.G. Lloyd. 2007. ***Journal of Medicinal Chemistry*** **50:** 5301-5310.
6. Li, Z. and T. Lazaridis. 2007. ***Physical Chemistry Chemical Physics*** **9:** 573-581.
7. Radestock, S., M. Bohm, and H. Gohlke. 2005. ***Journal of Medicinal Chemistry*** **48:** 5466-5479.
8. Robeits, B.C. and R.L. Mancera. 2008. ***Journal of Chemical Information and Modeling*** **48:** 397-408.
9. Seifert, M.H.J., J. Kraus, and B. Kramer. 2007. ***Current Opinion in Drug Discovery & Development*** **10:** 298-307.
10. Shi, Y.H. 2007. ***Drug Discovery Today*** **12:** 440-445.
11. Thomsen, R. and M.H. Christensen. 2006. MolDock: ***Journal of Medicinal Chemistry*** **49:** 3315-3321.
12. van Dijk, A.D.J. and A. Bonvin. 2006. ***Bioinformatics*** **22:** 2340-2347.
13. Verdonk, M.L., G. Chessari, J.C. Cole, M.J. Hartshorn, C.W. Murray, J.W.M. Nissink, R.D. Taylor, and R. Taylor. 2005. ***Journal of Medicinal Chemistry*** **48:** 6504-6515.
14. Whittle, M., V.J. Gillet, and P. Willett. 2006. ***Journal of Chemical Information and Modeling*** **46:** 2193-2205.
15. Willett, P. 2006. ***QSAR & Combinatorial Science*** **25:** 1143-1152.
16. Wishart, D.S. 2005. ***Drug Metabolism Reviews*** **37:** 279-310.

三、曾獲國內外學術獎及其他學術榮譽之名稱及日期，並作簡要說明。

- 獲得國立交通大學 2006 傑出人士榮譽獎勵。
- 博士畢業(2001/1)後，六年內從助理教授(2001/08-2004/07)升等到副教授(2004/08-2007/07)及教授(2007/8 起)。在二階段的升等過程中，14 位升等外審學者皆一致**極力推薦 (最高級分)**我的升等申請案。大部分外審學者認為『我在電腦輔助藥物設計及結構生物資訊領域中，有獨特及持續性的研究，研究成果也經常被引用，具有重要貢獻』。
- 國科會生物資訊跨領域研究計畫總計劃主持人，研究主持費為每月 15,000 元。在 2007 年因執行績效優,國科會主動增核一名博士後研究。
- Win the prize of 2001 Best M.S. and Ph. D. Dissertation Award hosted by IICM
- 獲得 2007 **國家新創獎 (獲獎作品:iGEMDOCK: 整合自動分子嵌合、虛擬篩選與分析之圖形介面化藥物設計系統)。**「國家新創獎」由國家生技醫療產業策進會主辦，旨在提供國內生技醫療領域研發成果一個競逐舞台，並經過產、官、學、研、行銷、財金、創投等專業學者組成之評審團審核，藉由公正、專業的評審機制及市場洞見，一方面獎勵卓越研發成果，一方面針對無形資產、智慧財產進行公正評價及引薦技術轉移合作。

  【評審評語】

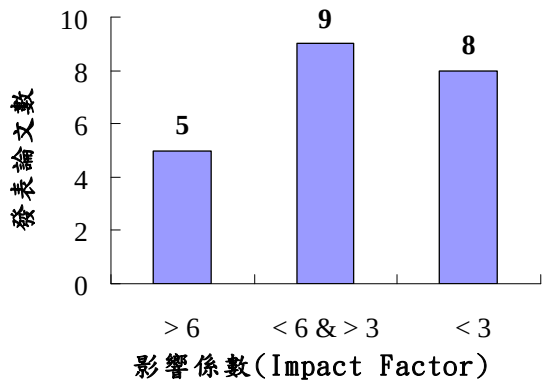
  電腦輔助藥物設計軟體：iGEMDOCK 是一套自動化分子嵌合、虛擬篩選以及篩選後分析整合程式，具操作簡便的圖形介面，並可即時(real-time)將分子立體結構視覺化。目前 iGEMDOCK 已成功應用在 sulfotransferase、胺氧化酵素(amine oxidase)、醯亞胺水解酵素(imidase)三種酵素上，並且經實驗證實後發現三個的新抑制劑(inhibitors)或基質(substrates)。在虛擬藥物篩選上，也發現兩個新的 dengue virus 鞘蛋白抑制劑。iGEMDOCK 建構於 GEMDOCK，應用在虛擬藥物篩選上具備高準確度、操作方便、快速、易於觀察分子嵌合構形等優點，並且提供篩選後分析的功能，為先導藥物開發提供了一個快速而可靠的平台。

五、其他資料：如擔任國際重要學術學會理監事、國際知名學術期刊編輯或評審委員等。(以上四項均請填寫申請截止日前五年內之資料)

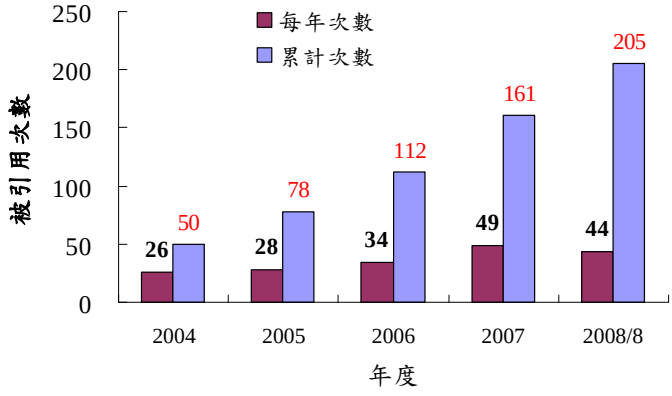
- 2007/2~迄今　台灣生物資訊學會理事
- 2005/8-2008/7　國科會**生物資訊跨領域**研究計畫**總計劃主持人**
- 2008/8-2011/7　國科會**生物資訊跨領域**研究計畫**總計劃主持人 (**計畫名稱: 物系統內分子交互作用及生化路徑之大規模分析--(總計畫與子計畫一)以生化網路演化關係研究分子交互作用與生化路徑)
- 2008/5-2011/4　國科會基因體醫學國家型科技計畫**主持人**　(計畫名稱：分子交互作用網路及結構功能演化在醫藥應用之研究)
- 2001/08 至 2004/07　國立交通大學生物資訊研究所 **助理教授**
- 2004/08 至 2007/07　國立交通大學生物資訊研究所 **副教授**
- 2007/08 起 訖今　國立交通大學生物資訊研究所 **教授兼所長**
- 論文指導獎: 中華民國資訊學會碩士論文獎 （學生沈再威, 2004）

- 論文指導獎: 中華民國資訊學會碩士論文獎 （學生董其樺, 2005）
- 指導碩士生陳永強獲得交大生物科技學院海報論文比賽 第二名（2006）
- 指導博士生董其樺獲得交大生物科技學院海報論文比賽 第一名（2007）
- 指導碩士生陳祐德獲得交大生物科技學院海報論文比賽 第一名（2008）
- 下列期刊評審委員:
    - *Nucleic Acids Research*
    - *Proteins: Structure, Function, and Bioinformatics*
    - *BMC Bioinformatics*
    - *BMC Structural Biology*
    - *Acta Pharmacologica Sinica*
    - *Journal of Computational Chemistry*
    - *Journal of Chemical Information and Modeling*
    - *IEEE Transactions on Knowledge and Data Engineering*
    - *Engineering Optimization*
    - *Letters in Drug Design & Discovery*
    - *Journal of Information Science and Engineering*

近五年我共發表 22 篇 SCI 期刊論文，其中影響係數(Impact Factor, IF)超過 6.0 共有五篇(圖一)，這五篇本人皆為通信作者。每年平均發表的 SCI 論文篇數約 4 篇，每篇論文的影響係數平均為 3.59。另外，在論文被引用次數方面(根據 WOS)，近五年總共被引用次數為 192 次(圖二)，我的 h-index 為 9，從 2000 至 2008 共發表 33 篇 SCI 論文，總共被引用次數為 205 次，平均每篇文章被引用次數為~6.2 次。在論文發表及被引用次數皆是逐年提升。



圖一: 期刊論文數與影響係數之關係圖



圖二: SCI 論文被引用次數與年份之關係圖

Journal Papers (* corresponding author) (order by publication date)

1. Y.-Y. Chiu, J.-K. Hwang, **J.-M. Yang***, "Soft energy function and generic evolutionary method for discriminating native from non-native protein conformations," *Journal of Computational Chemistry*, vol. 29, pp. 1364-1373, 2008 (**IF: 4.297)**
2. Y.-L. Chang, H.-K. Tsai, C.-Y. Kao, Y.-C. Chen, Y.-J. Hu, and **J.-M. Yang***, "Evolutionary

conservation of DNA-contact residues in DNA-binding domains," *BMC Bioinformatics*, vol. 9 (S6), pp. S3.1~S3.9, 2008 (**IF: 3.493**).

3. C.-Y. Yang, C.-H. Chang, T.-C. Lin, Y.-L. Yu, S.-A. Lee, C.-C. Yen, **J.-M. Yang,** J.-M. Lai, Y.-R. Hong, T.-L. Tseng, K.-M. Chao, and C.-Y. Huang***,** "PhosphoPOINT: a comprehensive human kinase interactome and phospho-protein database," *Bioinformatics*, vol. 24, pp. i14-i20, 2008. (**IF: 5.039**)
4. M.-C. Yang, H.-H. Guan, M.-Y. Liu, Y.-H. Lin, **J.-M. Yang**, W.-L. Chen, C.-J. Chen, and Simon J. T. Mao*, "Crystal structure of a secondary vitamin D_3 binding site of milk ß-lactoglobulin," *Proteins: Structure, Function, and Bioinformatics*, vol. 71, pp. 1197-1210, 2008. (**IF: 3.354**)
5. Y.Y. Yao, K.L. Shrestha, Y.J. Wu, H.J. Tasi, C.C. Chen, **J.-M. Yang**, A. Ando, C.Y. Cheng, Y.K. Li*, "Structural simulation and protein engineering to convert an endo-chitosanase to an exo-chitosanase," *Protein Engineering Design & Selection*, vol. 21, pp. 561-566, 2008. (**IF: 2.662)**
6. C.-H. Tung, J.-W. Huang and **J.-M. Yang***, "Kappa-alpha plot derived structural alphabet and BLOSUM-like substitution matrix for fast protein structure database search," *Genome Biology*, vol. 8, pp. R31.1~R31.16, 2007. (**IF: 6.589;** Times Cited: 2)
7. C.-H. Tung and **J.-M. Yang***, "fastSCOP: a fast web server for recognizing protein structural domains and SCOP superfamilies," *Nucleic Acids Research*, pp. W438-W443, 2007. (**IF: 6.954;** Times Cited: 3)
8. Y.-C. Chen, Y.-S. Lo, W.-C. Hsu, and **J.-M. Yang***, "3D-partner: a web server to infer interacting partners and binding models, " *Nucleic Acids Research*, pp. W561-W567, 2007. (**IF: 6.954;** Times Cited: 2)
9. **J.-M. Yang**, Y.-F. Chen, Y.-Y. Tu, K.-R. Yen, and Y.-L. Yang***, "**Combinatorial computation approaches identifying tetracycline derivates as flaviviruses inhibitors," *PLoS ONE*, pp. e428.1- e428.12, 2007.
10. **J.-M. Yang*** and C.-H. Tung, "Protein structure database search and evolutionary classification," *Nucleic Acids Research*, vol. 34, pp. 3646-3659, 2006. (**IF: 6.954;** Times Cited: 8)
11. C.-C. Chen, J.-K. Hwang and **J.-M. Yang***, "$(PS)^2$: Protein structure prediction server," *Nucleic Acids Research*, pp. W152–W157, 2006. (**IF: 6.965;** Times Cited: 2)
12. **J.-M. Yang*** Y.-F. Chen, T.-W. Shen, B. S. Kristal, and D. F. Hsu, "Consensus Scoring Criteria for Improving Enrichment in Virtual Screening," *Journal of Chemical Information and Modeling*, vol. 45, pp. 1134-1146, 2005. (**IF: 2.986**; Times Cited: 25)
13. **J.-M. Yang*** and T.-W. Shen, "A pharmacophore-based evolutionary approach for screening selective estrogen receptor modulators," *Proteins: Structure, Function, and Bioinformatics*, vol. 59, pp. 205-220, 2005. (**IF: 3.354**; Times Cited: 13)
14. **J.-M. Yang*** and C.-C. Chen, "GEMDOCK: A generic evolutionary method for molecular docking," *Proteins: Structure, Function, and Bioinformatics*, vol. 55, pp. 288-304, 2004. (**IF: 3.354**; Times Cited: 28)

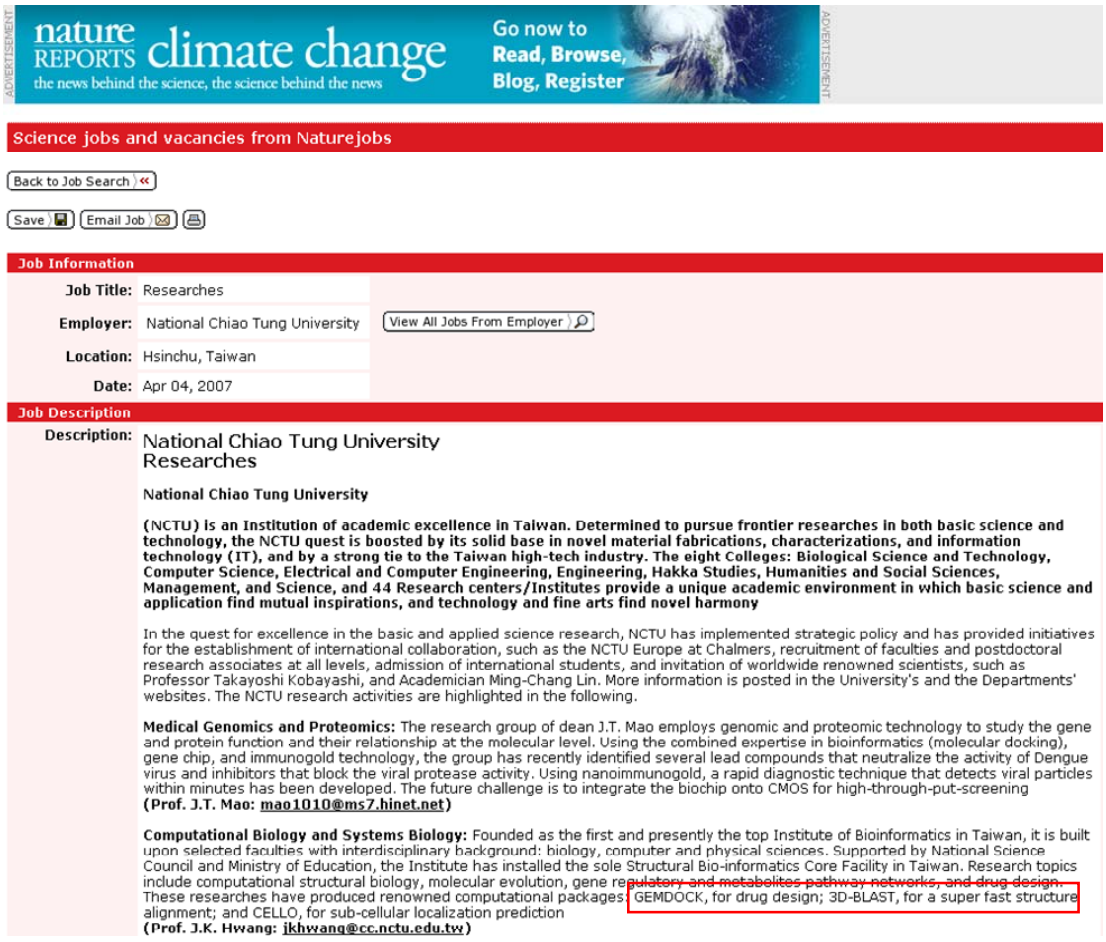
15. **J.-M. Yang*** "Development and evaluation of a generic evolutionary method for protein-ligand docking," *Journal of Computational Chemistry*, vol. 25, pp. 843-857, 2004. (**IF: 4.297;** Times Cited: 3)
16. H.-K. Tsai, **J.-M. Yang**, Y.-F. Tsai, and C-Y Kao, "An evolutionary algorithm for large traveling salesman problems," *IEEE Transactions on Systems Man and Cybernetics Part B-Cybernetics*, vol. 34, pp. 1718-1729, 2004. (**IF: 1.353;** Times Cited: 7)
17. H.-K. Tsai, **J.-M. Yang**, Y.-F. Tsai, and C-Y Kao, "An evolutionary approach for gene expression patterns," *IEEE Transaction on Information Technology in Biomedicine*, vol. 8, pp. 69-78, 2004. (**IF: 1.436;** Times Cited: 4)
18. H.-K. Tsai, **J.-M. Yang**, and C-Y Kao, "Issues of designing genetic algorithms for traveling salesman problems", vol. 8, pp. 689-697, *Soft Computing*, 2004. (**IF: 0.607**)
19. C.-C. Chuang, C-Y Chen, **J.-M. Yang**, P.-C. Lyu, J.-K. Hwang, "The detection of protein structural similarity using disulfide-binding patterns," *Proteins: Structure, Function, and Genetics*, vol. 53, pp. 1-5, 2003. (**IF: 3.354;** Times Cited: 22)
20. C.-S. Yu, J.-Y. Wang, **J.-M. Yang,** P.-C. Lyu, C.-J. Lin, J.-K. Hwang, "Fine-grained protein fold assignment by support vector machines using generalized n–peptide coding schemes and jury voting from multiple parameter sets," *Proteins: Structure, Function, and Genetics*, vol. 50, pp. 531-536, 2003. (**IF: 3.354;** Times Cited: 15)
21. Y.-W. Chu***** and **J.-M. Yang***, "Finding regularity in various types of secondary protein structures," *Journal of Information Science and Engineering*, vol. 19, pp.943-952, 2003. (**IF:0.202**)
22. E.-S. Lin, **J.-M. Yang**, and Y.-S. Yang, "Modeling the binding and inhibition mechanism of nucleotide and sulfotransferase using molecular docking," *Journal of the Chinese Chemical Society*, vol. 50, pp. 655-663, 2003. (**IF:0.643;** Times Cited: 1)
23. H.-K. Tsai, **J.-M. Yang**, Y.-F. Tsai, and C-Y Kao, "A heterogeneous selection genetic algorithm for traveling salesman problems," *Engineering Optimization*, pp. 297-311, 2003. (**IF:0.571;** Times Cited: 2)

Conference Papers

1. K-C Hsu, Y-F Chen, and **J-M Yang***, "Binding affinity analysis of protein-ligand complexes," *2nd International Conference on Bioinformatics and Biomedical Engineering*, pp. 167-171, 2008.
2. J-W Huang, C-C Chen, and **J-M Yang***, "Identifying critical positions and rules of antigenic drift for influenza A/H3N2 viruses," *2nd International Conference on Bioinformatics and Biomedical Engineering*, pp. 249-252, 2008.
3. K.-P. Liu and **J.-M Yang*,** "A Gaussian evolutionary method for predicting protein-protein interaction sites," *Lecture Notes in Computer Science*, vol. 4447, pp. 143-153, 2007.
4. Y.-L. Chang, H.-K. Tsai, C.-Y. Kao and **J.-M. Yang***, "Evolutionary conservation of DNA-contact residues in DNA-binding domains," *International Multi-Symposiums on Computer and Computational Sciences* (IMSCCS07), pp. 9-16, 2007.

5. **J.-M. Yang***, L.-S. Chang, and K.-P. Liu, "ARPPI: A knowledge-based model for protein-protein interactions," *Sixth International Conference on Bioinformatics* (InCoB2007), 2007.
6. Y.-C. Chen, H.-C. Chen and **J.-M Yang*,** "A 3D-domain annotated protein-protein interaction database," *Genome Informatics*, vol. 17, pp. 206-215, 2006.
7. Y.-Y. Chiu, J.-K. Hwang and **J.-M. Yang**, "GEMSCORE: A new empirical energy function for protein folding," *IEEE Symposium on Computational Intelligence in Bioinformatics and Computational Biology* (*CIBCB 2005*), pp. 303-310, 2005.
8. Y.-C. Chen, **J.-M Yang**, C.-H. Tsai, C.-Y. Kao, "GEMPLS: A new QSAR method combining generic evolutionary method and partial least squares", *Lecture Notes in Computer Science*, vol. 3449, pp. 125-135, 2005.
9. Y.-C. Chen, **J.-M Yang**, C.-H. Tsai, C.-Y. Kao, "Comparative molecular binding energy analysis of HIV-1 protease inhibitors using genetic algorithm-based partial least squares method," *Lecture Notes in Computer Science*, vol. 3103, pp. 385-386, 2004.

Appendix A [nature reports]: 3D-BLAST and GEMDOCK are selected by National Chiao Tung University and reported on "Science jobs and vacancies from Nature jobs"



Appendix B: Top ten of the most cited papers in my search career since 2000

Use the checkboxes to remove individual items from this Citation Report or restrict to items processed between 1977 and 2008 Go	2004 ◄	2005	2006	2007	2008 ►	Total	Average Citations per Year
	26	28	34	49	44	205	20.50
1. Title: GEMDOCK: A generic evolutionary method for molecular docking Author(s): Yang JM, Chen CC Source: **PROTEINS-STRUCTURE FUNCTION AND BIOINFORMATICS** Volume: **55** Issue: **2** Pages: **288-304** Published: **MAY 1 2004**	1	8	7	3	9	28	5.60
2. Title: Consensus scoring criteria for improving enrichment in virtual screening Author(s): Yang JM, Chen YF, Shen TW, et al. Source: **JOURNAL OF CHEMICAL INFORMATION AND MODELING** Volume: **45** Issue: **4** Pages: **1134-1146** Published: **JUL-AUG 2005**	0	0	6	9	10	25	6.25
3. Title: Relationship between protein structures and disulfide bonding patterns Author(s): Chuang CC, Chen CY, Yang JM, et al. Source: **PROTEINS-STRUCTURE FUNCTION AND GENETICS** Volume: **53** Issue: **1** Pages: **1-5** Published: **OCT 1 2003**	5	7	2	5	3	22	3.67
4. Title: Flexible ligand docking using a robust evolutionary algorithm Author(s): Yang JM, Kao CY Source: **JOURNAL OF COMPUTATIONAL CHEMISTRY** Volume: **21** Issue: **11** Pages: **988-998** Published: **AUG 2000**	4	1	0	1	0	16	1.78
5. Title: Fine-grained protein fold assignment by support vector machines using generalized npeptide coding schemes and jury voting from multiple-parameter sets Author(s): Yu CS, Wang JY, Yang JM, et al. Source: **PROTEINS-STRUCTURE FUNCTION AND BIOINFORMATICS** Volume: **50** Issue: **4** Pages: **531-536** Published: **MAR 1 2003**	3	2	3	5	1	15	2.50
6. Title: A pharmacophore-based evolutionary approach for screening selective estrogen receptor modulators Author(s): Yang JM, Shen TW Source: **PROTEINS-STRUCTURE FUNCTION AND BIOINFORMATICS** Volume: **59** Issue: **2** Pages: **205-220** Published: **MAY 1 2005**	0	2	4	5	2	13	3.25
7. Title: GEM: A Gaussian evolutionary method for predicting protein side-chain conformations Author(s): Yang JM, Tsai CH, Hwang MJ, et al. Source: **PROTEIN SCIENCE** Volume: **11** Issue: **8** Pages: **1897-1907** Published: **AUG 2002**	2	2	1	3	1	10	1.43
8. Title: A robust evolutionary algorithm for training neural networks Author(s): Yang JM, Kao CY Source: **NEURAL COMPUTING & APPLICATIONS** Volume: **10** Issue: **3** Pages: **214-230** Published: **2001**	2	0	3	2	2	10	1.43
9. Title: An evolutionary algorithm for the synthesis of multilayer coatings at oblique light incidence Author(s): Yang JM, Kao CY Source: **JOURNAL OF LIGHTWAVE TECHNOLOGY** Volume: **19** Issue: **4** Pages: **559-570** Published: **APR 2001**	4	1	2	0	2	10	1.25
10. Title: Protein structure database search and evolutionary classification Author(s): Yang JM, Tung CH Source: **NUCLEIC ACIDS RESEARCH** Volume: **34** Issue: **13** Pages: **3646-3659** Published: **2006**	0	0	0	3	5	8	2.67