



DIPLOMSKI RAD BR. 2016

Klasifikacija histopatoloških snimaka dijelova limfnih čvorova pomoću strojnog učenja

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ZAGREB, 3.7.2019.

Sadržaj

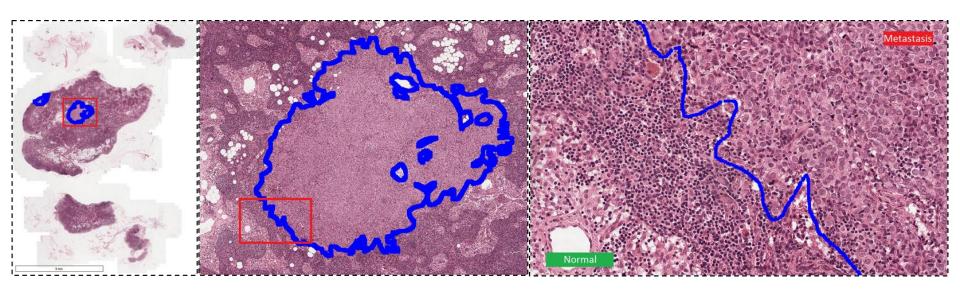
- Histopatološke slike
- Skup podataka
- Korišteni modeli
- Usporedba načina učenja
- Usporedba transformacija za proširivanje skupa podataka

- Rezultati
- Zaključak

Histopatološke slike

- Histopatologija
- Tehnika snimanja čitavog preparata (WSI)
- Camelyon16 natjecanje

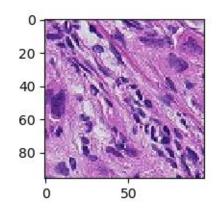
Primjer



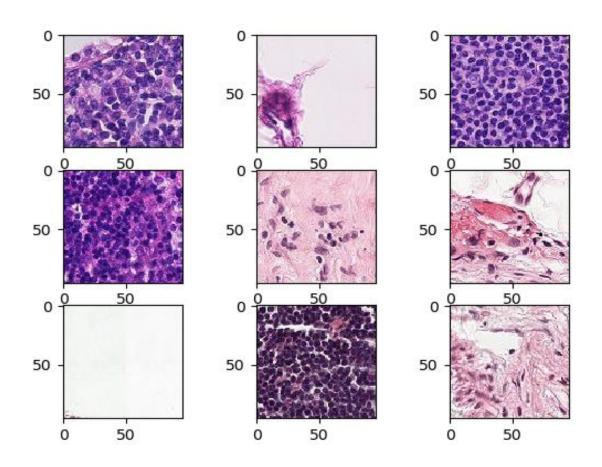
- Izvor: Camelyon 16 natjecanje
- Veličina: $200,000 \times 100,000$ slikovnh elemenata

Skup podataka - PatchCamelyon

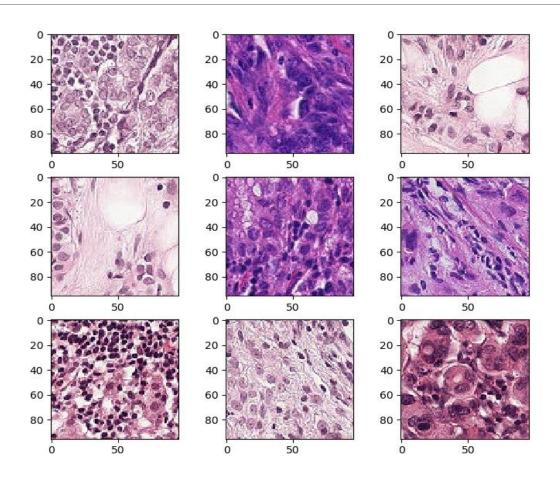
- ■96 × 96 slikovna elementa
- Binarne oznake
 - 0 ne sadrži tumor
 - 1 sadrži tumor
- ■Veličina 327,680 slika
 - Skup za učenje 80%
 - Skup za validaciju 10%
 - Skup za testiranje 10%
- Jednaki omjer pozitivnih i negativnih primjera



PCam - negativni primjeri



PCam - pozitivni primjeri



Zadatak klasifikacije

- Binarna klasifikacija
 - Slika -> {0, 1}
- ■Odabir pristupa → modeli dubokog učenja

Korišteni modeli

Naziv modela	Broj parametara	Broj slojeva s
		aktivacijskom funkcijom
AlexNet	57,877,824	8
ResNet18	11,186,645	18
DenseNet121	6,954,881	121
Inception-v3	27,161,264	98

Eksperimenti 1/2

- Usporedba korištenih modela
- Korištenje različitih stopa učenja
- Analiza utjecaja učenja prijenosom značajki
 - Učenje ispočetka
 - Učenje prijenosom značajki i mijenjanje svih slojeva
 - Učenje prijenosom značajki i mijenjanje zadnjeg sloja
- > Prijenos značajki sa skupa podataka ImageNet

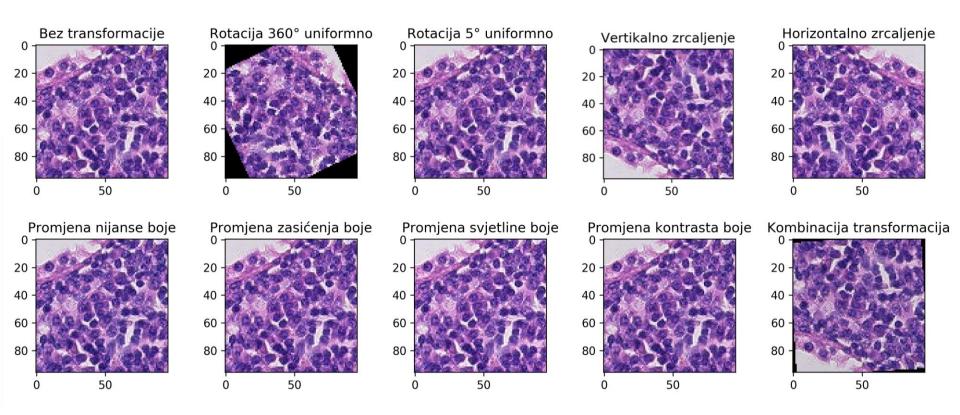
Dodatne napomene

- Algoritam za učenje ADAM
- Veličina mini-grupe: 32
- Rano zaustavljanje
- •Stopa učenja: $\{10^{-3}, 10^{-4}, 10^{-5}, 10^{-6}\}$
- Gubitak unakrsne entropije
- Mjere usporedbe: točnost, F1, površina ispod krivulje ROC

Eksperimenti 2/2

- Analiza utjecaja transformacija za proširivanje skupa podataka
- Model DenseNet
 - Prijenos značajki sa skupa podataka ImageNet
 - Stopa učenja: 10^{-4}

Transformacije



Rezultati – učenje ispočetka (1)

Naziv	Stopa učenja	Točnost	Mjera F1	AUC ROC
AlexNet	10^{-5}	0.7847	0.7763	0.8662
ResNet	10^{-3}	0.8123	0.7898	0.9042
DenseNet	10^{-3}	0.8125	0.7862	0.8788

Rezultati – učenje prijenosom značajki – svi slojevi (2)

Naziv	Stopa učenja	Točnost	Mjera F1	AUC ROC
AlexNet	10^{-4}	0.7991	0.7720	0.9048
ResNet	10^{-4}	0.8518	0.8334	0.9295
DenseNet	10^{-4}	0.8670	0.8522	0.9409
Inception-v3	10^{-3}	0.8884	0.8872	0.9489

Rezultati – učenje prijenosom značajki – zadnji sloj (3)

Naziv	Stopa učenja	Točnost	Mjera F1	AUC ROC
AlexNet	10^{-6}	0.7592	0.7301	0.8496
ResNet	10^{-4}	0.7822	0.7676	0.8637
DenseNet	10^{-3}	0.8065	0.8009	0.8874
Inception-v3	10^{-4}	0.8210	0.8149	0.9022

Rezultati – usporedba načina učenja

Naziv modela	AUC ROC (1)	AUC ROC (2)	AUC ROC (3)
AlexNet	0.8662	0.9048	0.8496
ResNet	0.9042	0.9295	0.8637
DenseNet	0.8788	0.9409	0.8874
Inception-v3	-	0.9489	0.9022

- (1) učenje ispočetka
- (2) prijenos značajki svi slojevi
- (3) prijenos značajki zadnji sloj

Rezultati - transformacije

Transformacija	Točnost	Mjera F1	AUC ROC
Bez transformacija	0.8670	0.8522	0.9409
Rotacija slike 360°	0.8447	0.8266	0.9110
Rotacija slike 5°	0.8719	0.8619	0.9407
Vertikalno zrcaljenje	0.8881	0.8816	0.9563
Horizontalno zrcaljenje	0.8766	0.8701	0.9419
Promjena nijanse	0.8704	0.8577	0.9473
Promjena zasićenja	0.8566	0.8425	0.9271
Promjena svjetline	0.8669	0.8549	0.9346
Promjena kontrasta	0.8714	0.8637	0.9425
Kombinacija	0.8867	0.8798	0.9589

Zaključak 1/2

- Uspoređeni su različiti modeli za klasifikaciju histopatoloških snimaka limfnih čvorova
 - AlexNet, ResNet, DenseNet, Inception-v3
- Učenje prijenosom značajki sa skupa podataka ImageNet i učenje čitavog modela se pokazalo najbolje
- Model s najboljim rezultatima Inception-v3
- Ispitan je utjecaj transformacija za proširivanje skupa podataka
 - Najbolji rezultat: vertikalno zrcaljenje, kombinacija transformacija
 - Negativan rezultat: promjena zasićenja, velika rotacija

Zaključak 2/2

- Nastavak rada
 - Vrednovanje modela na snimkama snimanim metodom WSI
 - Istraživanje primjene metoda interpretabilnosti

Literatura 1/2

- D. Komura i S. Ishikawa, "Machine Learning Methods for Histopathological Image Analysis", Computational and Structural Biotechnology Journal, vol. 16, pp. 34-42, 2018.
- G. Litjens et al., "A survey on deep learning in medical image analysis", Medical Image Analysis, vol. 42, pp. 60-88, 2017.
- B. Sahiner et al., "Deep learning in medical imaging and radiation therapy", Medical Physics, vol. 46, no. 1, pp. e1-e36, 2018.
- G. Litjens et al., "1399 H&E-stained sentinel lymph node sections of breast cancer patients: the CAMELYON dataset", GigaScience, vol. 7, no. 6, 2018.
- B. Veeling, J. Linmans, J. Winkens, T. Cohen i M. Welling, "Rotation Equivariant CNNs for Digital Pathology", Medical Image Computing and Computer Assisted Intervention MICCAI 2018, pp. 210-218, 2018.
- B. Ehteshami Bejnordi et al., "Diagnostic Assessment of Deep Learning Algorithms for Detection of Lymph Node Metastases in Women with Breast Cancer", JAMA Journal of the American Medical Association, vol. 318, no. 22, pp. 2199-2210, 2017.
- K. He, X. Zhang, S. Ren i J. Sun, "Deep Residual Learning for Image Recognition", 2016 IEEE Conference on Computer Vision and Pattern Recognition (CVPR), pp. 770-778, 2016.
- M. Gurcan, L. Boucheron, A. Can, A. Madabhushi, N. Rajpoot and B. Yener, "Histopathological Image Analysis: A Review", IEEE Reviews in Biomedical Engineering, vol. 2, pp. 147-171, 2009.
- A. Krizhevsky, I. Sutskever, G. E. Hinton, "Imagenet classification with deep convolutional neural networks", Advances in neural information processing systems, pp. 1097-1105, 2012
- A. Krizhevsky, "One weird trick for parallelizing convolutional neural networks", 2014.
- S. Shalev-Shwartz, S. Ben-David, Understanding machine learning. Cambridge: Cambridge University Press, 2014.
- N. Tajbakhsh et al., "Convolutional Neural Networks for Medical Image Analysis: Full Training or Fine Tuning?", IEEE Transactions on Medical Imaging, vol. 35, no. 5, pp. 1299-1312, 2016.
- A. Zhang, Z. Lipton, M. Li, A. Smola, "Dive into Deep Learning". University of California, Berkley, 2019.

Literatura 2/2

- D. Masters i C. Luschi, "Revisiting Small Batch Training for Deep Neural Networks", 2018.
- T. Fawcett, "An introduction to ROC analysis", Pattern Recognition Letters, vol. 27, no. 8, pp. 861-874, 2006.
- K. He, X. Zhang, S. Ren i J. Sun, "Delving Deep into Rectifiers: Surpassing Human-Level Performance on ImageNet Classification", 2015 IEEE International Conference on Computer Vision (ICCV), 2015.
- L. Pantanowitz, "Digital images and the future of digital pathology", Journal of Pathology Informatics, vol. 1, no. 1, p. 15, 2010.
- J. Kim, J. Hong i H. Park, "Prospects of deep learning for medical imaging", Precision and Future Medicine, vol. 2, no. 2, pp. 37-52, 2018.
- G. Huang, Z. Liu, L. Maaten i K. Weinberger, "Densely Connected Convolutional Networks", 2017 IEEE Conference on Computer Vision and Pattern Recognition (CVPR), pp. 2261-2269, 2017.
- E. Deniz, A. Şengür, Z. Kadiroğlu, Y. Guo, V. Bajaj and Ü. Budak, "Transfer learning based histopathologic image classification for breast cancer detection", Health Information Science and Systems, vol. 6, no. 1, pp. 1-7, 2018.
- P. Bandi et al., "From Detection of Individual Metastases to Classification of Lymph Node Status at the Patient Level: The CAMELYON17 Challenge", IEEE Transactions on Medical Imaging, vol. 38, no. 2, pp. 550-560, 2019.
- O. Russakovsky et al., "ImageNet Large Scale Visual Recognition Challenge", International Journal of Computer Vision, vol. 115, no. 3, pp. 211-252, 2015.
- Y. Lecun, L. Bottou, Y. Bengio i P. Haffner, "Gradient-based learning applied to document recognition", Proceedings of the IEEE, vol. 86, no. 11, pp. 2278-2324, 1998.
- X. Zhang, J. Zou, K. He i J. Sun, "Accelerating Very Deep Convolutional Networks for Classification and Detection", IEEE Transactions on Pattern Analysis and Machine Intelligence, vol. 38, no. 10, pp. 1943-1955, 2016.
- C. Szegedy et al., "Going deeper with convolutions", 2015 IEEE Conference on Computer Vision and Pattern Recognition (CVPR), 2015.
- S. Ioffe, C. Szegedy, "Batch Normalization: Accelerating Deep Network Training by Reducing Internal Covariate Shift", 2015,
- C. Szegedy, V. Vanhoucke, S. Ioffe, J. Shlens and Z. Wojna, "Rethinking the Inception Architecture for Computer Vision," 2016 IEEE Conference on Computer Vision and Pattern Recognition (CVPR), Las Vegas, NV, 2016, pp. 2818-2826.





Hvala

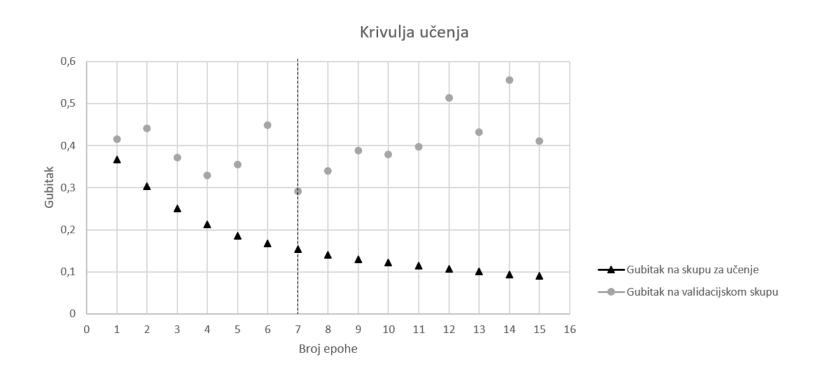
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Krivulja učenja



Rezultati modela učenih ispočetka s različitom stopom učenja

Naziv modela	Stopa učenja	Točnost	Mjera F1	AUC ROC
AlexNet	10 ⁻³	0.4998	0.6665	0.5000
AlexNet	10 ⁻⁴	0.7838	0.7697	0.8711
AlexNet	10 ⁻⁵	0.7847	0.7763	0.8662
AlexNet	10 ⁻⁶	0.7688	0.7694	0.8479
ResNet	10 ⁻³	0.8123	0.7898	0.9042
ResNet	10 ⁻⁴	0.7853	0.7827	0.8743
ResNet	10 ⁻⁵	0.7892	0.7857	0.8720
ResNet	10 ⁻⁶	0.7613	0.7492	0.8382
DenseNet	10 ⁻³	0.8125	0.7862	0.8788
DenseNet	10 ⁻⁴	0.7910	0.7583	0.8999
DenseNet	10 ⁻⁵	0.7872	0.7690	0.8714
DenseNet	10 ⁻⁶	0.7752	0.7684	0.8581

Rezultati modela inicijaliziranih prijenosom značajki sa skupa podataka ImageNet. Prilikom učenja svi parametri su prilagođavani.

Naziv modela	Stopa učenja	Točnost	Mjera <i>F1</i>	AUC ROC
AlexNet	10^{-3}	0.4997	0.6664	0.4999
AlexNet	10-4	0.7991	0.7720	0.9048
AlexNet	10^{-5}	0.7812	0.75336	0.8815
AlexNet	10 ⁻⁶	0.7800	0.7477	0.8764
ResNet	10 ⁻³	0.8297	0.8144	0.9184
ResNet	10-4	0.8518	0.8334	0.9295
ResNet	10 ⁻⁵	0.8485	0.8386	0.9266
ResNet	10^{-6}	0.8200	0.7978	0.9164
DenseNet	10^{-3}	0.8150	0.7858	0.9088
DenseNet	10-4	0.8670	0.8522	0.9409
DenseNet	10 ⁻⁵	0.8555	0.8408	0.9354
DenseNet	10^{-6}	0.8201	0.7920	0.9271
Inception-v3	10 ⁻³	0.8884	0.8872	0.9489
Inception-v3	10-4	0.8741	0.8661	0.9430
Inception-v3	10 ⁻⁵	0.8501	0.8327	0.9483
Inception-v3	10 ⁻⁶	0.8587	0.8436	0.9459

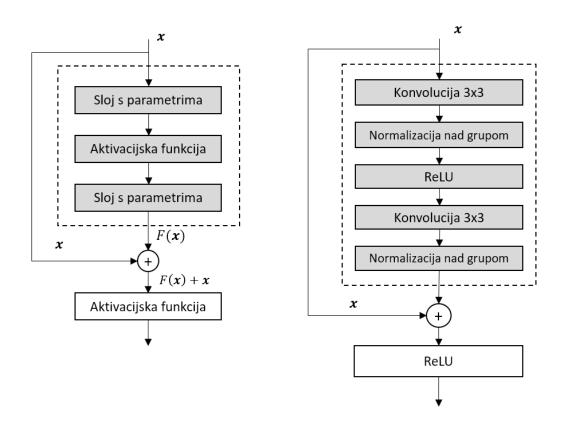
Rezultati modela inicijaliziranih prijenosom značajki sa skupa podataka ImageNet. Prilikom učenja samo zadnji potpuno povezani slojevi su prilagođavani.

Naziv modela	Stopa učenja	Točnost	Mjera <i>F1</i>	AUC ROC
AlexNet	10 ⁻³	0.7569	0.7398	0.8308
AlexNet	10^{-4}	0.7453	0.7061	0.8287
AlexNet	10 ⁻⁵	0.7589	0.7359	0.8395
AlexNet	10^{-6}	0.7592	0.7301	0.8496
ResNet	10 ⁻³	0.7760	0.7767	0.8547
ResNet	10^{-4}	0.7822	0.7676	0.8637
ResNet	10 ⁻⁵	0.7795	0.7685	0.8599
ResNet	10^{-6}	0.7492	0.7447	0.8156
DenseNet	10^{-3}	0.8065	0.8009	0.8874
DenseNet	10^{-4}	0.7988	0.7906	0.8818
DenseNet	10^{-5}	0.7904	0.7783	0.8766
DenseNet	10^{-6}	0.7630	0.7546	0.8406
Inception-v3	10^{-3}	0.8270	0.8204	0.9018
Inception-v3	10-4	0.8210	0.8149	0.9022
Inception-v3	10^{-5}	0.8121	0.8059	0.8948
Inception-v3	10 ⁻⁶	0.7728	0.7704	0.8536

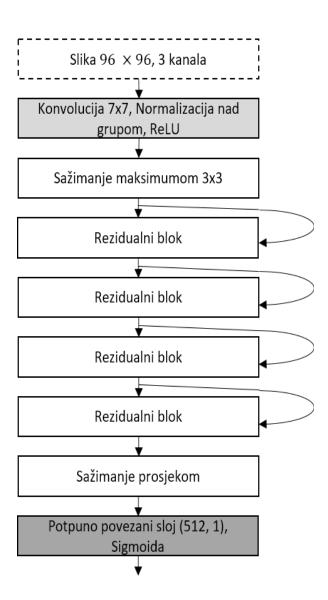
AlexNet



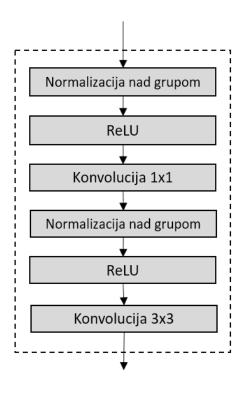
ResNet – rezidualni blok

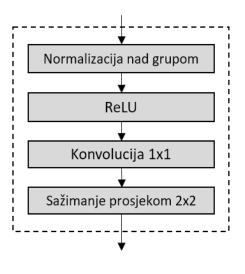


ResNet



DenseNet - slojevi

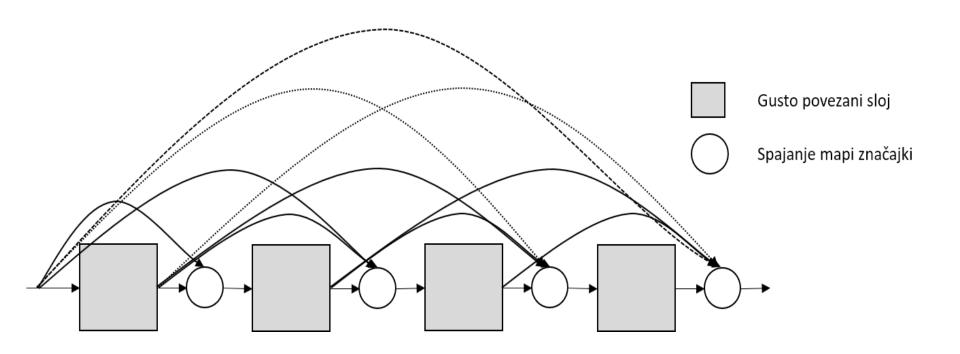




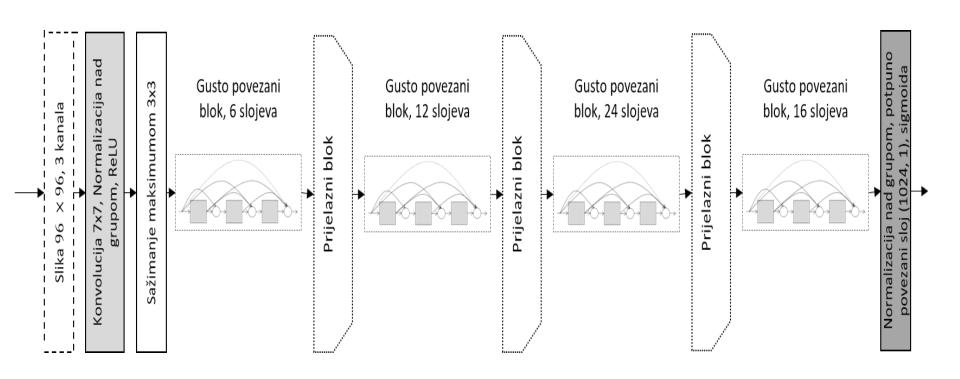
Gusto povezani sloj

Prijelazni sloj

DenseNet - blokovi



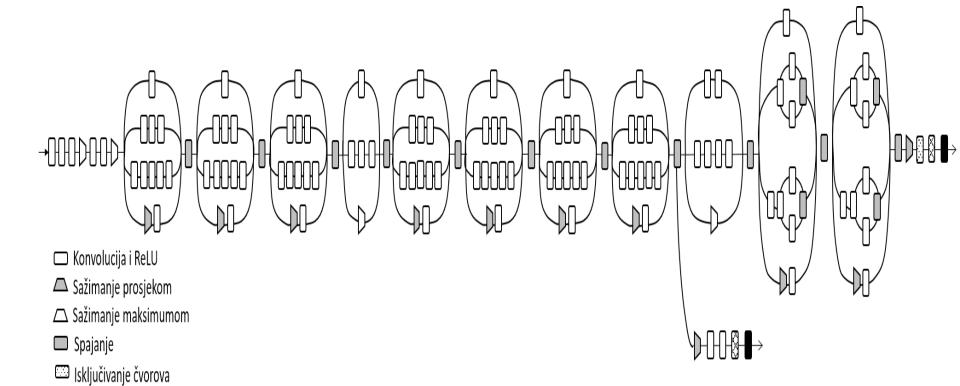
DenseNet



Inception-v3

Potpuno povezani sloj

Sigmoida



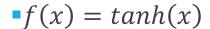
Algoritam Adam

```
Algorithm 8.7 The Adam algorithm
Require: Step size \epsilon (Suggested default: 0.001)
Require: Exponential decay rates for moment estimates, \rho_1 and \rho_2 in [0,1).
   (Suggested defaults: 0.9 and 0.999 respectively)
Require: Small constant \delta used for numerical stabilization. (Suggested default:
   10^{-8}
Require: Initial parameters \theta
   Initialize 1st and 2nd moment variables s = 0, r = 0
   Initialize time step t = 0
   while stopping criterion not met do
       Sample a minibatch of m examples from the training set \{x^{(1)}, \dots, x^{(m)}\} with
      corresponding targets \boldsymbol{y}^{(i)}.
      Compute gradient: \mathbf{g} \leftarrow \frac{1}{m} \nabla_{\boldsymbol{\theta}} \sum_{i} L(f(\mathbf{x}^{(i)}; \boldsymbol{\theta}), \mathbf{y}^{(i)})
      t \leftarrow t + 1
       Update biased first moment estimate: \mathbf{s} \leftarrow \rho_1 \mathbf{s} + (1 - \rho_1) \mathbf{g}
       Update biased second moment estimate: \mathbf{r} \leftarrow \rho_2 \mathbf{r} + (1 - \rho_2) \mathbf{g} \odot \mathbf{g}
       Correct bias in first moment: \hat{s} \leftarrow \frac{s}{1-\rho_1^t}
       Correct bias in second moment: \hat{r} \leftarrow \frac{\hat{r}}{1-a^t}
       Compute update: \Delta \theta = -\epsilon \frac{\hat{s}}{\sqrt{\hat{r}} + \delta} (operations applied element-wise)
       Apply update: \boldsymbol{\theta} \leftarrow \boldsymbol{\theta} + \Delta \boldsymbol{\theta}
   end while
```

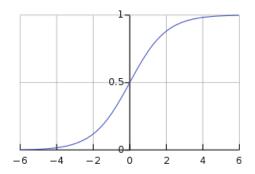
Predmet Duboko učenje, FER

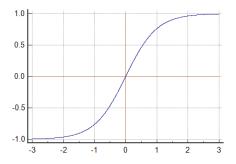
Aktivacijske funkcije

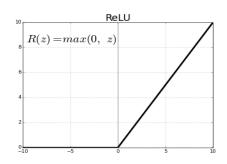
$$\sigma(x) = \frac{1}{1 + e^{-x}}$$



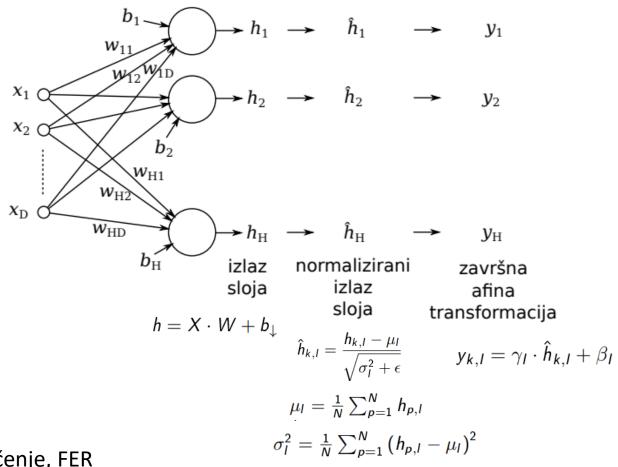








Normalizacija nad grupom



Predmet Duboko učenje, FER

He inicijalizacija

- •He et al, 2015
- •Srednja vrijednost $\mu = 0$

$$Varijanca \ \sigma = \sqrt{\frac{2}{layersize[l-1] + layersize[l]} }$$

Težine u l-tom sloju

$$W^{[l]} = np.random.randn(size_l, size_l-1) * np.sqrt(2 / (size_l-1 + size_l))$$